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Review article

Detection and rehabilitation of age-related motor skills impairment: Neurophysiological biomarkers and perspectives

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ABSTRACT

Age-related decline in motor control, manifesting as impaired posture, gait, and slowed movement execution, significantly diminishes the quality of life in older adults. These functional deficits are associated with alterations in neurophysiological data, which are analyzed using advanced techniques including spectral analysis, complexity measures, and functional connectivity network analysis. These methodologies provide valuable insights into the neurobiological mechanisms underpinning age-related motor function impairments, linking physiological changes to non-invasively recorded electrophysiological and hemodynamic responses. Recent investigations have demonstrated an age-dependent impairment in access to working memory during motor tasks, evidenced by significant correlations between electroencephalographic biomarkers and neural response latencies. Furthermore, these functional biomarkers are associated with the degradation of motor learning abilities in older individuals. There is a broad consensus that non-invasive assessment of brain activity accurately reflects the processes underlying age-related motor decline, thereby opening avenues for targeted intervention strategies. A key area of investigation is the utilization of motor system function for the early detection of neurodegenerative diseases. Seemingly, simple motor tasks engage cortical regions responsible for attention, vision, and memory through a process known as sensorimotor integration. Sensorimotor training implemented via brain-computer interfaces with neurofeedback demonstrates potential for ameliorating both cognitive and motor deficits in both healthy older adults and those with age-related conditions. This review synthesizes current research on age-related changes revealed through neuroimaging data analysis, highlighting how biomarkers derived from brain electrical and hemodynamic activity reflect both normative and pathological aging processes. Finally, we emphasize the considerable potential of neurophysiological data analysis for advancing the field of aging research. Digital medicine platforms, including brain-computer interfaces and a range of wearable monitoring devices, hold significant promise for transforming the diagnosis of age-related diseases. These technologies empower continuous, objective monitoring of older adults, paving the way for personalized, precision-based medical interventions.

1. Introduction

Aging brings multifaceted changes that can profoundly impact quality of life, especially in motor control (Ketcham and Stelmach, 2004; Boisgontier and Nougier, 2013). The decline in motor functions, marked by diminished posture and gait control, decelerated fine motor responses, and increased difficulty in daily activities, not only threatens independence but also raises the risk of injury due to falls and slower reaction times (Brach et al., 2007; Montero-Odasso et al., 2012). This decline in motor abilities is increasingly linked to specific age-related

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changes in neurophysiological processes (Seidler et al., 2010), which can now be probed through advanced neuroimaging and electrophysiological analyses. Recent studies indicate that even subtle age-related impairments in motor initiation are detectable via neurophysiological probes, revealing a gradual slowing of motor responses in elderly individuals (Frolov et al., 2020). This slowing down correlates with a broad spectrum of sensorimotor alterations, which become progressively evident in older adults.

Significant advances in understanding these changes have come from spectral analysis of neurophysiological signals. Studies demonstrate that motor-related theta activity diminishes with age, disrupting the brain's ability to process and initiate motor responses efficiently (Yordanova et al., 2020). Furthermore, analysis of alpha and beta band oscillations has revealed age-related shifts that contribute to slower reaction times and poorer coordination in motor tasks (Hong and Rebec, 2012; Liu et al., 2017; Shih et al., 2021). In parallel, complexity analyses, such as entropy measures and fractal analysis, have shown that aging increases the unpredictability of motor responses, a sign of decreased efficiency in neural control over motor output (Zappasodi et al., 2015; Wang, Initiative, 2020; Frolov et al., 2023). These findings underscore how the subtle decline in neural processing affects everyday motor functions and suggest that spectral dynamics offer a window into the neural aging process (Chettouf et al., 2022).

A related body of work has emphasized functional connectivity alterations in aging, specifically in regions associated with sensorimotor integration. For example, Maes et al. (2020) found that functional connectivity in the dorsal premotor cortex declines with age, contributing to slower and less precise motor responses, particularly as task complexity increases. Functional connectivity mapping further reveals that aging disrupts coordinated activity between the primary motor cortex and regions responsible for executive control and sensory processing (Goble et al., 2009; Seidler et al., 2010). These connectivity patterns are instrumental in tasks requiring sensorimotor integration, such as balance, reaction to environmental changes, and the maintenance of fine motor skills. Understanding these dynamics is critical because it illustrates how age-related changes in motor function are rooted in altered neural communication pathways.

An emerging area of research highlights the role of cognitive systems, including working memory, in modulating motor responses in aging. Studies demonstrate that age-related reductions in working memory capacity correlate with poorer performance in tasks that demand simultaneous cognitive and motor engagement, such as dual-task walking or balance exercises (Beurskens and Bock, 2012; Chai et al., 2018). As working memory becomes less accessible with age, elderly individuals face greater challenges in managing tasks that combine cognitive demands with motor precision, further exacerbating motor decline (Lindenberger and Baltes, 1997; Kahya et al., 2022). EEG-based biomarkers have proven valuable for tracking these dynamics, as they reflect both slower neural response times and decreased synchrony across regions involved in motor planning and memory access (Pitsik, 2021).

Numerous successful attempts to connect such functional probes with the deterioration of motor learning skills in elderly individuals (Espenhahn et al., 2019; Bootsma et al., 2021). Generally, there is a consensus that the data of non-invasive assessment of brain activity provides an adequate image on the processes behind the age-related impairment of motor skills, which opens new possibilities for development of various intervention strategies. One of such perspectives that draws a considerable attention of neuroscientists and gerontologists is creation of systems for early detection of neurodegenerative diseases associated with ageing.

Evidence increasingly supports that neurophysiological data analysis can offer early indicators of cognitive and motor impairments associated with neurodegenerative diseases, such as Alzheimer's and Parkinson's diseases. For example, functional MRI (fMRI) studies reveal distinct connectivity patterns associated with mild cognitive impairment and early Alzheimer's, characterized by reduced functional connectivity within motor and prefrontal networks during motor tasks (Dang et al., 2023). Likewise, Takahashi et al. (2022) employed functional near-infrared spectroscopy (fNIRS) to demonstrate that adults with mild cognitive impairment exhibit differing prefrontal activation during simple motor tasks, such as finger-tapping, suggesting early disruption of sensorimotor processing pathways. These findings underscore the potential for neurophysiological biomarkers to aid in the early detection of neurodegenerative diseases, which are often accompanied by gradual motor impairment.

Aging-related decline in sensorimotor integration—a complex interaction between sensory processing and motor response—is a fundamental contributor to motor difficulties. Degardin et al. (2011) showed that elderly adults exhibit declined integration of sensory cues into motor responses, making tasks that require quick adjustments, such as avoiding obstacles while walking, increasingly difficult. Similarly, multisensory integration deficits have been associated with higher risks of falls and balance issues, as shown by Zhang et al. (2020) in their systematic review. Importantly, sensorimotor integration is not static and can be enhanced through targeted training programs. Brain-computer interface (BCI) systems, in particular, show promise for rehabilitating motor function in older adults. BCI-based neurofeedback, which allows real-time monitoring and feedback on neural activity, has demonstrated success in enhancing both motor skills and cognitive function in aging populations ((Hramov et al., 2021a).

Considering these advances, our review aims to provide a comprehensive examination of neurophysiological biomarkers of age-related motor function decline. We explore how neuroimaging and electrophysiological data illuminate the physiological underpinnings of motor aging in both healthy and pathological contexts. Additionally, we discuss the potential for these biomarkers to inform early diagnostic and rehabilitative interventions, which could mitigate the impact of motor decline on quality of life. In this context, we review the modern methods of rehabilitation for age-related motor disorders.

By synthesizing current research on neurophysiological changes associated with aging, we hope to underscore the transformative potential of neurophysiological data analysis within geriatric healthcare and aging research.

2. Neurophysiological biomarkers of age-related motor skills impairment

When considering the neural correlates of motor-related activity in human brain, the modern scientific research provides a big variety of practices related to methodological as well as physiological aspects. In this section of the review, we consider known biomarkers of motor-related activity (Fig. 1) and how aging affects the motor skills impairment.

2.1. Neural correlates of motor-related activity

The rapid development of techniques for measuring various neurophysiological processes led to accumulation of large amounts of medical data including magneto- and electroencephalographic signals (M/EEG), neuroimaging data, brain hemodynamics and oxygenation (fMRI, CT, PET, etc.). While these datasets are of interest primarily to medical professionals, there is a well-established practice to determine biomarkers of neural activity by analyzing neurophysiological data using mathematical methods. Such biomarkers reflect real physiological processes, and allow to get an idea of how different kinds of activity are neurally represented. In particular, motor-related activity is known to cause an EEG phenomenon, observed since 1950s (Klass and Bickford, 1957; Chatrian et al., 1959) as blocking of the Rolandic mu-rhythm (8–13 Hz), and lated thoroughly described by Pfurtscheller et al. (Pfurtscheller and Da Silva, 1999; Neuper et al., 2006) as an event-related desynchronization (ERD). Motor-related ERD of alpha

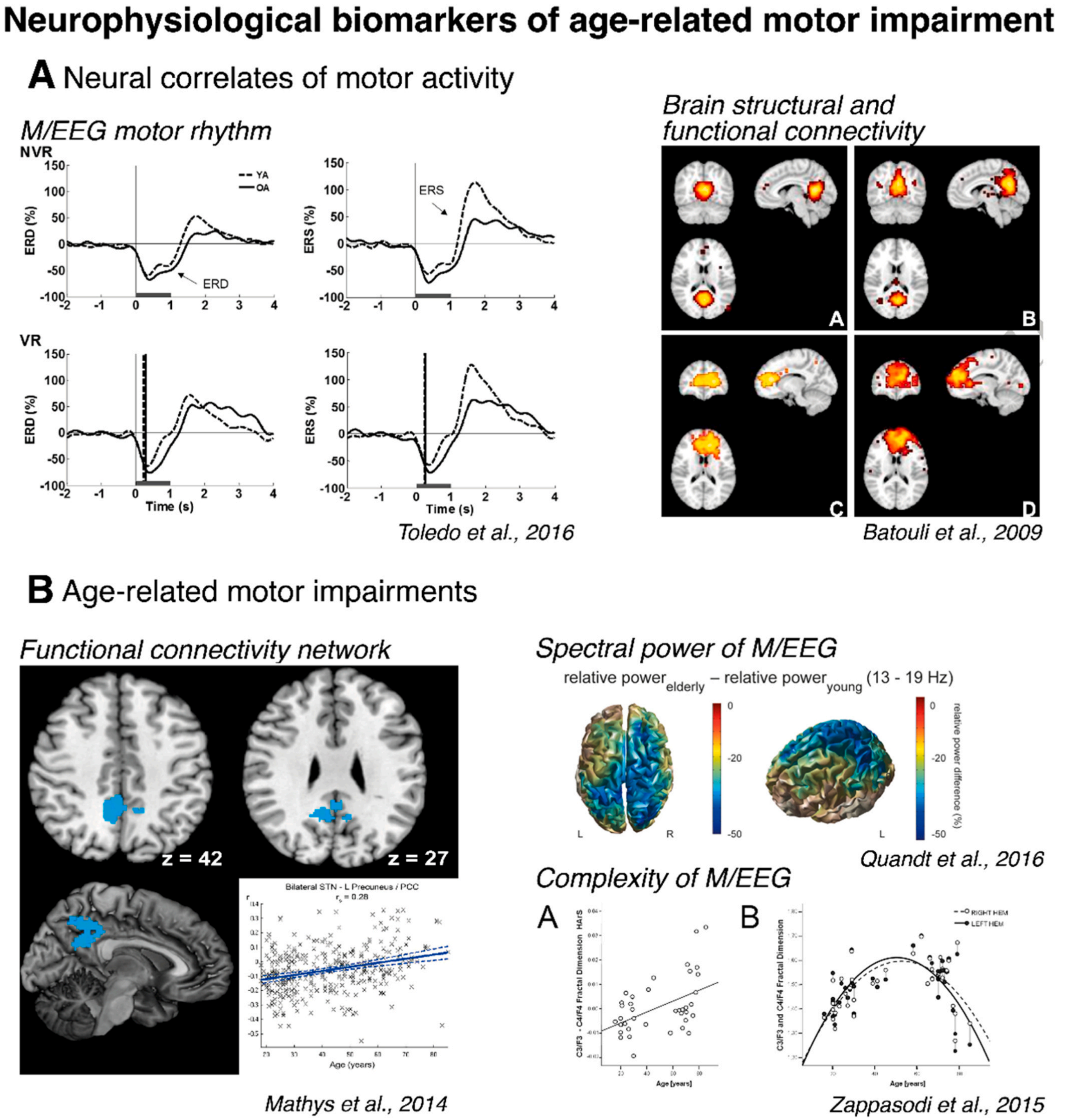

Fig. 1. A — Neural correlates of motor activity. Left panel (Toledo et al., 2016a) — ERD and ERS time series from Cz EEG channel for young and older adults. Right panel (Batouli et al., 2009) — resting state fMRI. Activation pattern of posterior cingulate cortex in young group (A) and elderly group (B); activation of prefrontal area in young group (C) and elderly group (D). B — Age-related motor impairments. Top panel (Mathys et al., 2014) — age-related decrease in anticorrelation with the subthalamic nucleus (STN). Bottom left (Quandt et al., 2016) — the difference of motor-related spectral power (13–19 Hz) between elderly and young groups. Bottom right (Zappasodi et al., 2015) — scatter plot of hemispheric symmetry between F3/C3 and F4/C4 over age (A) and scatter plot of mean fractal dimension values of left (white circle) and right (black circle) hemisphere over age.

frequencies is a spatio-temporal feature that emerges before movement onset and during both motor execution and motor imagery and is localized primarily in central area on the opposite hemisphere to the performed motor action (Pfurtscheller, 2000).

ERD of mu-rhythm associated with movement is a well-known electrophysiological correlate of neuronal activity in the particular area of the cortex (Pfurtscheller, 2001) and reflects desynchronized behavior of the small localized groups of neurons of cortical network (Crone et al., 2008). Emergence of mu-ERD during motor action is also closely associated with so-called beta-rebound, or immediate post-movement event related synchronization (ERS) of beta-rhythm (Pfurtscheller et al., 2005, Sisti et al., 2024). This modulation of beta-rhythm can be observed after both motor execution and imagery for almost any type of movement and is believed to originate from subcortical structures such as thalamus or basal ganglia (Bevan et al., 2002; Bizovičar et al., 2014). However, this statement is not quite definitive, as there is also the compelling evidence that such type of oscillation is generated in the cortex itself (Jurkiewicz et al., 2006). Da Silva (1991) describes the observation that beta-rebound coincides with decreased corticospinal pathways, which can indicate that post-movement beta-ERS may be a correlate of deactivation of motor cortex.

One of the most significant contributions to research of neural correlates of motor-related ERD\S was made by Prof. Pfurtscheller and colleagues, who published comprehensive research on basic principles of neural response to motor activity and methods for their quantification. For example, Neuper and Pfurtscheller, (2001) show that the rebound effect of beta-rhythm associated with any type of motor task not necessarily involving muscular activity, might reflect cortical networks slowdown related to the motor processing. While mu-ERD is considered a marker of active neural processing of the movement, beta-ERS following motor action reflects a shift of the cortical network into an idling (or passive) state (Pfurtscheller et al., 1996).

Beyond the electrical activity of cortical networks, more comprehensive methods exist to study the brain's functional correlates. Although different measurement modalities capture distinct aspects of neural activity, they often reflect the same underlying neuronal mechanisms. By establishing correlations between these modalities, researchers can gain deeper insights into how various cortical processes unfold. For example, EEG combined with hemodynamic measures (fMRI or fNIRS) allows for such cross-modal analysis. Pang and Robinson (2018) demonstrated that low-frequency EEG oscillations (<4 Hz) strongly correlate with blood-oxygen-level-dependent (BOLD) signals, to the extent that EEG spectral power can serve as a proxy for BOLD fluctuations. Notably, this low-frequency EEG activity shows the same inverse relationship with resting-state alpha power as BOLD signals. One possible explanation for this link is neurovascular coupling—the process by which active neurons trigger localized increases in blood flow and oxygenation to meet metabolic demands (Devor et al., 2011; Kaplan et al., 2020). Yeung and Chu's (2022) review highlights that simultaneous EEG-fNIRS recordings are particularly effective for assessing neurovascular coupling, the critical interplay between neural activity and cerebral blood flow. Disruptions in this mechanism, often seen in neurological disorders, can be detected through advanced signal processing techniques (Hillman, 2014).

2.2. Age-related impairment of brain motor system

Cerebral functional and structural properties change with aging, causing decline in cognitive and motor performance and affecting daily quality of life. Elderly population is subjected to the risk of development of various neurodegenerative conditions, most of which are vital to detect early in order for successful therapy. Among various ways in which aging affects the quality of life of elderly individuals, behavioral changes associated with motor control bear the most prominent risks. Decline of motor functions in advanced age, which includes an impaired posture and gate control, slowing down of fair motor actions and complication of daily activities, can be confidently correlated with motor-related functional probes processed via state-of-the-art analysis of neurophysiological data (Degardin et al., 2011; Li et al., 2018; Frolov et al., 2020).

The Aging Biomarkers Consortium (the ABC) proposed a unified approach to define aging biomarkers, emphasizing that a robust biomarker must be specific, systemic and serviceable (Ren et al., 2023). These characteristics mean that the biological measure must be able to define the extent and rate of aging of particular physiological systems in a meaningful way that allows to use them in clinical practice. The ABS aims at promoting the studies of age-related diseases by proposing the standards for measurement of aging biomarkers, including brain aging. Aging Biomarker Consortium et al. (2023) proposed a framework with three directions of brain aging biomarkers screening: functional, imaging and body fluid markers, first including motor coordination monitoring. The ABC stated that the changes in the brain functionality affecting fine motor ability is a robust biomarker of brain aging prediction. Previously, the decline of motor skills in healthy aging population was successfully assessed using functional probes based on mathematical analysis of cortical activity (Quandt et al., 2016; Frolov et al., 2020; Eswari et al., 2024). Based on our goal, we can highlight the next groups of biomarkers and corresponding methods of analysis: neuroimaging and functional connectivity networks and analysis of brain electrical activity based on spectral power and complexity measures.

Neuroimaging. Neuroimaging techniques, such as PET and fMRI, allow to assess both structural and functional changes in brain structure associated with aging. Structural changes are well covered in the scientific literature and include decrease of brain volume (Batouli et al., 2009) that intensifies with advanced age and differs across regions, with the most prominent changes in frontal and parietal areas and less significant — in occipital and other inferior subregions (Dennis and Cabeza, 2011). Taubert et al. (2020) conducted a comprehensive research using MRI data of 966 subjects (age 46–86) aimed at demonstrating an impact of aging on brain anatomical properties. Besides the age-related loss of brain volume found in almost all cortical structures, authors specifically report a rapid decline of white matter in primary motor cortex. The review by MacDonald and Pike (2021) provides an extensive amount of evidence on how various MRI measurements can detect age-related changes in brain morphology. Structural and functional connectivity are mutually connected (Zhou et al., 2022), however the nature of their relationship is rather complex. Some studies report a certain level of independency between these two measures, since they react differently on aging, with functional connectivity showing moderate decline across the lifespan (Fjell et al., 2017). Another study suggests that age-related decline in brain structural properties leads to increased functional connectivity due to the compensatory mechanism (Marstaller et al., 2015).

When speaking of «functional» properties of the brain, researchers refer to the functional brain networks that reflect the correlation between BOLD signals of the brain regions of interest. Besides fMRI, functional connectivity can be assessed using almost any type of neural activity recording, including M/EEG signals. There is a considerable amount of methods developed to evaluate the correlation between the brain areas based on the recorded time series, both linear and non-linear (Hramov et al., 2021b). M/EEG-based approaches are suffering from limitations that originate from poor spatial resolution of these techniques that can compromise the results of functional connectivity evaluation. The main limitation is the field spread problem, meaning that M/EEG sensors can record the activity of the same source (Schoffelen and Gross, 2009). Although this caused development of various mathematical tools aimed at reduce the impact, such as phase lag index (PLI), the field spread problem is a main motivator for source-level analysis of brain connectivity networks (Michel and He, 2019; Kurkin et al., 2023).

In normal aging, most studies are focused on the default mode network (DMN) — a large-scale cortical topology that includes medial frontiparietal network and is primarily activated in the resting state (Raichle, 2015). DMN functional significance includes high-level cognitive activity and is hypothesized to process «scattered» state of attention and passive monitoring of the environment (Mevel et al., 2011). DMN shows decreased connectivity with age (Onoda et al., 2012, Vidal-Piñeiro et al., 2014; Tang et al., 2022), indicating general decline in memory and cognitive functions. The weaker activation pattern in DMN in elderly population is broadly reported, and the local changes in subnetworks of DMN can indicate development of age-related neurodegenerative diseases (Greicius et al., 2004; Mohan et al., 2016; Ruppert et al., 2021). Considering the broad knowledge on both structural and functional properties of DMN, the dysfunctions in it are actively discussed as a robust biomarkers that can be used as a supporting indicators of age-related neurodegenerative conditions (Ibrahim et al., 2021; Jobson et al., 2021). For instance, functional connectivity analysis revealed decreased posterior and anterior DMN couplings in group of presymptomatic Alzheimer's disease (AD) subjects (Zhao et al., 2020), which is proposed to be a possible indicator for early diagnosis of AD. Another study shows that functional connectivity based on Pearson's correlation allows to confidently distinguish four subtypes of AD, with decreased DMN being a typical identifier of one of them (Chen et al., 2023). Considering motor-related activity, age-related differences in fMRI-based functional connectivity of motor-related cortical areas are shown to be correlated with physiological effects of aging such as frailty, with frail elderly patients demonstrating lower connectivity in the supplementary motor area (SMA) (Lammers et al., 2020). Based on this results, SMA-targeted therapy is promising for frailty treatment.

To capture more subtle effects, such as sensorimotor integration and motor planning, use of M/EEG-based functional connectivity restoration is more appropriate to the poor time resolution of fMRI. This approach allows to focus the research on particular motor-associated frequency bands, such as previously discussed alpha- and beta-ranges, as well as slower theta-range to study topological effects related to sensory processing aspect of cue-induced movements, working memory and motor control. The MEG-based functional connectivity analysis using mutual information method revealed the reconfiguration of functional connectivity network during motor planning and motor execution (Yeom et al., 2020). The sensitivity of these changes allows to use them in more practical applications, such as machine learning (ML) based classification systems of the different types of movements (Gu et al., 2020; Shamsi et al., 2021; Mirzaei and Ghasemi, 2021). Considering age-related changes, EEG-based functional connectivity analysis reveals patterns consistent with known cognitive and structural impairments related to aging. In the pre-movement phase, differences in functional connectivity topologies suggest different patterns of motor planning processing by cortical network in young and elderly population that suggest age-related decline in working memory (Frolov et al., 2020). Our previous research on motor-related functional connectivity revealed pattern consistent with compensatory mechanism in elderly population, which corresponds to hyper activation of local cortical network in order to preserve the same level of cognitive performance (Pitsik et al., 2022). Compensation can be detected in various form of cognitive pathologies (Chen et al., 2020; Mao et al., 2021; Tang et al., 2021), but is observed in healthy aging as well (Aron et al., 2022; Kang et al., 2022).

Features of M/EEG time series. The motor-related biomarkers of healthy aging can be quantified in many ways. In this section, we review spectral and complexity-based features, since these two groups of methods are most commonly used in both fundamental and practical research of healthy aging of human motor system.

The common practice of defining mu-ERD is through spectral power alterations. As we previously pointed out, ERD/S events are the most promising and well-studied in the area of motor-related cortical activity. However, the impact of age on mu-ERD is rather rarely referred to, with most of the studies focusing on pathological changes and rehabilitation prospects (Inamoto et al., 2023). One of the known effects of aging is the loss of hemispheric asymmetry: while young adults demonstrate pronounced contralaterality of mu- and beta-ERD when moving both hands, healthy aging is associated with rather symmetric activation pattern (Vallesi et al., 2010; Przybyla et al., 2011). The ERD pattern is more localised in young subjects, detectable primarily in the central region contralateral to the performed movement, whereas in elderly subjects the motor-related activity can be detected in fronto-central and parieto-central areas as well (Derambure et al., 1993). Elderly subjects are prone to demonstrate larger beta-ERD during motor action combined with slower cortical processes and compensatory strategy (Toledo et al., 2016b).

Besides mu- and beta-ERD, there is a rich body of evidence that a slow theta rhythm (4–8 Hz) plays a major role in the motor control and preparation and can be a good indicator of motor system aging. For instance, unlike young adults, elderly subjects do not demonstrate the increase in midfrontal theta-power in demanding sensorimotor tasks (Depestele et al., 2023), which suggests disruption in theta upregulation. Theta power depression is also oftenly reported to be the hallmark of working memory decline that underlies many cognitive and motor deficits in elderly population (Nowak et al., 2021). There is also evidence that theta activation during sensorimotor tasks is related to the motor coordination, and it's age-related impairment might be the reflection of decline in functional control of upper limbs responses (Yordanova et al., 2020). The pattern of age-related theta power decrease is also observable during sensorimotor balance-maintaining task (Gujar, 2019).

Evaluation of M/EEG signals complexity is a very promising approach to reveal underlying dynamical properties of cortical activity. Depending on the method, resting state neuronal oscillations are known to become more complex (Anokhin et al., 1996; Pierce et al., 2000) or less complex with advanced age (Zappasodi et al., 2015). Complexity measurements show age-related changes in the areas mainly responsible for working memory (Ishii et al., 2018; Javaid et al., 2024). Complexity of the baseline EEG correlates with the mu-ERD during cued motor task, and this correlation is shown to be changing with age (Pitsik, 2021). Such measures are oftenly discussed as appropriate features for ML-based classification methods (Marcos-Martínez et al., 2021; Li et al., 2022), being quite sensitive to subtle changes in EEG dynamics to show clear changes in single-trial analysis (Pitsik et al., 2020).

Generally, there's a consensus that age reflects in the cortical activity in the form of overcompensation which affects all physiological systems of the human body (Inamoto et al., 2023). Primarily studied via fMRI technique, compensatory mechanism usually refers to involvement of broader functional network topologies by elderly adults to perform the task that requires more localised activation in younger subjects. Spectral and dynamical characteristics of brain electrical activity suggest the same by quantification of neurophysiological time series in spatio-temporal domain.

3. Modern methods of rehabilitation for age-related motor disorders

Age-related diseases are defined as those that become more prevalent with advancing age. The most effective method for preventing age-related diseases is through the implementation of a comprehensive health and wellness program that encompasses both physical and mental training, with the objective of reducing a chance of developing such illnesses (Bacanoiu and Danoiu, 2022). Additionally, there is a SENS research strategy focused on developing and delineating the measures necessary to entirely neutralize the adverse effects of senescence (Zealley and de Grey, 2013). Nevertheless, the proposed solutions have yet to be implemented in practice.

However, contemporary approaches to disease prevention merely serve to reduce the probability of developing specific disorders. Presently, ailments that manifest in old age are regarded as inevitable, requiring either treatment or symptom compensation. Furthermore, a prevalent consequence of the aging process that is not associated with a particular disease is frailty, defined as the inability to perform tasks that are simple for a young person. Motor disorders are the most conspicuous in everyday life and have a markedly deleterious effect on overall quality of life. Furthermore, as age advances, motor disorders result in restricted mobility, recurrent falls and, in some cases, mortality (Pratali et al., 2014).

This section examines various methods of treatment and rehabilitation of motor disorders associated with age-related diseases. Fig. 2 illustrates the different rehabilitation methods used in the treatment of major movement disorders.

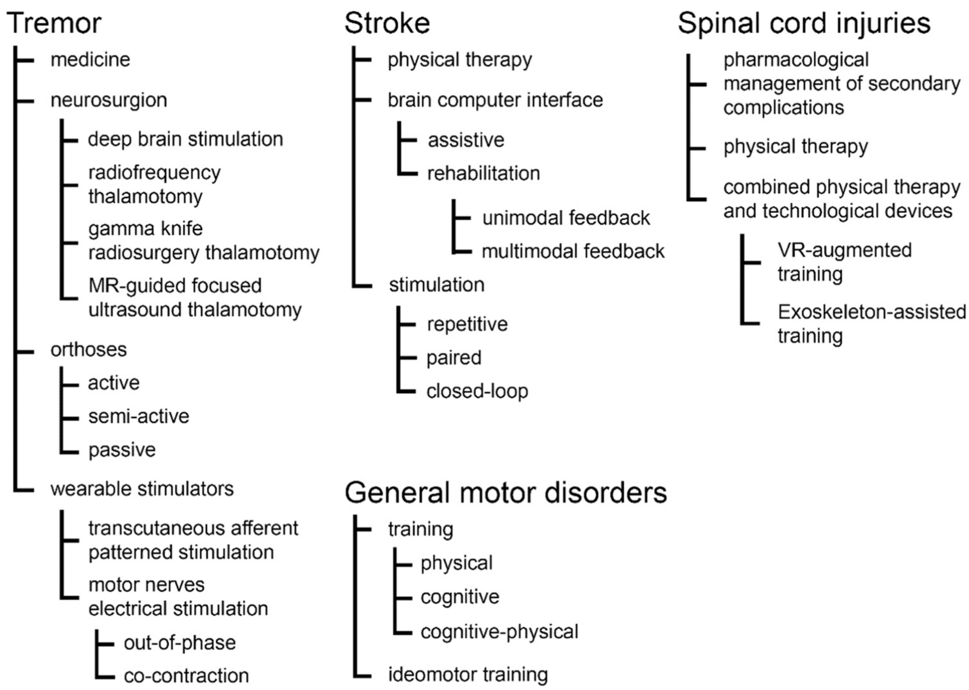

Fig. 2. Age-related diseases causing motor dysfunction and related rehabilitation methods.

3.1. Tremor

Pathological tremor is defined as the occurrence of involuntary rhythmic muscle contractions, resulting in shaking movements in one or more parts of the body (Bhatia et al., 2018). Tremor is the most prevalent movement disorder in adults (Elble et al., 2013), and is most commonly observed in two age-related diseases: Parkinson's disease and essential tremor (Raethjen et al., 2000). Potential treatment or suppression options for tremor include neurosurgery, device implantation, wearable devices, and drug therapy.

Pharmaceutical drugs represent one of the most commonly employed treatments for tremor associated with Parkinson's disease and essential tremor (Frei and Truong, 2022). It is unfortunate that this approach is ineffective in approximately half of tremor cases and has serious negative side effects (Louis, 2005; Gallego et al., 2010; Matsumoto et al., 2013). Consequently, over half of patients cease taking the medication due to adverse effects or lack of efficacy (Diaz and Louis, 2010; O'Connor, Kini, 2011), and instead pursue alternative avenues. For a comprehensive review of pharmaceutical drugs used for tremor treatment, see Frei and Truong (2022).

Neurosurgical interventions for tremor therapy encompass a range of techniques, including: deep brain stimulation (DBS), radiofrequency thalamotomy (RT), gamma knife radiosurgery thalamotomy (GKRS), and MR-guided focused ultrasound thalamotomy (MRgFUS) (Dallapiazza et al., 2019). Characteristics of these neurosurgical options are shown in Fig. 2. The objective of these surgical procedures is to target a specific region of the thalamus, namely the ventral intermediate nucleus included in ventral posterior nucleus. This region is responsible for generating oscillations that are transmitted to the body parts affected by essential and parkinsonian tremors. The use of DBS involves the placement of a pair of electrodes in the target area of the thalamus, which stimulate the target area at a frequency calculated on an individual basis in order to compensate for the tremor (Lyons and Pahwa, 2008). RT is a surgical procedure that involves the destruction of a portion of the thalamus cells using a radio wave emitter, performed on an open skull (Larcipretti et al., 2024). GKRS is a non-invasive procedure that involves irradiating a section of the thalamus with a gamma radiation beam, which results in the death of a portion of the cells that induce tremor(Gunawan et al., 2022). MRgFUS utilizes a number of ultrasound emitters focused at a single point in order to destroy the thalamic cells that induce tremor (Rohani and Fasano, 2017). Fig. 3 illustrates the specific details of the aforementioned methods.

DBS has emerged as a highly efficacious treatment for a range of tremors. For instance, while the efficacy of pharmacological intervention in reducing tremor has been observed to range from 23 % to 59 % in patients with Parkinson's disease (Koller, 1986), the effectiveness of DBS has been demonstrated to be 90 % (Elble and Deuschl, 2011). However, DBS is an invasive treatment and carries a risk of surgical complications due to the implantation of electrodes into the brain (Katayama et al., 2005; Hariz et al., 2008). More progressive techniques, including GKRS and MRgFUS, are non-invasive and do not entail the surgical complications associated with traditional treatments. Consequently, they are gaining popularity (Yamamoto et al., 2022).

Alternatives to tremor compensation include wearable devices such as orthosis, nerve and muscle stimulators (Fig. 4).

Wearable tremor suppression orthoses can be classified into three categories based on the suppression mechanism: passive, semi-active, and active systems (Nguyen and Luu, 2021). The passive system employs a variety of energy absorption techniques to mitigate involuntary movements. The semi-active system employs a sensor-based estimation of the tremor level to regulate the resistance of the system, thereby modulating the amplitude of involuntary movements. The semi-active mechanism also unintentionally suppresses tremor movements through the absorption of energy. The active mechanism provides movement in the direction opposite to that of the tremor (estimated by various sensors) with the intention of reducing it. In active devices, electric DC and servo motors are employed as actuators, driving the upper-limb joints via a gearbox or cable transmission system.

One of the earliest active orthoses developed to suppress tremor was the wearable orthosis for tremor assessment and suppression or WOTAS (Rocon et al., 2007). The exoskeleton is affixed to the shoulder, forearm, and hand of an individual via Velcro fasteners and provides three degrees of freedom: elbow flexion-extension, wrist flexion-extension, and forearm pronation-supination. The exoskeleton is equipped with sensors that record human movements. These sensors are of two types: kinematic (angular velocity) and kinetic (force of interaction between the

	DBS	FUS	GKRS	RF
Frame application	Yes *Can be performed framelessly	Yes	Yes	Yes
Hair removal	Partial	Completely	None	Partial
Cranial burr hole	Yes	No	No	Yes
Target confirmation	MER, electrical stimulation, procedural evaluation	Test lesions, procedural evaluations	Indirect anatomical targeting	MER, electrical stimulation, test lesions, procedural evaluations
Treatment effects	Immediate	Immediate	Delayed (typical delay 4 months)	Immediate
Adjustable	Yes	No	No	No
Reversible	Yes	No	No	No
Bilateral treatment	Yes	No	Yes	No
Implanted devices	Yes	No	No	No
Other considerations	Device maintenance and programming	MRI guided Skull penetration	Radiation	Variable thermal dosing

ET, essential tremor; DBS, deep brain stimulation; FUS, focused ultrasound; GKRS, gamma knife radiosurgical thalamotomy; RF, radiofrequency.

Fig. 3. Comparison of alternative neurosurgical procedures to for tremor management (Dallapiazza et al., 2019).

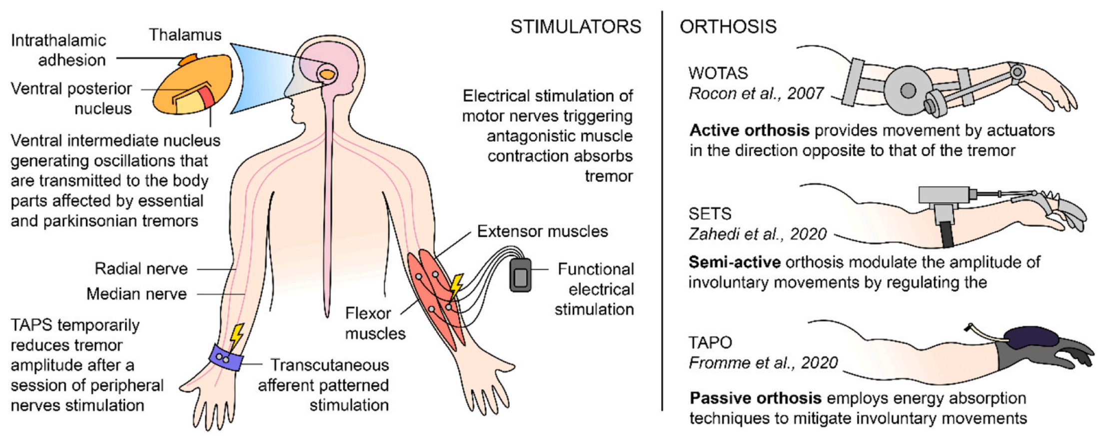

Fig. 4. Stimulation techniques and orthoses for tremor treatment. Different options for orthoses are given with examples and names of prototypes.

limb and the orthosis). Data obtained from these sensors is filtered in order to distinguish tremor from intentional movement. Fluctuations caused by tremors are compensated by the exoskeleton motors. A total of ten individuals diagnosed with tremors of varying etiologies participated in the device testing phase. The device was capable of significantly reducing tremor in test participants when performing three tasks: holding an arm outstretched, pointing a finger to the nose and relaxing the arm. The average reduction in tremor was 70 %. It was observed by the researchers that the greater the strength of the tremors experienced by the participants was, the more effectively the orthosis was able to compensate for them. Therefore, this device is more appropriate for patients with a lengthy medical history and a high-amplitude tremor.

Modern active orthoses, such as the Tremor Suppression Orthosis (TSO) developed by Herrnstadt et al. (2019), which controls the elbow joint, have been shown to effectively compensate tremor, with an average reduction of 94.37 ± 7.27 % in test results. Nevertheless, the primary issue with active orthoses remains their weight and dimensions. The TSO, which exhibits excellent compensation indicators, weights 1700 g, while theWOTAS, without its computer parts, weighs 850 g. Furthermore, it is notable that, in contrast to passive orthoses, none of the existing developments of active orthoses have been introduced to the market.

In semi-active mechanisms, magnetorheological fluid is frequently used to produce the damping force reducing tremor (Zahedi et al., 2021; Case et al., 2016; Yi et al., 2019). The viscosity of magnetorheological fluid can be modified by varying the strength of the magnetic field exposure. Additionally, it is characterised by a high strength-to-weight ratio, which is a crucial attribute for wearable exoskeletons (Perry et al., 2007). The weight of semi-active devices is comparable to that of passive devices, at approximately 200 g. However, the dimensions of semi-active devices are still constrained by the presence of active components.

A notable disadvantage of passive orthoses over active devices is their lack of a system for tracking individual tremor rhythms. However, a key benefit of passive devices is their lightweight design. Furthermore, they are frequently more compact than active and semi-active orthoses, allowing for concealment beneath clothing and minimal interference with daily activities. One of the most recent developments is the Task-Adjustable Passive Orthosis - TAPO (Fromme et al., 2020), presented in the form of a fabric glove with a built-in capsule filled with air. The capsule is positioned externally to the hand, in the region above the wrist joint. By modifying the volume of the capsule, it is possible to attain a reduction in tremor while simultaneously elevating the effort necessary to move the wrist. The efficacy of TAPO was demonstrated in a clinical trial, wherein a patient exhibited a reduction in tremor of up to 82 %. In addition to analogous passive orthoses comprising air chambers, there are also options incorporating rotation dampers (Katz et al., 2017), which serve to counteract tremor by physically limiting joint movement. A comparable damper technology is employed by the STIL Orthosis (STIL, Netherlands), which is currently available on the market.

Another category of wearable devices for tremor suppression employs electrical stimulation. Two principal approaches to electrical stimulation for tremor treatment include peripheral nerve activation and antagonistic muscles activation (Mo et al., 2021). Both approaches utilize sensors to assess the individual tremor oscillation rate and perform stimulation of sensory or motor neurons based on the acquired data.

The objective of high-frequency transcutaneous electrical nerve

Ageing Research Reviews 113 (2026) 102923

stimulation is to selectively stimulate the large, myelinated peripheral proprioceptive A-beta (Aβ) sensory fibers (Johnson, 2007). These Aβ fibers convey proprioceptive sensory information into the thalamic circuits that are implicated in tremor generation (Garcia et al., 2024). Prior research has demonstrated that electrical stimulation of peripheral nerves at the wrist evokes activity within the ventral intermediate nucleus, thereby facilitating the development of a non-invasive neuromodulation therapy - transcutaneous afferent patterned stimulation or TAPS (Hanajima et al., 2004; Klostermann et al., 2009). TAPS comprises electrical bursts at a frequency that is calibrated to the specific tremor patterns of each individual patient.

Latest research of TAPS home-use in large group of patients ($n > 200$) at a daily 3-month period showed that 92 % of participants experienced a reduction in tremor power, with 54 % reporting a $\geq$ 50 % decrease in tremor power (Isaacson et al., 2020). The findings of this study indicate that non-invasive neuromodulation therapy, when used repeatedly at home, is an effective and safe method for reducing hand tremor in patients with essential tremor. TAPS is currently being utilized in a form of a wrist-worn device, the Cala kIQ (Cala Health, USA), which is currently available on the market. The watch-like device needs to be activated for 40 min to provide near an hour of decreased tremor power in targeted arm (Yu et al., 2020). While the effect of such treatment is transient, it has been approved by a number of clinical studies (Dai et al., 2023; Lu et al., 2023).

Functional electrical stimulation (FES) provides stimulation to motor nerves triggering muscle contraction. To suppress tremor, FES aims to activate antagonistic muscles (Javidan et al., 1990). The current approaches in utilizing FES to suppress tremors can be broadly classified into two main strategies: out-of-phase and co-contraction stimulations (Dideriksen et al., 2017; Meng et al., 2022).

The MOTIMOVE (3F-Fit Fabricando Faber, Serbia) device is an example of an out-of-phase stimulator. The multichannel stimulator activates electrodes placed on the forearm and upper arm above the flexor and extensor muscle points, thereby enabling selective muscle activation via distributed, asynchronous electrical stimulation. A pilot study of the MOTIMOVE device demonstrated an average reduction in tremor intensity of 67 % in six patients diagnosed with ET or PD (Popović Maneski et al., 2011). However, the system has certain limitations:. it requires precise electrode placement for optimal functionality and a compact computing device for mobility. Additionally, a combined multimodal out-of-phase FES and active orthosis system has demonstrated favorable outcomes, exhibiting a reduction in the tracking error for voluntary motion (Habibollahi et al., 2023).

The hardware and software design of the co-contraction stimulators is identical to that of the out-of-phase system. However, the co-contraction strategy is based on the model that at a single joint, an agonist and antagonist muscle receive tremorgenic input, resulting in involuntary mechanical oscillations (Gallego et al., 2015). In this strategy, the simultaneous application of electrical stimulation above the motor threshold in both the agonist and antagonist muscles serves to increase the impedance of the joint, thereby minimizing the involuntary oscillations (Gallego et al., 2013).

3.2. Stroke

Stroke continues to represent the primary cause of disability among the adult population (Stinear et al., 2020). As mortality after stroke declines, demand for stroke rehabilitation services is increasing, primarily for the rehabilitation of limb mobility, the lack of which has the greatest impact on quality of life (Langhorne et al., 2009). The primary objectives of rehabilitation treatment and physical therapy interventions following a stroke are to enhance the patient's functional capabilities, foster self-reliance, and enhance their overall quality of life (Langton-Frost et al., 2023).

Stroke is a highly heterogeneous disease, which means that its treatment with the goal of patient recovery of patients would be greatly facilitated by a personalized approach to medicine. Consequently, the field of stroke recovery therapeutics encompasses a multitude of intervention classes and treatment targets (Richards and Cramer, 2023). Among these, physical therapy represents one of the most prevalent forms of rehabilitative treatment provided after a stroke. Physical therapists work individually with patients who have suffered a stroke in order to improve their strength, coordination, and balance, thereby assisting them to regain the ability to perform the activities that constitute their everyday lives. For a comprehensive review of a plethora of post-stroke physical therapy interventions, see Shahid et al. (2023).

In the last decade, brain-computer interface (BCI) systems have emerged as a promising tool for the restoration of motor function. A BCI is defined as a software and hardware system that can be used to control external objects by decoding and interpreting brain activity (Wolpaw, 2013). The most prevalent methodology for the registration of brain activity in the context of BCI is electroencephalography. This approach is advantageous due to the relatively inexpensive and portable equipment utilized, coupled with a high signal discretization rate (Värbu et al., 2022). In the context of post-stroke rehabilitation, BCI decodes the patient's intention to move their affected limb and provides contingent feedback in various forms, including visual feedback, haptic feedback, multimodal feedback, actual movement and, more recently, virtual reality (Mane et al., 2020). It is therefore crucial that BCI-based interventions bridge the gap between the motor intention and sensory feedback of movement, in order to achieve functional recovery (Remsik et al., 2016; Cassidy and Cramer, 2017).

The advancement of BCI technologies for post-stroke patients is progressing in two distinct directions: the rehabilitation of lost motor functions and the development of alternative solutions to replace them. Rehabilitation BCI involves training to activate neuroplasticity mechanisms and partially or completely restore a former repertoire of movements (Chaudhary et al., 2016). In cases of severe stroke, when recovery through alternative methods is not possible, an assistive BCI is required to replace the most critical activities (Tariq et al., 2018).

Rehabilitation BCI employs motor imagery as a training task, which makes it suitable for patients who lack the requisite minimum movement capabilities to be eligible for conventional rehabilitation paradigms (Buch et al., 2008). There are various techniques for performing motor imagery. However, evidence suggests that the use of kinesthetic imagery facilitates more effective training and engages the motor cortex, thereby enhancing the efficacy of rehabilitation (Neuper et al., 2005). It is important to note that goal-directed kinesthetic motor imagery (Pereira et al., 2017) has been demonstrated in a number of studies to result in greater source activation compared to non-directed motor imagery (Yong and Menon, 2015; Kitahara et al., 2017). This approach is promising in terms of rehabilitation.

The modality of feedback is an important feature in BCI for rehabilitation. Visual feedback is a commonly used approach due to its simplicity of execution, whereas orthosis or exoskeleton feedback has the ability to produce actual movement in a limb affected by stroke and engaging additional neural pathways. These two approaches represent the primary paradigms of feedback in recent research on BCI (Khan et al., 2020). Simple and unintuitive visual feedback via monitor is being actively replaced by various examples of virtual/augmented reality (Wen et al., 2021; Kohli et al., 2022). Virtual reality provides an immersive experience, where the patient's intention of hand movement transfers into visually congruent action of a virtual hand. It should be noted that virtual reality does not provide a haptic stimulus, which could be beneficial for patients with residual tactile sensitivity in terms of rehabilitation. Robotic devices as BCI feedback in rehabilitation training have been shown to be an effective means of restoring motor activity in the extremities (Robinson et al., 2021). This technology still has many challenges to overcome, therefore widespread clinical adoption of robotic BCI training is yet to come (Colucci et al., 2022). The latest research trend in the field of non-electrical stimulation feedback in BCI is the development of multimodal systems. An illustrative example of this technology is the VR-BCI hand function enhancement rehabilitation system incorporating multi-sensory stimulation, as proposed by Shao et al. (2024). The system includes stimulation via virtual reality, sound and tactile gloves, which results in increased activation of motor brain areas during the training process. As concluded in this work, complete immersive experience could further accelerate rehabilitation process via two-way facilitation of sensory and motor conduction pathways. Basic construction of a modern BCI with common feedback modalities illustrated in Fig. 5.

A variety of stimulation techniques are currently being investigated for potential inclusion in rehabilitation as standalone techniques or as a form of reinforcement. The potential applications of non-invasive techniques, including transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS), and invasive epidural cortical stimulation (ECS), have been extensively investigated (Lefaucheur, 2009; Edwardson et al., 2013; Ting et al., 2021). The incorporation of stimulation into stroke rehabilitation strategies is typically performed in one of two ways: as a preprogrammed stimulation session, which is conducted concurrently with physical and occupational therapy, or as feedback in a closed-loop session. In preprogrammed stimulation, specific stimulation parameters are provided regardless of the patient's intentions. In contrast, closed-loop stimulation responds to patient's intentions to activate certain structures.

Two principal categories of preprogrammed stimulation are established: repetitive and paired. The objective of repetitive stimulation is to manipulate cortical excitability (particularly the motor cortex) in order to restore an interhemispheric activity balance disrupted by stroke (Murase et al., 2004). Repetitive TMS (rTMS), theta burst stimulation (TBS), and tDCS are frequently employed for this objective, as all of these techniques may either enhance the activity of a lesioned hemisphere (Fitzgerald et al., 2006; Plow et al., 2016, Khan, 2017; Chieffo et al., 2021) or reduce the activity of an intact hemisphere (Vines et al., 2008; Chung et al., 2016; Sharma et al., 2020). Paired stimulation induces a simultaneous pre- and post-synaptic neuronal activation, which elicits spike-timing-dependent plasticity (Feldman, 2012). This stimulation paradigm frequently features motor cortex TMS and spinal cord or peripheral nerves FES (Castel-Lacanal et al., 2007; Castel-Lacanal et al., 2009). It is noteworthy that neither type of preprogrammed stimulation takes into account the intricate and dynamic patterns of neuronal activity that occur in a patient.

In contrast to paired stimulation, closed-loop stimulation delivers a signal to the postsynaptic compartment in response to voluntary corticospinal activity of a patient, thereby increasing the likelihood of direct translation into functional gains (Ethier et al., 2015). A study conducted on a rat model demonstrated that closed-loop stimulation facilitated enhanced overall recovery following spinal cord injury and ischemic strokecompared to only rehabilitation procedures or simple stimulation of an extremity (Ganzer et al., 2018; Meyers et al., 2018). This general approach has also been successfully tested in human subjects (Popovic et al., 2011; Hara et al., 2013). However, this method is contingent upon the patient being able to exert a certain degree of control over the affected limb to generate signals that are compatible with the aforementioned approach. However, the integration of closed-loop stimulation with BCI bypasses this limitation (Buch et al., 2008). It has been demonstrated that a motor imagery-based BCI with FES feedback enables stroke patients to enhance their upper and lower limb functionality (Marquez-Chin et al., 2016; Mrachacz-Kersting et al., 2016; Biasiucci et al., 2018; Liao et al., 2023).

A variety of post-stroke rehabilitation devices are currently available on the market, catering to both clinical and individual settings. A comprehensive review of upper limb training systems currently available on the market was conducted by Sheng et al. (2023). With regard to rehabilitation systems for the legs, it is notable that such devices are rare and only available for clinical use. To illustrate, the system for the rehabilitation of upper and lower limbs, recoveriX Neurotechnology (g.tec medical engineering GmbH, Austria), is a motor imagery BCI with visual and FES feedback (Sebastián-Romagosa et al., 2020). This system serves as an illustrative example of a multimodal closed-loop BCI that has recently gained prominence due to its immersive structure, which is believed to enhance training outcomes (Lupu et al., 2020; Ren et al., 2020).

3.3. Spinal cord injuries

The human spine comprises specialized tissues and structures that function synergistically to facilitate a wide range of motion and withstand substantial mechanical loads—crucial for daily physical activities. The spinal cord, protected by the vertebral column, remains highly susceptible to external trauma, the leading cause of spinal cord injuries (SCI), primarily resulting from falls and road traffic accidents (Patek, Stewart, 2023). However, neurological impairments, whether transient or permanent, may also arise from various non-traumatic causes (Clark,

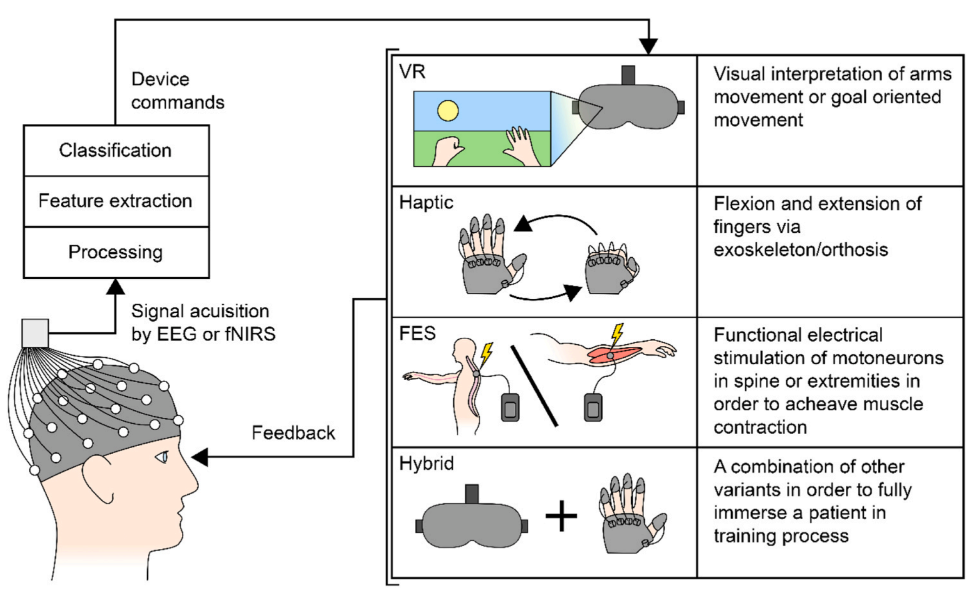

Fig. 5. BCI building blocks with feedback options for stroke rehabilitation. EEG – electroencephalography, fNIRS – functional near-infrared spectroscopy, VR – virtual reality, FES – functional electrical stimulation.

Marshall, 2017). Most non-traumatic spinal cord injuries (NTSCI) are classified as acquired abnormalities according to standardized taxonomy (New and Delafosse, 2012).

With aging, the spinal cord undergoes progressive degenerative changes (Geertsen et al., 2017), and the incidence of acquired abnormalities leading to NTSCI exhibits a positive correlation with advanced age (Van den Berg et al., 2010). Thus, acquired spinal cord pathologies may be age-dependent.

The recognized etiological factors of NTSCI include spinal stenosis, neoplastic lesions, inflammatory disorders, infectious processes, and vascular pathologies (Vervoordeldonk et al., 2013). Despite diverse etiologies, NTSCI lacks pathological specificity in clinical and imaging features, leading to empirical treatment based on differential diagnoses. Progressive degeneration of neural tissue manifests as gradually worsening motor deficits, including muscle weakness, gait disturbances, and impaired coordination, frequently accompanied by sensory abnormalities and neuropathic pain (Ko, 2022). Many patients develop secondary complications such as urinary tract infections, spasticity, and urinary incontinence, further impairing their quality of life (Gupta et al., 2009; Nair et al., 2005).

Regardless of etiology, severity, or extent of spinal cord damage, patients demonstrate improved performance in activities of daily living—including self-care, personal hygiene, transfers, and mobility—following rehabilitation intervention, alongside significant neurological recovery (Ronen et al., 2005; Catz et al., 2004). Additionally, pharmacologic management of pain and secondary complications alleviates symptoms, enabling motor rehabilitation (Pataraia, Crevenna, 2019; Dworkin et al., 2007; Stiens et al., 1997). Traditional physiotherapy sessions focus on enhancing mobility, strength, and overall physical function, promoting neurological and functional recovery (Gupta et al., 2009). Nevertheless, studies confirm that combining conventional methods with technological devices maximizes rehabilitation effectiveness (Maggio et al., 2024; Semprini et al., 2018; Zanatta et al., 2023).

Balance impairment is a significant consequence of NTSCI. Since maintaining balance is essential for performing daily activities, its impairment can lead to difficulties in mobility, posture control, and gait. Evidence suggests that integrating VR into rehabilitation enhances effectiveness, particularly in balance restoration (Miguel-Rubio et al., 2020). Virtual reality-based interventions have emerged as a promising adjunct to conventional therapy, offering intensive repetitive practice while maintaining patient motivation (Peñasco-Martín et al., 2010). By delivering multisensory feedback within an immersive environment, these interventions further support rehabilitation (Fager, Burnfield, 2014). VR treatment typically involves observation and training in a virtual environment with embodied virtual limbs and lasts approximately six weeks, with three sessions per week (An, Park, 2018; Van Dijsseldonk et al., 2018). For improved accessibility, such training can also be conducted in home-based settings (Villiger et al., 2017).

Patients with severe motor impairments require additional support during rehabilitation. In such cases, exoskeletons serve as assistive devices for training (Tamburella et al., 2022). Robotic devices are commonly used to improve gait (Bach Baunsgaard et al., 2018; Chang et al., 2018) and motor function (Tsai et al., 2020; Yatsugi et al., 2018). Robotic Exoskeleton-Assisted Rehabilitation Systems (REARS) represent a promising modern approach experimentally tested for NTSCI rehabilitation (Gupta et al., 2023). REARS consists of two components: a mobile body-weight support system for overground walking and balance training, and a powered wearable exoskeleton. A 24-session REARS protocol, lasting one hour per session, includes training in transfers, trunk and pelvic balance, upper extremity range-of-motion exercises, hand function, grip strengthening, and activities of daily living. Following REARS training, patients demonstrate improved independence and reduced reliance on assistive devices. Thus, technological rehabilitation approaches contribute significantly to functional recovery and quality of life.

3.4. General decrease in motor abilities

The timing of multi-joint actions has been demonstrated to be dependent on the function of the proprioceptive system in patients (Sainburg et al., 1995). Patients with cerebellar damage show deficits similar to those observed in older individuals (Bastian et al., 1996), indicating that age-related degeneration of the cerebellum (Raz et al., 2001, Raz et al., 2005) and the proprioceptive system (Goble et al., 2009) may contribute to deficits in multi-joint coordination observed in older adults. Such multi-joint actions include not only writing and various hand movements, which are regarded as the most complex, but also gait.

In the past, gait was generally considered as an automated motor task that did not require higher-order cognitive control. It is now known that aging causes a shift from automatic to more controlled motor processing, with additional brain regions activated to achieve the same level of motor or postural control (Boisgontier et al., 2013; Heuninckx et al., 2005). Modern publications also indicate that gait and cognition are interrelated (Montero-Odasso et al., 2012) and may share similar neural substrates, especially in older age (Parihar et al., 2013). It may therefore be posited that cognitive training could represent an effective method of enhancing motor performance in older age (Smith-Ray et al., 2015; Hwang et al., 2021).

Type 2 diabetes mellitus is one of the most common age-related diseases leading to frailty, physical and cognitive functions degeneration (Fulop et al., 2010; Vinik et al., 2015). Physical impairments leading to gait and balance disorders as well as muscle weakness, increase a chance of falling (Yang et al., 2016). It turned out that lower-extremity exercise and walking training alone could not help reduce fall rates, or improve functional performance and muscle tone (Kruse et al., 2010). Nevertheless, balance training has been demonstrated its effectiveness in fall prevention (Sherrington et al., 2017). However, this type of training alone has not been shown to enhance activity of daily living or social participation in older individuals (Silsupadol et al., 2009). Subsequently, Kraiwong et al. (2021) discovered that the implementation of cognitive-physical training over an eight-week period led to enhanced physical performance in elderly individuals with diabetes. However, no significant impact was observed in terms of depression and mood indicators. A year after the training program had begun, the number of falls experienced by those who had undergone the training was found to be insignificantly lower than that of the control group. However, the strength of the leg muscles and the speed of motor activity of the lower extremities remained higher, as did the activity of daily living.

A recent multi-level meta-analysis conducted by Rieker et al. (2022) investigated the impact of combined cognitive and physical interventions on cognitive functions in healthy older adults. The combined approach demonstrated a slight but significant advantage over the individual effects of physical or cognitive interventions, while maintaining its efficacy over time. In conclusion, the findings of Rieker et al. suggest that a simultaneous combination of cognitive and physical activity is more effective in improving executive functions, attention, and processing speed. Additionally, combined training yielded superior outcomes compared to single physical training in terms of balance performance. These findings suggest that combined cognitive and physical training may prove more efficacy in older adults with motor disorders.

A study by Boraxbekk et al. (2016) demonstrated the effects of six weeks of motor imagery training and real finger-tapping training in a group of older adults on finger tapping tasks (time required to perform a sequence of determined taps on a keyboard) and neural plasticity (brain activation measured by fMRI). Improvements in motor performance were observed following both mental and real training. Furthermore, the transfer of experience to untrained tasks was observed following motor imagery training (Boraxbekk et al., 2016). The combination of mental and motor activities yielded inconsistent outcomes that deteriorated over time. This phenomenon can be attributed to the inherent challenge of establishing a stable pattern of action when employing disparate training strategies in conjunction. Although research performed by Oh and Choi (2021) found that motor imagery alone improves balance control and reduces fall rates in older adults.

To conclude, a variety of methods for treating various motor disorders have been explored. See Table 1 for a summary of the most relevant studies.

4. Open research topics and perspectives

Modern medicine increasingly raises questions not only about the treatment of specific diseases, but also the prognosis of the course and therapy of chronic diseases (Hodson, 2016). Such a statement of the question requires the development of effective methods to identify whether a particular individual belongs to risk groups for various chronic diseases. Such an early detection allows physicians to conduct adequate preventive and supportive measures to cap the progression of the disease or keep it in a mild form. This has become especially relevant in recent times, when a significant increase in the standard of living, proper diet, psychological attitude to health care, preventive measures, and medical advances in the treatment of diseases have led to a significant increase in life expectancy. As a consequence, the treatment of such diseases that were rare half a century ago but are now becoming more and more prevalent among elderly patients, is becoming relevant.

Neurodegenerative diseases serve as a prominent example of this trend, as their risk increases sharply with the age of the patient. In particular, Parkinson's disease affects about 300 individuals per 100,000 people. Most people are diagnosed over the age of 70, with only 15 % of cases occurring among people under the age of 50. Recent estimates show that the number of people living with Parkinson's disease steadily increases with age (Driver et al., 2009; Hirsch et al., 2016). It is clear from the data presented that the burden of Parkinson's disease will increase in many countries as populations age. A similar situation occurs for Alzheimer's disease (Alzheimer's Association Report (2020). One in ten (10 %) people in the U.S. aged 65 and above has Alzheimer's disease. The percentage of people with Alzheimer's dementia increases with age: 3 % of people aged 65–74, 17 % of people aged 75–84, and 32 % of people aged 85 and older. Additional movement disorders such as essential tremor (ET) and Huntington's disease, which are characterized by a large spectrum of motor and non-motor symptoms, further exemplify age-related conditions requiring extensive attention.

There are still no reliable tests for early diagnosis of these diseases, nor objective prognostic biomarkers. This creates problems in assessing individualization and progression. Overall, the main challenge faced by healthcare systems is not confined to the treatment of specific diseases, but extends to disease prevention, early detection, and chronic disease management. In the scenario of personalized preventive care, healthcare providers are required to maintain a long-term relationship with the patient, who must learn to manage symptoms, organize adherence to treatment (e.g., taking medications regularly), and cope with stress and negative emotions. At the same time, this approach requires the accumulation of a large amount of personal organized data about the patient to enable automatic intelligent analysis of not only their current state, but also the prognosis of their health status and/or chronic disease. However, one problem lies in the functional mobility of personal visits to doctors of elderly patients with neurodegenerative diseases, who often have functional mobility impairments (Bouça-Machado et al., 2018). The Covid-19 pandemic has already significantly disrupted traditional clinical practice, forcing widespread adoption of telemedicine in healthcare delivery. The next promising phase of healthcare adaptation is the introduction of alternative modes of continuous assessment and treatment outside the clinic with minimal interaction with healthcare providers.

The latter is possible thanks to the advances of modern mobile electronics and digital technologies, which are fundamentally changing the social fabric of life in the twenty-first century. And now their level of development is such that digital technologies are ready to have a profound impact on healthcare, in fact, allowing for real-time "disease management", giving a real tool to transform classical medicine. Digital tools such as smartphones and wearable sensors, connected in a unified network of the Internet of Things (IoT), present the possibility to objectively, almost continuously and remotely assess age-related changes in people leading to motor impairment in various conditions (Age-Related Motor Skills Impairment - ARMSI). Historically, the core of medical care was related to solving health problems, and for a long time it was based on interaction between a patient and medical doctors, hospitals, and other parts of the health care system; however, with the introduction of mobile and wearable medical devices, medical care is being transferred to the patient's home, reducing the need for face-to-face interaction with healthcare providers.

Wearable mobile devices capable of monitoring our bodies and continuously collecting data on human physiology using digital medical devices opens up new opportunities for both biomedical research and clinical practice. Smartphones equipped with high-quality accelerometers, gyroscopes, global positioning technologies (GPS) are widely available and used daily by more than 3 billion people of a wide range of ages worldwide (Mobile network subscriptions worldwide, 2025). This makes them attractive mass digital tools for clinical treatment and research on age-related changes in motor function. Wearable monitoring devices offer an even greater range of possibilities. For example, they can be equipped with a wide range of specialized sensors (electromyography, electrocardiography, temperature sensors, etc.). Such sensors can be more autonomous than smartphones and will not require direct active participation of elderly users. They are capable of automating, continuously recording, analyzing, and sharing standardized physiological and biological data over high-speed communication links using IoT technology. This creates the possibility to conduct high-throughput phenotyping of individuals across the lifespan and offers the prospect of earlier identification of people at risk of developing diseases, increased sensitivity for detecting progression of motor diseases, which may accelerate the development of new therapies and improve clinical research.

Emerging systems with open and closed neurobiological feedback based on brain-computer interfaces (BCIs) (Hramov et al., 2021a), as well as the deep brain stimulation (DBS) systems they control (Lozano et al., 2019), illustrate some of the clinical applications of wearable technologies. Such systems will be able to directly measure electrophysiological and/or hemodynamic brain activity, which could potentially provide a scientific basis for the use of remote brain stimulation with adaptive DBS systems.

Thus, the new digital paradigm of medicine will be aimed at personalized proactive prevention of the development of a particular disease. As noted in the review (Coravos et al., 2019), this means that physicians will start routinely prescribing not only certain medications, but also software applications and mobile wearable devices approved by medical device regulators to monitor and manage chronic diseases. Perhaps, this approach will eventually extend to preventing acute episodes of chronic diseases.

As a new scientific trend in medical knowledge, digital medicine encompasses both a wide range of professional expertise and new responsibilities facing medical personnel related to the use of digital tools. Technologies capable of capturing digital user/patient data include digital biomarkers (e.g., using a voice biomarker to track changes in tremor in a patient with Parkinson's disease (Zhang, 2017; Arora et al., 2018; Singh and Xu, 2020), electronic assessments of clinical outcomes (e.g., electronic patient-reported outcome questionnaire), and tools to measure adherence and safety (e.g., wearable sensor that tracks falls, smart mirrors for passive monitoring at home, video cameras) (Council et al., 2011).

Continuous home monitoring also raises a new set of practical questions: Who will track the data? Who will be responsible for taking

Table 1
Articles demonstrating the main approaches to the treatment of various motor disorders.

Disease	Rahabilitation Method	Subjects	Effect	Reference
Tremor	Active orthosis	10 patients with tremor (essential or Parkinson)	81.2 % mean power reduction of tremor	Rocon et al., (2007)
Tremor	Active orthosis	9 patients with tremor (essential or Parkinson)	average tremor reduction of 94.3 %	Herrnstadt et al., (2019)
Tremor	Semi-active orthosis	10 datasets from patients with severe Parkinsonian and Essential Tremor	mean tremor power reduction 28.7 dB and 11.8 dB in first and second harmonic	Case et al., (2016)
Tremor	Semi-active orthosis	5 healthy subjects, self-initiated osclillations	amplitude of acceleration and angular velocity of simulated tremor reduction by 60.39 % and 55.07 %, respectively	Yi et al., (2019)
Tremor	Semi-active orthosis	5 healthy subjects, self-initiated osclillations	wrist tremor magnitude of acceleration and angular velocity reduction by 61.39 % and 56.22 %, respectively	Zahedi et al., (2021)
Tremor	Passive orthosis	1 patient with Parkinson's Disease	mean 78 % tremor power reduction	Fromme et al. (2020)
Tremor	Passive orthosis	10 patients with essential tremor	up to 80 % tremor amplitude reduction	Katz et al., (2017)
Tremor	TAPS	193 patients with essential tremor were included in final analysis	mean tremor power decrease 72.7 %	Isaacson et al., (2020)
Tremor	TAPS	276 patients with essential tremor	78.75 % mean power reduction of tremor	Dai et al., (2023)
Tremor	Out-of-phase FES	7 patients with Parkinson's disease and essential tremor	67 % decrease in the amplitude of tremor	Popović Maneski et al., (2011)
Tremor	Co-contraction FES	6 patients suffering from parkinsonian or essential tremor	reduced tremor amplitude up to a 52.33 %	Gallego et al., (2013)
Stroke	excitatory TBS over primary motor cortex	15 patients with first-ever middle cerebral artery ischaemic stroke	motor physiological parameters were significantly greater after continuous theta burst stimulation	Khan, (2017)
Stroke	Primary motor cortex exitatory rTMS	12 patients with first-ever stroke	significantly decreased spasticity, increase in the motor function of the paretic arm (measured by FMA)	Chieffo et al., (2021)
Stroke	Conventional physical therapy and low-frequency rTMS on contralesional premotor cortex	96 patients who had first ever ischemic stroke in the previous 15 days	improved functional independence in patients (measured by modified Barthel Index)	Sharma et al., (2020)
Stroke	Paired peripheral nerve FES and primary motor cortex TMS	6 patients in the first weeks after stroke	significant target muscle motor evoked potential facilitation after paired stimulation, increase in arm motor performance (measured by FMA)	Castel-Lacanal et al., (2009)
Stroke	MI-BCI with visual and FES feedback	51 stroke patients with upper extremity hemiparesis	significant increase in the motor function of the paretic arm (measured by FMA and Modified Ashworth Scale) persisted 6 months after the therapy ended	Sebastián-Romagosa et al., (2020)
Stroke	MI-BCI with VR and FES feedback	12 healthy subjects	MI-BCI with hibrid VR and FES feedback showed better results in classification metrics than only VR feedback	Ren et al., (2020)
Stroke	MI-BCI with FES feedback and physiotherapy	40 hospitalized patients with ischemic stroke	MI-BCI rehabilitation training and physiotherapy more effectively improve motor function compared with physiotherapy only (based on FMA, MAS)	Liao et al., (2023)
Spinal cord injuries	VR-augmented lower limb training	12 chronic SCI patients	significant improvements were shown in lower limb muscle strength (measured by LEMS), balance (measured by BBS), and functional mobility (measured by TUG)	Villiger et al., (2017)
Spinal cord injuries	VR- augmented treadmill training	15 chronic SCI patients	Significant improvements were found in walking speed, stride frequency, step width, and stability measures (measured by DSM)	Van Dijsseldonk et al., (2018)
Spinal cord injuries	Semi-immersive VR balance training	10 chronic SCI patients	after intervention stability (measured by LOS), balance (measured by BBS) and functional mobility (measured by TUG) were significantly increased	An, Park, (2018)
Spinal cord injuries	Exoskeleton-assisted gait training	7 chronic SCI patients	significantly increased walking speed (measured by walking tests) and minimum clinically important difference was achieved in functional mobility (measured by TUG)	Gupta et al., (2023)
Spinal cord injuries	Exoskeleton-assisted gait training	13 SCI patients	significant increase in movement speed and stride length (measured by walking tests)	Chang et al., (2018)
Spinal cord injuries	Exoskeletal-assisted walking training	10 SCI patients eligible for locomotor training	significant improvements were shown in lower limb muscle strength (measured by LEMS), and independency (measured by FIM)	Tsai et al., (2020)
General motor disorder	Cognitive training	51 older adults (aged 79 or older)	intervention participants performed significantly better than controls on Timed Up & Go test and distracted walking	Smith-Ray et al., (2015)
General motor disorder	Physical-cognitive training	37 older adults with T2DM and balance impairment	The Activity of Daily Living, Timed Up & Go test and alternate stepping test, hip extensors and abductors, knee extensors and flexors, ankle plantarflexors and dorsiflexors increased and remain 1-year follow-up	Kraiwong et al., (2021)
General motor disorder	Semi-immersive virtual reality-based cognitive training combined with locomotor activity	18 older adults	significantly greater improvement in the Trail Making Test A, Digit Span Test backward and 10-m Walking Test scores	Hwang et al., (2021)
General motor disorder	Motor imagery training	34 older adults who had experienced falls	significantly greater increase in Berg Balance Scale, Timed Up and Go Test, and Falls Efficacy Scale after motor imagery	Oh, Choi, (2021)

(*continued on next page*)

Table 1 (*continued*)

Disease	Rahabilitation Method	Subjects	Effect	Reference
			training intervantion compared with task-oriented trainin and control	
General motor disorder	Combined motor and motor imagery training	56 healthy older participants	cobination of motor imagery and motor training did not result in additional performance gains compared to motor-only training (measured by time of execution)	Boraxbekk et al., (2016)

TAPS – transcutaneous afferent patterned stimulation, FES – functional electric stimulation, TBS – theta burst stimulation, MI-BCI – motor imagery brain computer interface, VR – virtual reality, rTMS – repetitive transcranial magnetic stimulation, MAS – motor assessment scale, FMA – Fugl-Meyer Assessment, SCI – spinal cord injury, LEMS – Lower Extremity Motor Score, BBS – Berg Balance Scale, TUG – Timed Up and Go, DSM – dynamic stability margin, LOS – Limit of stability, FIM – Functional Independence Measure, T2DM – type 2 diabetes mellitus.

certain medical actions in cases where interventions are necessary? How will providers of such services be compensated for performing these tasks? A number of organizations, such as the Clinical Trials Transformation Initiative (USA), have had some success in addressing the first two issues, but for these tools to be truly integrated into clinical practice, legislative solutions to these issues are needed, which have not yet been done (Clinical Trials Transformation Initiative). Addressing these issues of regulation of modern digital devices in clinical practice and for home monitoring of patients is a matter of the near future if we are to use new digital technologies effectively and safely.

It should also be noted that the mass introduction of digital mobile devices will lead to the accumulation of huge amounts of digital medical data, which will require the automation of their processing and the development of recommendations to patients and/or doctors based on individual data. Processing of accumulated big data and searching for patterns in them is currently performed by computer analytical methods, among which artificial intelligence (AI) technologies show the greatest efficiency. These information technologies, which caused the recent "big data revolution", can immense volumes of various types of medical information and, in contrast to traditional statistical methods, have a number of undoubted advantages. In particular, the analysis of big data allows not only answering previously posed questions (i.e., confirming already stated hypotheses), but also formulating new hypotheses and/or establishing new regularities.

In summary, the aging population presents a significant challenge for healthcare systems, with ARMSI being a major concern. The digital medicine, BCI, and AI offer promising tools for detecting and rehabilitating ARMSI. Early detection of ARMSI is crucial to maximizing treatment outcomes and promoting patients' independence. Traditional methods of assessment are often time-consuming, subjective, and rely on clinical observation. Digital medicine, BCI, and AI offer more objective, sensitive, and scalable approaches for detecting ARMSI. The vision of present methods combination in detecting, proposing an intervention, and optimizing the treatment is shown in Fig. 6. In the following section these methods will be considered in more detail.

4.1. Digital Medicine

Wearable sensors and smartphone apps can monitor movement patterns, gait, and balance, providing valuable data for early detection of ARMSI. (Huang et al., 2024; Al-khafajiy et al., 2019). These technologies offer non-invasive, accessible, and cost-effective solutions for continuous monitoring and identification of potential risks. For example, accelerometers and gyroscopes in smartphones can track gait parameters like step length, cadence, and variability, which can be indicative of gait impairments associated with ARMSI. (Adams et al., 2021) Furthermore, smartphones and wearable devices can detect and quantify numerous motor symptoms of Parkinson's disease, including gait, falls, tremor, bradykinesia, motor fluctuations, and dyskinesias. In the recent papers (Ellis et al., 2015; Kim et al., 2018; Fiems et al., 2020; Yahalom et al., 2020) attempts have been made to use smartphone applications to assess postural sway, detect gait variability and faltering, etc. Fall detection and fall risk assessment are of particular benefit in Parkinson's disease. Continuous monitoring using mobile devices and

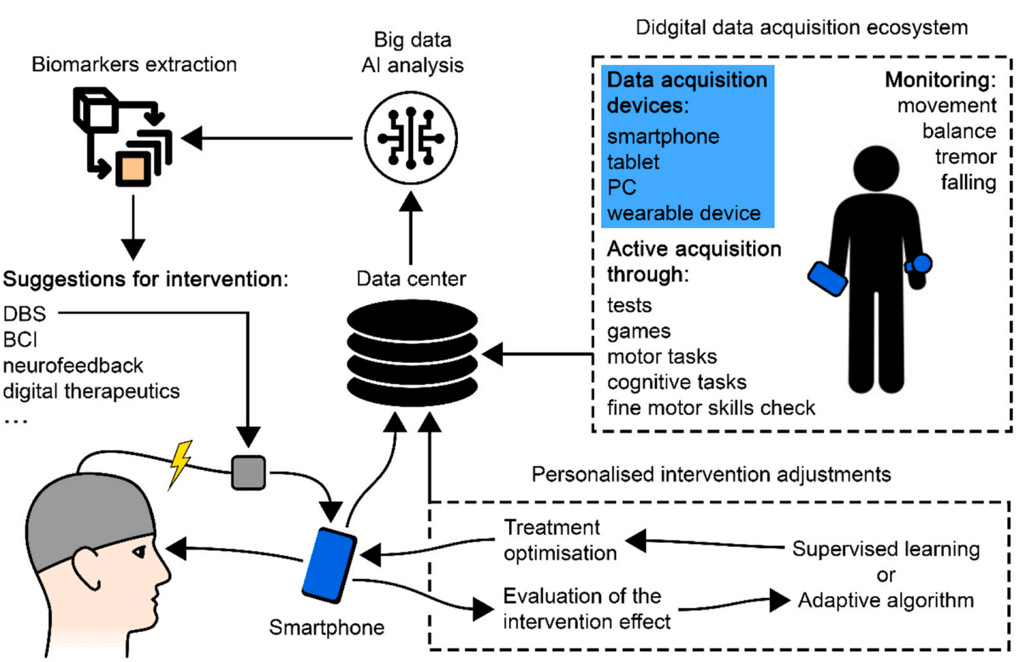

Fig. 6. Digital medicine in ARMSI monitoring, identification and treatment.

special applications provides an accurate and objective assessment of falls. Mobile digital medicine systems can also play a significant role in rehabilitation tasks as well. For example, interactive games on smartphones or tablet PCs and virtual reality (VR) platforms can provide engaging and motivating exercises to improve motor skills and cognitive functions (Adlakha et al., 2020; Ferreira and Menezes, 2020). Gamified rehabilitation programs can help increase patient engagement and adherence to therapy.

4.2. BCI and DBS

BCI systems allow individuals to control external devices using brain signals (Hramov et al., 2021a). While primarily focused on rehabilitation, BCIs could be used to assess subtle changes in brain activity related to motor function, potentially enabling earlier detection of ARMSI compared to traditional methods. Studies have shown that BCIs can differentiate between healthy individuals and those with Parkinson's disease based on their brain activity patterns during motor tasks. (Chaudhary et al., 2016; Lazarou et al., 2018) This suggests that BCIs could potentially be applied to detect early signs of ARMSI in other neurological conditions as well. Even greater benefits can be achieved by the incorporating DBS into the open/close feedback loops, which is effective for the treatment of ET, dystonia, motor complications, and medication-refractory tremor in Parkinson's disease (Benabid et al., 1991; Schuepbach et al., 2013; Moro et al., 2017). Digital devices, such as smartphones and wearable devices, can aid in the pre-, intra-, and postoperative assessment of the response to DBS adjustments as well as its remote programming (Lieber et al., 2015; Chockalingam et al., 2017). Electrophysiological data that can be acquired from electrodes implanted in the brain and correlated with symptoms and medications to optimize DBS programming during face-to-face patient visits or remotely. Directly measured pathophysiologic brain activity can be used as a source of information for novel biomarkers of disease activity and progression, as well as response to treatment. Therefore, integration of BCI and DBS technologies could allow individuals with ARMSI to regain some lost functionality by controlling assistive devices or stimulating specific brain regions (Lebedev and Nicolelis, 2006; Benabid et al., 2011). This can improve independence and quality of life for individuals with severe motor impairments.

4.3. Artificial intelligence

AI-based algorithms can analyze data from sensors, imaging studies, and even health records to identify patterns associated with ARMSI (Chudzik et al., 2024; Zolfaghari et al., 2023). AI-powered systems can also assist in the interpretation of complex data, potentially leading to more accurate and timely diagnoses of ARMSI (Bernal et al., 2024). For instance, AI algorithms have been developed to identify individuals at risk of falls based on their gait patterns captured by wearable sensors (Harris et al., 2022). This technology could be used to screen individuals for ARMSI and identify those who may benefit from early interventions. AI can personalize rehabilitation programs by tailoring exercises to individual needs and tracking progress (Arefin and Kipkoech, 2024). AI-powered systems can also provide real-time feedback and adaptive adjustments to enhance the effectiveness of therapy.

Thus, we can conclude that combining digital medicine, BCI, and AI offers a powerful approach for a holistic and personalized management of ARMSI. Future research should explore the potential of integration of these technologies for early intervention and prevention of ARMSI.

CRediT authorship contribution statement

SG, NG, EP, SK, VK and AH have designed and elaborated the manuscript as well as read and approved its final version.

Declaration of Competing Interest

The authors report no declarations of interest.

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Data availability

No data was used for the research described in the article.

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