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Review article

Experience-dependent plasticity of large-scale brain networks in aging: How different training modalities shape neural connectivity

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ABSTRACT

Brain regions are organized into large-scale networks through dynamic functional connections that support sensorimotor and cognitive processes across the lifespan. Age-related disruptions of these functional systems are associated with cognitive and motor decline and increased risk of neurocognitive disorders. A growing body of evidence suggests that structured physical training can modulate resting-state functional connectivity within these networks, offering a potential neuroprotective strategy. However, the relative efficacy of different training modalities, and the mechanisms by which simultaneous cognitive loading during motor training may confer neuroplastic benefits, remain incompletely characterized. This narrative review critically integrates evidence on network-level changes following cardiorespiratory, resistance and balance training, cognitive stimulation, and combined motor–cognitive interventions (with exergames (i.e., interactive physical and/or motor-cognitive exercises to control traditional or extended reality videogames) and mind–body practices) in older adults. We critically appraise evidence strength across three methodological tiers: direct neuroimaging (i.e., rs-fMRI), indirect measures (i.e., EEG and fNIRS), and conceptual frameworks, and apply this hierarchy to critically evaluate the guided-plasticity facilitation framework, a working hypothesis proposing synergistic neuroplastic effects when motor and cognitive demands overlap, for which direct neuroimaging support in humans remains limited. Key methodological gaps are identified: scarcity of direct comparison trials, inadequate dose-matching, limited long-term data, and near-absence of dynamic functional connectivity analyses. We outline research priorities to advance a mechanistic, individualized understanding of experience-dependent brain network plasticity in aging and neurocognitive disorders and propose network-level biomarkers as a candidate direction for future personalized training prescriptions. We also outline a prospective precision-medicine framework for exercise prescription in neurocognitive disorders, noting that prospective validation studies are needed before network-level biomarkers can inform clinical decision-making.

1. Introduction

Mens sana in corpore sano (translated: *a healthy mind in a healthy body*, from Decimus Junius Juvenalis, ~127 AD) is probably the most known ancient sentence stating that brain and body are intimately connected. In the seventeenth century, however, the concept of "mind-body dualism" emerged, and modern medicine adopted the idea that mind and body are separate (Fabiano et al., 2026). Nevertheless, an emerging

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risk syndrome such as the motor-cognitive risk syndrome (Semba et al., 2020), together with population-based evidence of bi-directionality between mental disorders and physical health conditions (Hanna et al., 2024), points to common causal underpinnings.

With populations aging worldwide and the number of individuals aged 65 years and older projected to double by 2050 (United Nations, 2020), identifying modifiable lifestyle factors that preserve the integrity of large-scale brain networks is a public health priority. Age-related disruption of these functional systems is among the most consistent neuroimaging signatures of cognitive aging and neurocognitive disorder risk (Fjell and Walhovd, 2010; Rodriguez-Sabate et al., 2019). Structured physical training represents one of the most manageable and scalable interventions targeting this disruption; yet the mechanistic pathways, the comparative efficacy of different training modalities, and the conditions under which motor-cognitive simultaneity may confer synergistic benefits remain poorly characterized at the neural networks level.

Today, after almost 2000 years, it is widely accepted that regular physical activity and training bring improvements that are beyond the musculoskeletal, cardiovascular, and respiratory systems. In fact, the Centers for Disease Control and Prevention (CDC; United States) recommends regular physical activity, given its systemic benefits, including neural and cognitive domains (Piercy et al., 2018). For example, regular practice of physical activity and exercise can counteract cognitive decline (Omura et al., 2020), depression and anxiety (Schuch et al., 2016), contributing to slowing the physiological aging process (Baek, 2016). Accordingly, the Lancet Commission's report on dementia prevention and intervention emphasized the role of physical activity in mitigating the risk of developing dementia (Livingston et al., 2020). Moreover, physical activity and training have recently been recommended for the primary, secondary, and tertiary prevention of neurocognitive disorders by a panel of international experts in a collaborative guideline (Veronese et al., 2023). Indeed, some individuals with mild Neurocognitive Disorder (mNCD) present abnormal accumulation of misfolded proteins in the brain, a process further exacerbated by oxidative stress, metabolic disorder, and neuroinflammation, leading to neuropathological damage. Throughout this review, MCI (Mild Cognitive Impairment) and mNCD (mild Neurocognitive Disorder) are used interchangeably as reported in the included trials, although they derive from distinct diagnostic frameworks: DSM-5R for mNCD and research consensus criteria for MCI. Furthermore, it should be noted that while trials are synthesized together in this review, diagnostic heterogeneity across historical MCI and DSM-5R mNCD criteria represents a potential confounding variable in clinical trial meta-analyses.

The mechanisms linking physical training to brain health in aging span multiple biological levels, from neurotrophic and myokine signaling (e.g., BDNF, IGF-1, VEGF) to hypothesized neurogenic effects, and ultimately to network-level functional reorganization, though direct evidence connecting molecular triggers to neural network outcomes in older humans remains limited. As this review focuses on the neural networks level, lower-level mechanisms are not detailed further but can be retrieved elsewhere (Huuha et al., 2022; Lu et al., 2023).

Importantly, lower-level cellular mechanisms such as adult hippocampal neurogenesis, are robustly established in rodents but remain controversial in humans (Boldrini et al., 2018; Sorrells et al., 2018). For instance, human trials rely on peripheral proxies (e.g., serum BDNF) or macro-level neuroimaging, which cannot directly infer on cellular neurogenesis. Consequently, mechanistic extrapolations from animal models to human network plasticity should be interpreted cautiously as working hypotheses. In addition to the reduction of neuropathological damage, physical training also allows the maintenance and increase of cognitive reserve (Huuha et al., 2022; Livingston et al., 2020), which empowers individuals to maintain a ‘normal’ level of functioning, even in the presence of neurodegenerative alterations (Barnes and Yaffe, 2011; Stern, 2009, 2002; Wallace et al., 2019). Two distinct pathways link physical activity to brain health in aging: (1) cardiorespiratory (or endurance) training, that involves continuous, rhythmic activity engaging large muscle groups and relying on oxidative metabolism to improve cardiovascular capacity and that operates through global neuroplastic and hemodynamic mechanisms (i.e., increased cerebrovascular perfusion, BDNF upregulation, and reduced neuroinflammation), producing broad changes across multiple brain regions and networks (Givralli et al., 2026); and (2) motor skill learning, that operates through functional reorganization and structural efficiency of specific neural circuits, producing targeted, task-specific plasticity (De Sá et al., 2024; Voelcker-Rehage and Niemann, 2013). Traditional cardiorespiratory training predominantly improves structural brain capacity, such as hippocampal volume (Erickson et al., 2011), though subsequent replication studies have yielded inconsistent results (Coen et al., 2011), warranting cautious interpretation of the robustness of this effect. By contrast, motor learning reshapes the functional organization of sensorimotor and executive circuits. In older adults, these pathways may interact, that is motor-cognitive training may recruit both, but they should not be conflated when interpreting modality-specific effects (Netz, 2019).

Physical training interventions may also be more effective when combined with concurrent cognitive tasks, an effect attributed to the guided-plasticity facilitation framework, a working hypothesis suggesting synergistic benefits from combined 'facilitation' and 'guidance' effects (Fabel and Kempermann, 2008; Herold et al., 2018; Kempermann et al., 2010), which we critically examine in Section 2.3. The overarching argument of this review is that the apparent divergence in training-modality effects on brain networks is largely artifactual rather than a genuine reflection of differential mechanistic specificity. This divergence is primarily a product of heterogeneous methodologies, absent dose-matching, and the near-exclusive reliance on proxy neuroimaging measures. Addressing this challenge requires a methodological step-change: direct comparison trials using appropriate neuroimaging tools, combined with dynamic connectivity analyses and individual-level moderator assessment. Until this methodological milestone is reached, confident prescription recommendations based on differential network effects remain premature. In this work, we outline the historical foundations and fundamental mechanisms of neural networks, and subsequently examine their adaptive responses to motor, cognitive, and combined motor–cognitive training interventions.

1.1. *Resting-state brain networks: a brief overview*

The discovery of resting-state brain networks emerged from two landmark observations. Shulman et al. identified a consistent pattern of blood flow decreases across multiple active cognitive tasks (Shulman et al., 1997), while Biswal et al. demonstrated temporally correlated spontaneous signals between bilateral sensorimotor cortices at rest (Biswal et al., 1995). Raichle, Shulman and colleagues subsequently formalized the concept of a 'default mode' of brain function, namely Default Mode Networks (DMN), referring to regions active during rest and deactivated during externally directed tasks (Raichle et al., 2001), catalyzing large-scale brain mapping initiatives including the Human Connectome Project (Van Essen et al., 2013). Today, resting-state fMRI is a standard tool for characterizing functional network organization, its disruption in aging and neurological disease, and its responsiveness to training interventions.

In addition to the DMN, these networks include the Salience Network (SN), the Central Executive Network (CEN; also termed Frontoparietal Network, FPN), and the Somatomotor Network (SMN) (Shirer et al., 2012; Yeo et al., 2011). Temporal correlations exhibit dynamic changes over time possibly induced by the environment and external stimuli, suggesting that the brain's adaptive capabilities are linked with functional connectivity. This also implies that artificially created environments that offer various types of perturbations (e.g., exergames) might be used to specifically target the brain’s adaptive capacities. Investigating neural network dynamics, from corticomuscular coupling to

large-scale cortical networks, can reveal the neurophysiological mechanisms underlying cognitive-motor performance and its decline across the lifespan (Artoni et al., 2017; Cross and Iacoboni, 2013; de Bruin et al., 2019; Gennaro and de Bruin, 2020; Petersen et al., 2012), as well as the network disruptions associated with neurological and psychiatric conditions, including stroke (Favaretto et al., 2022; Siegel et al., 2016), Parkinson's Disease (Cross et al., 2021; Roeder et al., 2020; Sparks et al., 2022), Alzheimer's Disease (Vogel et al., 2020), Huntington's disease (Pini et al., 2020), and psychiatric disorders (Zhang and Raichle, 2010).

Interestingly, brain networks seem intimately linked to the level of sport and exercise practiced. For instance, Ishihara and colleagues showed that participating earlier during childhood in sport activities can improve structural and functional aspects of the brain (Ishihara et al., 2021), and patterns of interactions within brain networks can differentiate, at a later stage, athletes from non-athletes (Gao et al., 2019). Whether similar long-term sport-related network differentiation occurs across aging and protects against age-related network decline remains an open question relevant to precision prevention strategies.

Among the major neural networks, the 'triple-network model' comprises the SN, which gates attentional switching; the DMN, involved in self-referential processing and episodic memory; and the CEN, supporting working memory, problem solving, and decision making (Bressler and Menon, 2010; Menon and Uddin, 2010). Notably relevant to motor control is the SMN, anchored in primary motor (M1) and somatosensory (S1) cortices and connected to subcortical motor circuits including the basal ganglia (Rodriguez-Sabate et al., 2019). The SMN is active during corticospinal interaction mechanisms and the efferent-afferent motor control loop underlying locomotion, as reviewed

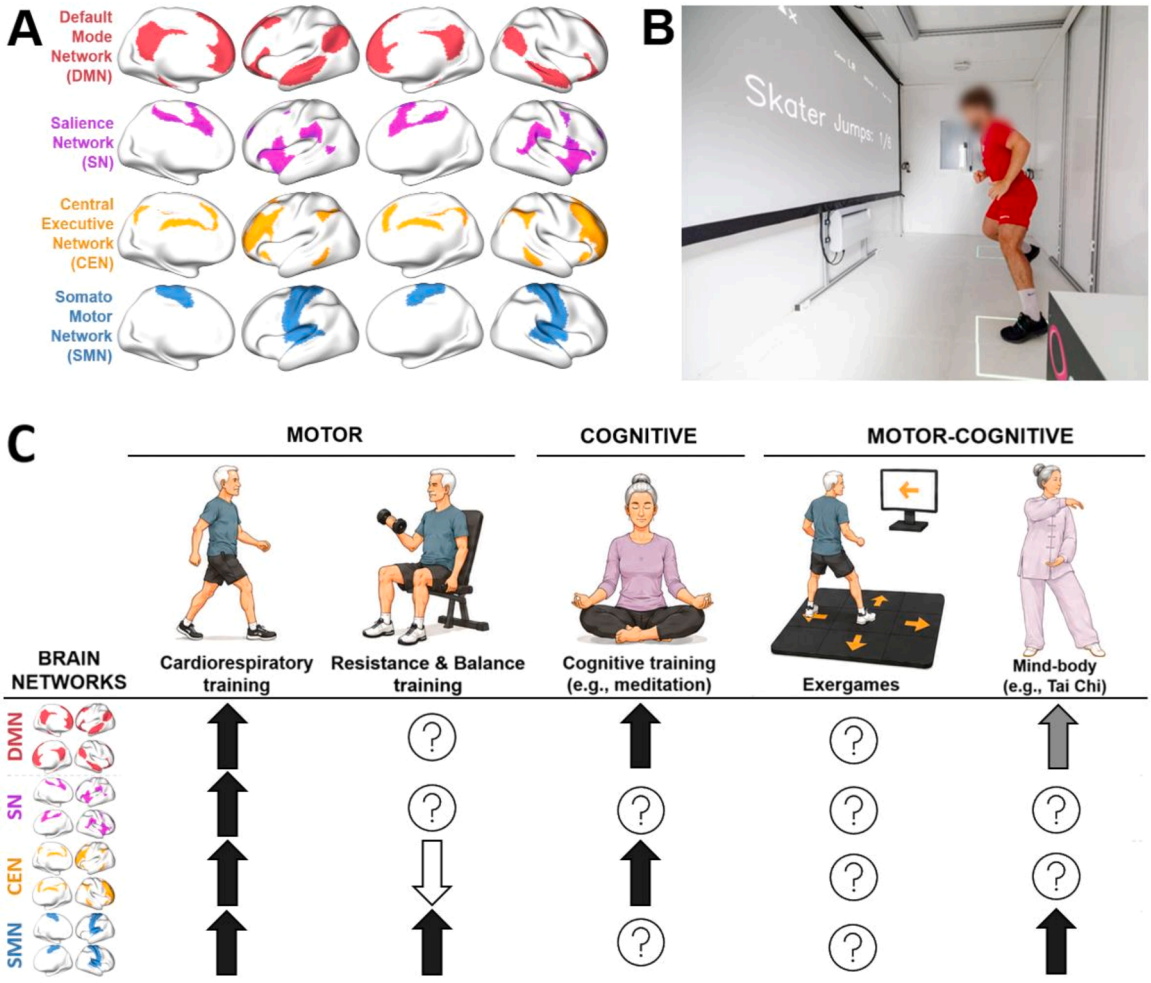


Fig. 1. (A) Large-scale resting-state brain networks reviewed in this manuscript, rendered by the authors from the study of Yeo and colleagues on the group-level seven-network parcellation (Yeo et al., 2011) (1000-subject reference solution; data obtained from the CBIG repository, https://github.com/ThomasYeoLab/CBIG). Surfaces were generated in MATLAB using FieldTrip(Oostenveld et al., 2011) to read the CIFTI parcellation file, projected onto the fs_LR 32k very-inflated cortical surface (Human Connectome Project standard mesh). Default Mode Network (DMN, red), Salience Network (SN, magenta), Central Executive Network (CEN, orange; also termed Frontoparietal Network, FPN), and Somatomotor Network (SMN, blue) are each shown across four views: left-hemisphere medial and lateral surfaces, and right-hemisphere medial and lateral surfaces. (B) Videogame-based exergame intervention suitable for both young and older adults. This image depicts one example of a step-based, cognitively enriched exergame platform and is included for illustrative purposes only; it does not constitute an endorsement of any specific system or institution. A newly developed system at the Department of Health, OST — Eastern Swiss University of Applied Sciences, St. Gallen, Switzerland. (C) Summary of the impact of different training interventions on large-scale brain networks. Arrow fill encodes evidence quality and direction of effect: solid black arrows indicate an increase supported by direct resting-state fMRI (Tier 1); solid grey arrows indicate an increase supported by indirect measures only (Tier 2: EEG, fNIRS, or behavioral outcomes); the unfilled (white) arrow indicates a decrease supported by direct resting-state fMRI (Tier 1); circled question marks indicate networks not yet directly tested for a given modality. The unfilled downward arrow (CEN, Resistance & Balance training) reflects an expertise-dependent shift from CEN-dominant to SMN-dominant processing with skill consolidation (see Section 2.1), representing a functional adaptation rather than an adverse effect. Full citations for each cell are provided in the corresponding sections of the main text and in Table 1 and Table 2. The decorative older adult figures in panel C were illustrated with the assistance of generative graphic tools.

elsewhere (Gennaro and de Bruin, 2018).

Depending on the synchronization of the spontaneous signal originating from the abovementioned neural networks, a neural network can exhibit a pattern of positive or negative signaling fluctuations correlation. Menon and Uddin (Menon and Uddin, 2010) suggested that the SN functions as a gate, regulating the recruitment of distinct neural circuits, including the DMN and the CEN. Engagement in external tasks prompts the deactivation of the DMN while activating the CEN, indicating a continuous competition for resources among these networks involved in various motor-cognitive functions. These interactions are recognized as pivotal for functional brain dynamics, facilitating resource reallocation from self-referential thought to task-related processing. Task engagement is generally characterized by activation of task-positive networks (SN/CEN for cognitive tasks, SMN for motor tasks) with concurrent and anti-correlated (task-negative) DMN deactivation reflecting competitive resource allocation(Menon and Uddin, 2010; Rodriguez-Sabate et al., 2019). Thus, the relationship between cognitive/motor performance and resting-state networks is intricate and multifaceted, as brain states can be characterized by both correlated and anticorrelated patterns linked with cognitive/motor processes (Laird et al., 2011; Liégeois et al., 2019).

All these neural networks (Fig. 1A) interact, albeit with different roles and to a different extent, leading to cognitive tasks or motor actions. The fine-tuned balance of the brain networks is critical to maintain a healthy psychophysiological system. Disruption in this within-network balance can contribute to the onset of physical, psychological and/or cognitive impairments and altered brain structures (Fjell and Walhovd, 2010; Krönke et al., 2020; Siegel et al., 2016).

Prefrontal cortical gray matter volume is a key structural determinant of executive function capacity (Yuan and Raz, 2014), consistent with the central role of the prefrontal cortex within the CEN. More intriguingly, consistent with the classic view of the DMN as a task-negative network, individual differences in pre-task DMN activation (assessed via EEG microstates) have been found to correlate with subsequent visuomotor task performance, with stronger DMN pre-activation predicting poorer performance (Penalver-Andres et al., 2022), likely reflecting greater susceptibility to internally-directed attention (e.g. mind-wandering) at the expense of external task engagement. These findings suggest that resting state large-scale brain networks as DMN, might also be (inversely) related to higher-level cognitive functions required during active and dynamic tasks. However, the relationship between sport and exercise training, both acute bouts and chronic practice, and the reorganization of large-scale brain networks remains insufficiently characterized. Clarifying these associations is essential for identifying the supraspinal neural mechanisms through which physical training shapes brain function, and for developing targeted, evidence-based interventions across both athletic and clinical populations.

Here we critically examine evidence including but not limited to experience-dependent plasticity of large-scale brain networks, in the context of motor, cognitive, and motor-cognitive training across the lifespan, with a focus on healthy aging. Evidence was evaluated according to an explicit three-tier hierarchy: (1) direct neuroimaging evidence from appropriate tools with high spatial resolution (i.e., resting-state fMRI); (2) indirect evidence from other neuroimaging and electrophysiological tools (i.e., EEG, fNIRS), as well as behavioral outcomes; and (3) conceptual frameworks, used for mechanistic contextualization only. Importantly, here, "direct" and "indirect" refer to the spatial resolution and specificity with which a method can localize network-level activity, not to the proximity of the signal to neuronal firing itself; both rs-fMRI and EEG/fNIRS ultimately index neural activity through indirect physiological proxies (BOLD and electromagnetic/hemodynamic signals, respectively).

Structural connectivity, as assessed by diffusion tensor imaging (DTI)-based white matter tractography, lies outside the scope of this synthesis and is not reviewed here. While GRADE-adapted criteria exist for clinical endpoints, applying a structured, multi-tier evidence hierarchy specifically to network-level exercise neuroimaging represents a novel methodological contribution. Practically, this framework enables researchers and clinicians to critically appraise the available evidence: Tier 1 establishes definitive network reorganization, whereas Tier 2 and Tier 3 findings identify candidate mechanisms requiring further fMRI validation before clinical translation.

2. Motor, cognitive, and motor-cognitive training: effects on neural connectivity

2.1. Motor adaptations

Evidence in this section derives primarily from rs-fMRI and structural MRI studies, providing relatively direct assessments of network-level plasticity. In older adults, performing walking activities for at least 1 year has been shown to modulate resting-state neural networks, such as DMN and CEN (Voss et al., 2010), but even 12 weeks of exercise training might be sufficient to achieve enhancements in cross-interactions across DMN and SN networks (Won et al., 2023). These effects transcend age, as exercise-induced brain connectivity adaptations are evident in both older and younger individuals, where in the former the improvements may be more pronounced due to a lower baseline of network efficiency and altered brain structure and function (Colcombe and Kramer, 2003; Fjell and Walhovd, 2010; Voss et al., 2010). Indeed, both age and cardiovascular fitness level independently contribute to resting-state connectivity strength within the CEN and DMN, with lower levels amplifying the age-related decline in network efficiency (Gust et al., 2022). Collectively, these findings underscore the coupling between network functionality and physical activity across the lifespan, although this association may vary across individuals.

Interestingly, one study recently compared expert young adult endurance athletes and age-matched non-athletes, showing that engaging in endurance training can lead to enhanced connectivity between the correlated CEN and SMN, and the anti-correlated pattern with DMN (Raichlen et al., 2016). Considering that maximal oxygen uptake (VO2max) represents one of the main physiological indexes of cardiorespiratory performance (Bassett and Howley, 2000), the abovementioned findings suggest that higher endurance intensity, and, thus, higher percentage of VO2max, may necessitate higher cognitive efforts that, in turn, may require increased neural plasticity and enhanced efficiency of large-scale functionally connected brain networks (Raichlen et al., 2016). Further evidence suggests that cardiorespiratory training, but not physical activity per se, has been associated with DMN strengthening. Whether these effects are truly superior to those induced by other training modalities, however, remains an open question addressed in Section 2.4.

Cardiorespiratory training might not be the unique target modifier for brain networks adaptations. Beyond this type of training, sport-specific skill-based activities, such as artistic gymnastics, which combines high motor complexity with both aerobic and anaerobic metabolic demands, have also been shown to modulate the functional organization of large-scale brain networks. For instance, CEN underwent neuroplastic changes in gymnasts, while increasing the inverse correlation between this neural network and SMN as a function of years of experience (Wang et al., 2016). That is, in the early stages of skill acquisition, gymnastics demands both attentional resources and motor execution linked to CEN and to SMN, respectively; however, as complex routines become consolidated through deliberate practice, motor sequences are increasingly automatized, progressively reducing the need for top-down cognitive control and shifting processing toward more efficient SMN-dominant execution (Wang et al., 2016). Balance training has similarly been associated with adaptations in motor-related network structures. For instance, a previous investigation reported that six weeks of dynamic balance training produced increases in gray matter volume and enhanced resting-state functional connectivity within the SMA and

pre-SMA, regions involved in movement preparation and sequencing within the SMN, with structural changes persisting for several months after training cessation (Taubert et al., 2011), suggesting durable consolidation of motor learning.

Critical note: Before drawing conclusions on the relative merits of each training modality, a fundamental caveat must be acknowledged. Cardiorespiratory training appears to produce broad network-level changes, yet this does not establish its superiority over other approaches. Resistance training at moderate-to-high intensity has been associated with improvements in executive-function performance and hippocampal connectivity markers (Hortobágyi et al., 2022; Wu and Huang, 2025), though this evidence derives primarily from behavioral proxies and structural MRI rather than direct resting-state functional connectivity analyses. Interestingly, the progressive shift from CEN to SMN dominance observed in expert gymnasts reflects expertise-dependent automatization rather than a general down-regulation of higher-order networks. However, firm conclusions on modality-specific superiority cannot yet be drawn in the absence of rigorously matched direct comparison trials. Notably, the reported intensity-dependent effect sizes (Hortobágyi et al., 2022) were driven primarily by young adult cohorts and did not replicate in healthy older adults or clinical populations, warranting caution when extrapolating these findings to the older adult population that is the focus of this review.

2.2. Cognitive adaptations

Evidence in this section relies predominantly on rs-fMRI and structural MRI, with some behavioral outcome data. Cognitive training has been examined in several studies to evaluate its potential effects on neural networks adaptations. For instance, a multi-domain cognitive training approach that included visuo-spatial and other cognitive domains, showed to be successful in improving the cross-interaction of functional connections across DMN and CEN (Cao et al., 2016). It should be noted that this multi-domain protocol included a physical activity component (Cao et al., 2016), precluding attribution of the observed connectivity changes solely to cognitive stimulation, which represents a methodological limitation that future trials isolating pure cognitive training should address. Studies on cognitive training have employed different intervention strategies, such as playing music. Indeed, one investigation showed that music practice may lead to structural and functional neuroplastic changes in the DMN (Fauvel et al., 2014). Another strategy might be represented by board games, which require the integration of multiple cognitive resources for problem solving. For instance, expert chess players exhibit neuroplastic modifications within the DMN compared to novices (Duan et al., 2012). Moreover, growing evidence indicates improvements in DMN in long-term meditation practitioners (Jang et al., 2011), with initial benefits of meditation already observed after 8 weeks of practice in brain regions associated with the DMN, such as the prefrontal cortex and the anterior insula (Tomasino and Fabbro, 2016). Additional studies have explored targeted cognitive stimulation protocols, such as task batteries involving semantic processing and retrieval mechanisms, demonstrating that these approaches can induce both structural plasticity and changes in functional connectivity within the DMN (De Marco et al., 2016).

Across these diverse cognitive training modalities (i.e., domain-specific protocols, music practice, board games, meditation, semantic stimulation), a consistent concept emerges: the DMN is the most reliably modulated network, reflecting its central role in internally directed processing. Modalities that impose higher executive load (e.g., multi-domain protocols or chess) tend to additionally engage the CEN, while those emphasizing sustained attention and interoception (e.g., meditation) show more heterogeneous patterns. What remains poorly characterized is whether these modality-specific patterns reflect genuinely distinct mechanisms or simply differences in task demands and study methodology, representing a limitation that applies equally to motor and motor-cognitive training research.

Critical note: Cognitive training also modulates other task-positive networks, such as the dorsal attention network (DAN) and ventral attention network (VAN), and their dynamic anti-correlations with the DMN. However, these interactions are less frequently reported than changes within the DMN and CEN (Van Balkom et al., 2020), despite being essential for understanding ecological validity.

2.3. Motor-cognitive adaptations

Evidence in this section derives largely from indirect measures, such as EEG, fNIRS, and behavioral indices of executive function, with direct rs-fMRI data remaining scarce; claims are qualified accordingly. If both isolated cognitive and physical training independently promote neuroplasticity, it is reasonable to assume that their combination may yield additive and even synergistic effects. This premise is consistent with the guided-plasticity facilitation framework (Fabel and Kempermann, 2008; Herold et al., 2018; Kempermann et al., 2010), which suggests that concurrent engagement of multiple systems enhances experience-dependent plasticity. Although studies directly linking large-scale functional network reorganization to combined motor-cognitive interventions (or exergame-based training) remain sparse, a large body of evidence provides indirect but converging support for this notion. However, we emphasize that this remains a working hypothesis. For instance, no study has directly tested the proposed BDNF-priming mechanism using neuroimaging in older humans, and support to this is currently inferred from rodent literature or dual-task behavioral paradigms in humans.

Specifically, exergame-based interventions have been associated with neuroplastic adaptations assessed through different methodologies, such as functional near-infrared spectroscopy (fNIRS), surface electroencephalography, and cognitive testing of executive functions (linked to the CEN), across a wide range of age groups (Adcock et al., 2020b, 2020a, 2019; Eggenberger et al., 2016, 2015; Eng et al., 2020; Schättin et al., 2016). Complementing this evidence, one study demonstrated that neural drive to skeletal muscles during dual-task walking is modulated following exergame training (de Bruin et al., 2019). From a functional connectivity perspective, the sensorimotor network (SMN) serves as the primary cortical hub for coordinating motor execution and processing sensory feedback during movement tasks (Gennaro and de Bruin, 2018). Thus, rather than operating in isolation, the SMN must dynamically synchronize with higher-order cognitive networks to effectively integrate these motor outputs with ongoing cognitive demands. The interplay between SMN and higher-order control systems (e.g., CEN), alongside their dynamic segregation from the DMN, represents a plausible candidate mechanism through which motor-cognitive training may drive functional adaptations, though direct rs-fMRI confirmation remains limited. Accordingly, future studies should prioritize direct assessments of functional connectivity across these networks, including their state-dependent anti-correlations, to better characterize the neural signatures of exergame-induced adaptations. Importantly, the degree of benefit is contingent on appropriate load calibration: the same shared neural architecture that enables synergy under optimal concurrent demands will produce dual-task interference when those demands are excessive, hinting towards a principle that should guide both exergame design and training prescription.

A recent systematic review and meta-analysis pooling 31 randomized controlled trials examined which training components moderate the cognitive benefits of exergame-based training in middle-aged and older adults(Manser et al., 2024). Body position emerged as a significant moderator of global cognitive outcomes, with standing, stepping-based exergames outperforming seated or weight-shifting variants. Complex attention outcomes were moderated by the type of motor-cognitive training, the training location, and how training was administered; and executive function outcomes were moderated by exercise intensity. Notably, none of the included studies reported sufficient information to

evaluate the level of concurrent cognitive demand as a moderator, so the critical load threshold at which motor-cognitive synergy transitions into interference remains uncharacterized and represents an urgent research priority for exergame dosing in older adults.

To illustrate the practical architecture of motor-cognitive interventions, exergame-based training represents one of the most studied contemporary implementations of simultaneous motor and cognitive engagement in older adults. Technological innovations, such as exergames (Fig. 1B), provide new avenues for engaging participants in simultaneous motor-cognitive training (Dove and Astell, 2017). Exergaming is defined as *"technology-driven physical activities, such as video game play, that requires participants to be physically active or exercise in order to play the game"* (Witherspoon, 2013). Videogame-based interventions offer several advantages over conventional ones, fostering both skill acquisition and neuroplastic adaptations (Kühn et al., 2014). Accordingly, exergame-based training is emerging as a promising complementary approach in older adults, though comparative superiority over traditional modalities has not been established at any level of analysis (Cai et al., 2023; Eggenberger et al., 2015; Schättin et al., 2016). Importantly, these benefits are contingent upon the use of purpose-designed exergames rather than entertainment-oriented ones. Specifically, exergames should be intentionally developed to enhance players' skills and performance, thereby aligning with the principles of so-called serious games(Manser et al., 2025).

When the overarching goal is to induce structural brain plasticity, experimental evidence demonstrates that playing commercial video games for at least two months (30 min/day) can significantly increase gray matter volume in the right hippocampal formation, right dorsolateral prefrontal cortex, and bilateral cerebellum (Kühn et al., 2014). Targeting such brain structures is essential for preserving and enhancing executive functions (e.g., working memory) and other cognitive functions, including spatial navigation and strategic planning, as well as motor performance, all of which may be particularly compromised in older adults. Thus, exergame-based training has been associated with improvements in global cognition, learning and memory, executive function, and verbal fluency in older adults with neurocognitive disorders (Cai et al., 2023), suggesting a potential role in attenuating cognitive decline in these populations. Whether such behavioral improvements reflect underlying preservation of hippocampal, prefrontal, or cerebellar structure and connectivity remains limited. While exercise generally induced fMRI-measured functional connectivity and activation adaptations across networks associated with cognition, findings on behavioral correlates remain mixed: evidence from systematic reviews indicates that improvements in the hippocampus and cingulate frequently correlate with cognitive gains, although associations between neuronal and cognitive changes are not consistently reported across studies(Xu et al., 2024). Over the past decade, significant progress has been made in the investigation of exergame-based interventions (Li et al., 2023; Swinnen et al., 2022), which have been shown to simultaneously enhance cognitive (Swinnen et al., 2022) and physical functions, particularly in complex locomotor activities such as gait, where movement is coupled with cognitively demanding secondary tasks (Eggenberger et al., 2015; Schättin et al., 2016). Current evidence supports that exergame-based training is safe, has high attendance adherence, and can improve global cognition, complex attention, and executive functions (Manser et al., 2024) in middle-aged and older adults, both with (Aminov et al., 2018; Cai et al., 2023; Chen et al., 2023; Li et al., 2023; Swinnen et al., 2022; Zhao et al., 2020) and without (Gallou-Guyot et al., 2020; Jiang et al., 2022; Torre and Temprado, 2021) clinical conditions. However, direct neuroimaging evidence linking these behavioral improvements to specific brain network changes remains scarce and represents a key gap that the present review aims to highlight. Among the design features that most reliably enhance cognitive outcomes, step-based exergames performed in a standing position appear superior to seated or weight-shifting variants (Manser et al., 2024; Manser and de Bruin, 2021). This advantage likely reflects the greater cognitive demands imposed by whole-body motor control and the higher ecological validity of stepping tasks, which share neural substrates with real-world locomotion (Artoni et al., 2017; Gennaro et al., 2020; Gennaro and de Bruin, 2020, 2018; Petersen et al., 2012), consistent with the guided-plasticity facilitation framework (Fabel and Kempermann, 2008; Herold et al., 2018; Kempermann et al., 2010), although, as noted above, this framework remains a working hypothesis rather than an established mechanism. Such motor-cognitive synergy is based on the neurophysiological evidence demonstrating that supraspinal cortical control is active throughout the entire locomotion cycle, not only at its initiation, making step-based exergames particularly effective tools for simultaneously engaging motor and higher-order cognitive neural circuits (Artoni et al., 2017; Gennaro et al., 2020; Gennaro and de Bruin, 2020, 2018; Petersen et al., 2012).

The first systematic review, specifically examining neurobiological effects of exergame interventions in older adults with and without neurocognitive disorders, found evidence of changes in brain structure and neuroplasticity, modifications in the cerebral bases of motor tasks in healthy older adults, and alterations in key regions including the DMN in participants with neurocognitive disorders, while noting that many findings await replication in adequately powered direct-neuroimaging studies (Attoh-Mensah et al., 2025).

Notably, motor-cognitive integration is not unique to modern digital environments. Long before the advent of exergames and virtual reality, several traditional practices embedded cognitive demands with motor execution. These include disciplines such as Tai Chi Chuan (Taijiquan), Baduanjin, Yoga, Chi Kung (Qi Gong), and other meditation-based practices, often collectively referred to as "mind-body" practices due to their explicit integration of cognitive and motor processes (Benson and Klipper, 1975; Esch and Stefano, 2022). Although mechanistically distinct from exergames, these practices seem to similarly engage distributed neural systems. A growing body of literature indicates that mind-body interventions can mitigate age-related motor-cognitive decline (Lam et al., 2012; Solloway et al., 2016; Sungkarat et al., 2017) and modulate functional connectivity within the DMN, although with heterogeneous patterns of reorganization (Liu et al., 2019). Furthermore, Tai Chi Chuan has been shown to differently engage the SMN compared to more conventional physical activities, such as walking (Yue et al., 2020). However, this field still lacks studies that simultaneously assess large-scale network dynamics and behavioral improvements within the same experimental framework. Recent work has begun to bridge traditional and technological approaches. For example, Tai Chi Chuan movements have been incorporated into exergame platforms (Adcock et al., 2020b, 2020a, 2019) and biofeedback-guided breathing protocols have been integrated into an interactive training environment (Manser and de Bruin, 2024, 2021). These hybrid paradigms represent a promising avenue for enhancing validity while leveraging the scalability and adaptability of digital interventions.

Critical note: Despite consistent evidence for improvements in cognitive and motor outcomes following exergame and mind–body training, direct investigations of large-scale functional network reorganization, particularly using resting-state functional connectivity (rsFC), remain strikingly scarce. Current evidence relies predominantly on proxy measures (e.g., fNIRS, EEG-derived metrics, or behavioral indices of executive function). Rigorous randomized controlled trials directly comparing exergame interventions with traditional endurance or resistance training, while controlling for dose, intensity, and duration, and incorporating dynamic rsFC and network-level metrics (e.g., integration, segregation, and temporal flexibility) are critically needed. Until randomized trials directly measuring resting-state network changes following exergame versus matched endurance training are completed, with adequate dose control, the network-level superiority of motor-cognitive approaches remains a hypothesis, not a finding. This conclusion is partially supported by Attoh-Mensah et al., who confirmed neurobiological effects of exergaming in this population while underscoring the need for stronger evidence from direct neuroimaging

paradigms (Attoh-Mensah et al., 2025).

2.4. Direct comparisons and moderating factors

The modality-specific patterns described below should be interpreted considering the methodological heterogeneity identified in our core rationale. That is, they reflect current evidence patterns rather than established differential efficacy. Few randomized controlled trials have directly compared the effects of different training modalities (i.e., cardiorespiratory, resistance, balance, cognitive and motor-cognitive training) on resting-state functional connectivity using harmonized designs (e.g., matched dose, duration, and analytical approaches). As a result, firm conclusions regarding the relative superiority of any single modality remain premature.

Nonetheless, current evidence suggests a degree of modality-specific convergence. Cardiorespiratory training appears to induce robust and widespread adaptations across large-scale networks, including DMN, CEN, SN, and SMN. At the same time, emerging data indicate that high-intensity resistance training may elicit comparable or even superior improvements in executive-control networks and hippocampal connectivity when intensity is appropriately matched, pointing to a potentially underexplored role of neuromuscular load in shaping brain plasticity. Motor-cognitive interventions, including exergames and mind-body practices, represent a promising yet still under-characterized domain. These approaches are inherently suited to probe ecologically valid brain–behavior interactions, especially through mechanisms involving SMN-DMN coupling and anti-correlations. However, the current evidence relies predominantly on indirect or proxy measures (e.g., EEG, fNIRS, behavioral indices), with a notable scarcity of gold-standard rs-fMRI investigations capable of capturing large-scale network reorganization and its temporal dynamics. Several motor-cognitive activities remain underrepresented in the literature synthesis. Table 1 provides a structured overview of the network-level adaptations documented across all training modalities reviewed, together with their key moderators and principal methodological limitations. Among the motor-cognitive activities overlooked in the direct comparison literature, dance merits particular attention. Like some mind-body practices and step-based exergames, dance integrates rhythmic coordination, spatial navigation, and social-cognitive demands, but with a uniquely simultaneous engagement of all three. Recent randomized controlled trials have demonstrated that structured dance programs produce robust within-network DMN connectivity increases and enhanced DMN–CEN functional coupling in older adults, with effect sizes in several trials exceeding those of an inactive control condition (Balazova et al., 2021), suggesting that the cognitive density embedded within complex movement, rather than physical load alone, may be a primary driver of network-level neuroplasticity. A comprehensive synthesis of this evidence was beyond the scope of the present review; however, incorporating dance as a dose-matched direct comparator alongside endurance, resistance, and exergame conditions is a priority for future systematic reviews and meta-analyses.

An emerging methodological development central to this review's core argument is dynamic functional connectivity (dFC), which captures time-varying changes in network configuration rather than static average correlations. Where static rsFC characterises the mean connectivity strength across an entire scan session, dFC metrics (e.g., sliding-window correlation variance, hidden Markov model state-switching rates, and phase-coherence dynamics) reveal how flexibly networks reconfigure over time. Evidence consistently shows that aging reduces dFC flexibility, producing a more rigid network architecture in which the brain becomes less able to transition between functional states, and this reduced flexibility correlates with poorer executive and motor performance (Liégeois et al., 2019). Critically, if structured training restores temporal network flexibility rather than solely increasing mean connectivity strength, static rsFC analyses will systematically underestimate true training effects, representing a measurement gap that partly explains the inconsistency across studies reviewed here. Future intervention studies should therefore incorporate dFC alongside static rsFC as co-primary neuroimaging endpoints.

Importantly, training-induced network adaptations are not uniform, but are strongly moderated by a range of factors (see Table 2). Among these, training intensity emerges as a primary determinant, with higher-intensity protocols generally associated with larger effect sizes and more pronounced network reconfiguration. Total dose and intervention duration are also critical, with evidence suggesting that a minimum exposure of approximately 12 weeks is required to induce stable, chronic changes in functional connectivity. Individual characteristics further shape responsiveness, including age and baseline fitness level, with larger gains typically observed in older adults or less fit individuals, consistent with greater plasticity reserves. Finally, the degree of motor–cognitive simultaneity appears to be a key, yet insufficiently isolated, variable, potentially modulating the balance between network integration and segregation. In parallel, expertise-dependent adaptations indicate a progressive shift from higher-order control (i.e. CEN-

Table 1
Summary of training modalities and neural network adaptations.

Modality	Networks Adaptations	rs-fMRI studies identified[a]	Acute vs Chronic	Key Moderators	Main Limitations
Cardiorespiratory training	DMN, CEN, SN, SMN	Won et al., (2023) Gust et al., (2022) Raichlen et al., (2016)* Voss et al., (2010)	Both[b]	Intensity, VO2max gain, age	Dose rarely matched to other modalities
Resistance & balance training	CEN–SMN reconfigurations reported, but evidence limited to skill-specific populations (i.e., gymnastics, balance)	Wang et al., (2016) Taubert et al., (2011)	Mainly chronic	Years of practice, intensity	Few rsFC studies; expertise-dependent
Cognitive only	DMN, CEN	Cao et al., (2016) De Marco et al., (2016) Fauvel et al., (2014) Jang et al., (2011)	Chronic	Task complexity	Limited real-world motor transfer
Motor-cognitive (i.e., exergames & brain-body)	SMN–DMN anti-correlation, CEN	Yue et al., (2020) (for SMN–DMN anti-correlation) Liu et al., (2019) (for CEN)	Chronic	Simultaneity, stepping	Direct rsFC data scarce; current evidence relies predominantly on indirect measures (EEG, fNIRS, behavioral).

*Study conducted in young adult endurance athletes; included to illustrate the VO2max–related network efficiency mechanism

[a] Direct rs-fMRI studies (Tier 1 evidence) cited for this modality in the main text; studies relying exclusively on EEG, fNIRS, or behavioural proxies are discussed in the main text but not listed here.

[b] Acute effects are primarily neuroendocrine (e.g., BDNF elevation, increased cerebral blood flow); chronic effects reflect structural and connectivity-level reorganization. These mechanisms are distinct and should not be conflated

Table 2
Moderators of training-induced brain network plasticity.

Moderator	Effect on Neuroplasticity	Evidence Level
Training intensity	• High > low (larger effect sizes g = 0.40 vs 0.19)[a,b]	Moderate
Dose & duration	• ≥ 12 weeks for conventional endurance/resistance training; motor-cognitive/exergame training may show cognitive effects with shorter exposure when task complexity is high[c]	Low-Moderate to Strong*
Age & baseline fitness	• Stronger gains in older/lower-fitness individuals	Moderate
Motor-cognitive simultaneity	• Proposed synergistic effects within ~60-min post-exercise BDNF window[d]	Low–Moderate
Expertise level	• Shifts reliance from CEN to SMN in athletes	Moderate
Training Type	• Cardiorespiratory training produces global network-level changes (DMN, CEN, SN, SMN); • skill-based and motor-cognitive training produces more circuit-specific adaptations	N/A

Evidence levels: Strong = replicated rs-fMRI findings across multiple independent intervention samples; Moderate = consistent indirect or mixed evidence (EEG, fNIRS, behavioral, or limited rs-fMRI); Low–Moderate = evidence primarily indirect with no direct rs-fMRI support; N/A = insufficient data to classify

[a] **Note:** for exergame-based training, motor-cognitive task complexity may partially substitute for physical intensity in driving neuroplastic outcomes.

[b] Effect sizes reported in previous work (Hortobágyi et al., 2022). These values apply to conventional endurance/resistance training; effect size data for exergame-based training under varying intensity-complexity conditions are not yet available from direct rs-fMRI studies.

[c] Based on previous literature (Manser et al., 2024; Voss et al., 2010; Won et al., 2023), head-to-head comparison of minimum effective duration across modalities has not been established in older adults using direct rs-fMRI endpoints. *Low-moderate to strong evidence level, for exergames and conventional training, respectively.

[d] The ~60-minute post-exercise BDNF window is an approximation based on animal and exercise-physiology literature (Ferris et al., 2007), precise duration varies with exercise intensity, modality, and individual factors. This requires further empirical confirmation in older adult populations specifically

dominant processing) toward more efficient, automatized sensorimotor processing (i.e. SMN dominance), as exemplified in highly trained populations such as gymnasts.

2.5. Clinical implications: from healthy aging to cognitive decline

The training-induced network adaptations described in the above sections carry specific implications for aging populations and individuals with or at risk of neurocognitive disorders. Disruptions of resting-state network integrity, particularly reduced DMN connectivity, impaired CEN–SMN coupling, and diminished triple-network balance, are among the earliest neuroimaging biomarkers of pathological cognitive aging, preceding clinical symptom onset by years (Fjell and Walhovd, 2010; Rodriguez-Sabate et al., 2019). If structured training can modulate these same networks, even partially, this opens a mechanistic rationale for exercise as a neuroprotective strategy targeting early-stage neural networks vulnerability.

Available evidence is most consistent for cardiorespiratory training in healthy older adults, where DMN and CEN connectivity improvements have been reported following interventions of ≥ 12 weeks (Voss et al., 2010; Won et al., 2023). Motor-cognitive training, including exergaming, has shown promising behavioral effects in MCI and early dementia in older populations (Cai et al., 2023; Manser and de Bruin, 2024; Swinnen et al., 2022), with further confirmation of neurobiological changes by recent works (Attoh-Mensah et al., 2025), including DMN alterations in older adults with neurocognitive disorders following exergame interventions, while underscoring the need for stronger validation.

Critically, the magnitude and durability of network-level training effects in clinical aging populations likely depend on disease stage, residual plasticity capacity, genetic moderators, such as APOE ε4 and BDNF Val66Met, and/or baseline functional brain connectivity. The BDNF Val66Met polymorphism warrants specific mention. In fact, Met allele carriers exhibit attenuated activity-dependent BDNF secretion, potentially blunting the neuroplastic response to physical training and constituting a major source of the inter-individual variability in the exercise-BDNF-plasticity axis (Brown et al., 2014) described throughout this review. These individual-level factors are rarely assessed in existing trials, limiting the generalizability of current evidence. Among these underexamined moderators, biological sex warrants dedicated attention. Evidence indicates that aging trajectories in resting-state network connectivity differ between males and females: women show a regionally dissociated pattern of DMN connectivity change relative to men, with an increased posterior DMN connectivity alongside a decreased medial-prefrontal connectivity, that is most pronounced around the menopausal transition (Ficek-Tani et al., 2023). This divergence has been mechanistically linked to the decline in estrogen-mediated synaptic and neuroprotective signaling that accompanies menopause (Hara et al., 2015). Whether training-induced connectivity changes in the DMN and CEN differ in magnitude by sex, and whether postmenopausal women show heightened responsiveness to cardiorespiratory interventions targeting DMN connectivity, remain unknown. Addressing these gaps through sex-stratified secondary analyses of existing trials and prospectively designed, sex-balanced RCTs is a priority for future research. These sex- and genotype-specific connectivity patterns highlight important avenues for future research, suggesting that precision-medicine frameworks may eventually need to account for biological sex and genetic variation, once validated in prospective clinical trials. Future research should prioritize stratified trial designs that match training modality and dose to individual network profiles, moving toward a precision medicine framework for exercise-based neuroprotection in aging.

3. Conclusion and critical synthesis

Taken together, the evidence discussed across the above sections supports three integrative conclusions. First, cardiorespiratory training holds the strongest and most replicated direct rs-fMRI evidence base, with consistent effects across the DMN, CEN, SN, and SMN; yet even this modality lacks dose-matched direct comparison against alternatives. Second, the apparent modality-specificity of network effects is very likely a methodological artefact. That is, the near-exclusive reliance on proxy measures for motor-cognitive and cognitive-only conditions, combined with the absence of harmonized experimental study designs, limits mechanistic interpretation of the observed differences. Third, as synthesized in Fig. 1C, the evidence landscape is asymmetric. In fact, what looks like differential network specificity across modalities largely reflects differential methodological aspects, rather than differential neurophysiological underpinnings. Fig. 1C illustrates how the evidence base varies across modalities, providing a clear overview of both the field's maturity and the critical empirical gaps that remain. Despite growing interest in the field, several critical gaps persist. There is a striking paucity of randomized controlled trials directly comparing training modalities under rigorously matched conditions (i.e., dose, intensity, and duration), and even fewer studies incorporating static vs dynamic functional connectivity metrics. Moreover, the long-term durability (>12 months) of training-induced adaptations and their transfer to ecologically valid motor and cognitive performance have rarely been investigated using direct neuroimaging endpoints.

Inter-individual variability represents another major limitation. Key moderators (genetics, biological sex, psychological factors, and baseline network efficiency) are rarely systematically assessed, limiting the development of personalized training prescriptions and protocols. In

addition, the relationship between acute and chronic effects remains poorly understood; specifically, it remains unclear how transient neuroendocrine responses to exercise translate into stable, large-scale network reorganization. This question requires systematic investigation, particularly in older adults at varying stages of cognitive reserve depletion.

Within this context, the guided-plasticity facilitation framework (Fabel and Kempermann, 2008; Herold et al., 2018) offers a theoretically coherent, but still hypothesis-level, interpretative model for the hypothesized additive benefits of combined motor–cognitive training. According to this model, exercise-induced neurobiological priming, hypothesized to involve BDNF among other factors, may create a transient window of heightened plasticity, during which concurrent cognitive engagement can more effectively guide network reorganization. Meta-analytic evidence provides support for this framework, particularly in individuals with neurocognitive disorders. However, several important caveats must be acknowledged.

Synergistic effects appear to be temporally constrained, with optimal benefits occurring within a limited post-exercise window (approximately 60 min). Furthermore, adherence may decline when dual-task demands become excessively complex, and benefits tend to be more robust in clinical populations than in healthy individuals. Critically, very few studies have adequately controlled for total training dose or disentangled the relative contributions of physiological facilitation versus cognitive guidance. As such, claims regarding the universal superiority of motor–cognitive interventions in improving functional brain connectivity should be interpreted with caution.

In summary, while experience-dependent plasticity of large-scale brain networks is robustly supported across multiple training modalities, the field must now shift from descriptive, modality-specific approaches toward mechanistically driven, comparative, and dynamic frameworks. Future research should prioritize rigorously controlled designs, time-resolved connectivity analyses, and the identification of individual moderators. Such advances will be essential for optimizing training interventions, from healthy aging to early intervention in individuals at risk of neurocognitive disorders and may extend to athletic populations as a performance optimization tool, though this remains secondary to the neuroprotective applications prioritized here. A specific priority is to characterize the load–response curve for motor–cognitive simultaneity, establishing at what intensity and complexity the transition from synergy to interference occurs within shared neural networks, which will be essential for optimal training prescription in both healthy and clinical populations. This review extends and integrates prior work on exergame training components (Manser et al., 2024) and training intensity effects on neuroplasticity markers (Hortobágyi et al., 2022), and addresses the network-level mechanistic gap identified by previous work (Attoh-Mensah et al., 2025), that confirmed neurobiological effects of exergaming in older adults but found direct network-level evidence to be critically absent. By systematically applying our proposed evidence hierarchy, future research can move beyond heterogeneous proxy measures and design targeted Tier 1 trials that directly verify how specific training modalities reshape large-scale networks. For the field of aging neuroscience, the most consequential next step is to establish whether resting-state network profiles, measured non-invasively and at low cost, can serve as stratification biomarkers for personalized exercise prescription in older adults at risk of neurocognitive decline.

CRediT authorship contribution statement

FG: Conceptualization, Writing – Original Draft, Visualization. LP, MC, EdB, PM, TM, MB, AP: Writing – Review & Editing. All authors read and approved the final version of the manuscript.

Declarations

The individual's identity in Fig. 1B has been anonymized via facial blurring; no other identifying features are visible. The decorative older adult figures in Fig. 1C were illustrated with the assistance of generative graphic tools.

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