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From Disease To Health: Physical Therapy Health Promotion Practices for Secondary Prevention in Adult and Pediatric Neurologic Populations

Lori Quinn, EdD, PT and
Department of Biobehavioral Sciences, Teachers College, Columbia University

Don Morgan, PhD
Department of Health and Human Performance, Middle Tennessee State University

Abstract

Background and Purpose—Over the last decade there has been a substantial increase in efforts to better understand how targeted physical activity and exercise interventions can be used to minimize secondary consequences arising from neurological damage in both adult and pediatric populations. This paper overviews contemporary research that address mediators of functional and neuroplastic adaptations to physical activity and exercise, and seeks to highlight the important role that physical therapists can play to increase participation and improve well-being in adults and children with neurological disorders. We further highlight potential strategies to foster translation of evidence-based findings for use by clinicians and consumers.

Summary of Key Points—Engagement in physical activity can serve as a powerful promoter of health and well-being in adults and youth with neurologic disease, and may have the potential to alter the course of disease processes. Physical therapists can play a key role in promoting fitness and wellness by encouraging active living, providing early diagnosis of disease and prescribing targeted activity interventions to improve fitness and participation and helping individuals overcome personal and environmental barriers to an active lifestyle.

Recommendations for Clinical Practice—Physical therapists must adopt a model of rehabilitation that emphasizes secondary prevention in adults and youth with neurological diseases. Physical therapists can play a unique role in developing forward-thinking approaches in using innovative health and wellness strategies to promote positive changes in activity and exercise behaviors.

Health promotion and secondary prevention in adult neurologic populations

Dr. Robert Butler, founding director of the National Institute on Aging, National Institutes of Health has said “if exercise could be packaged into a pill it would be the single most widely prescribed and beneficial medicine in the nation”. Over the past decade, there has been

Corresponding author: Lori Quinn, EdD, PT, Associate Professor, Department of Biobehavioral Sciences 525 West 120th St. Box 199, Teachers College, Columbia University New York, NY 10027.

substantial research aimed at understanding the beneficial effects of physical activity and exercise in the general population, as well as in adults and children with a range of diseases and disorders. In adults with chronic diseases such as diabetes and heart disease exercise interventions have similar, if not potentially better, outcomes compared to drug interventions.[1] Aerobic exercise and multi-modal exercise interventions are well known for their effect on cardiorespiratory fitness, muscle strength, depression and cognition[2]. There is also increasing acceptance of the potential that exercise may have in achieving disease modification in neurological conditions due to its positive influence on brain function and health[3,4]. In adults with neurological conditions, exercise and physical activity have been shown to have the potential both to decrease risk of disease onset,[5–7] and to improve motor and cognitive function and quality of life.[8–16] The concept of “living well” with chronic diseases has never been as possible as it is today.

Neuroplasticity and disease progression

Early intervention is key to successful implementation of lifestyle strategies such as exercise. An important component of this implementation requires therapists to understand the natural course of diseases. Figure 1[17] illustrates the clinical progression of Huntington's disease (HD), a neurodegenerative disease predominantly affecting the medium spiny neurons of the striatum and resulting in a triad of mobility, cognitive, and behavioral symptoms. The neurodegenerative pathway is similar to many other diseases, however it has the advantage of being a genetic disease with 100% penetrance, meaning that individuals can know with complete certainty if they have the gene that causes HD. Disease progression starts at the earliest presymptomatic stage, where overt clinical signs are not yet present but degenerative changes in the brain are evident up to 10 years before age of onset[18], progressing to prodromal stage, where neuronal loss occurs but overt clinical signs may be subtle, followed by early, moderate and advanced clinical stages, where significant impairments and activity limitations emerge and worsen over time.

While primary prevention of neurodegenerative diseases is most urgently needed, delaying disease onset, even by several years, or slowing disease progression can significantly impact functional abilities and quality of life. Intervention in the earliest stages of the disease, either at or prior to diagnosis, may have the greatest potential to slow progression of neurodegenerative diseases such as Parkinson disease (PD), multiple sclerosis (MS) and Huntington disease (HD).

Physical activity

Physical activity refers to movements of the body that use energy, and can encompass a range of everyday activities including walking, gardening, and climbing stairs, but also includes specific forms of sport or exercise, such as playing soccer, running on a treadmill, or doing Pilates or yoga. There is increasing evidence that physical activity has the potential to prevent or delay the onset of certain neurodegenerative diseases such as Alzheimer's disease (AD), PD and dementia.[5–7] Physical activity levels may help to drive compensatory neural networks in individuals with neurological diseases and disorders,[19–21] that may in turn compensate for the failing brain and alter disease trajectories. Physical activity has been shown to reduce the risk of developing Alzheimer's disease by up to 45%.[6] Furthermore, a study of over 1,700 elderly individuals reported an incidence of dementia of 13.0 per 1000 person-years for those who exercised three or more times per week (≥15 min/session of walking, cycling, swimming, aerobics, strength training, stretching, or other activities) compared with 19.7 per 1,000 person-years for those who exercised fewer than three times per week.[22] Similarly in PD, studies have provided preliminary evidence that low levels of physical activity and exercise may contribute to an increased lifetime risk of PD.[5,23]

Despite the evidence in support of exercise and physical activity in adult neurologic populations, exercise uptake is not consistent[11,24,25] and is limited by significant barriers.[26–28] These include individual safety and fear of falling, low outcome expectation from exercise, lack of time to exercise, and the location at which exercising takes place.[26–28] The American College of Sports Medicine (ACSM) current guidelines recommend the four key components of aerobic, resistance, flexibility and neuromotor for maintaining cardiorespiratory, musculoskeletal and neuromotor fitness in apparently healthy adults.[29] The ACSM recommends moderate intensity cardiorespiratory exercise training for at least 30 minutes or more per day on 5 days per week and for a total of 150 minutes, vigorous-intensity cardiorespiratory exercise training for at least 20 minutes per day on 3 days per week (≥75 min/wk), or a combination of moderate and vigorous intensity exercise to achieve a total energy expenditure of 500–1000 MET min per week. Resistance exercises should be performed for each of the major muscle groups 2-3 days per week; neuromotor exercise involving balance, agility, coordination, and flexibility exercises of each the major muscle–tendon groups (a total of 60 s per exercise) should be performed 2 days per week. While there are no specific guidelines for individuals with neurologic conditions, the evidence in support of aerobic[10,13,15,30–34] and strengthening[8,35,36] exercises in these populations suggests that these recommendations can and should be applied to patients with neurological conditions.

Physical therapists must take an active role in implementing strategies to facilitate exercise uptake, ideally from early in the disease process. There has been a substantial number of programs developed in the last 10 years with the aim of increasing levels of physical activity through coaching and behavioral change interventions in individuals with neurological diseases. Programs such as the LIFE program in the UK[37], the Blue Prescription for MS in New Zealand[38,39], ParkFIT for PD in the Netherlands[40,41], and Engage-HD for people with HD in the UK[42,43] have used similar models of behavioral change interventions, grounded in theoretical constructs to facilitate uptake and adherence. While these studies are not without their limitations, they provide initial guidance for therapists to begin implementing similar coaching strategies, as well as providing important foundations for future research in this area.

In order for such programs to be widely implemented and translated into clinical practice, detailed information about protocol implementation, therapist training, outcome measures and costs are needed.[43] Speelman et al.[40] have suggested that specific training for therapists should include education on behavior change theories and concrete and specific examples of exercise goals. Keys to successful physical activity interventions include incorporating personalized programs that consider disease pathophysiology, current stage or movement-system classification,[44,45] and the individualized needs and personal preferences of the patient and their family. For a patient with PD, for example, consideration of the stage of disease (e.g. Hoehn and Yahr scale) and motor phenotype (e.g. tremor-predominant, akinetic-rigid, postural-instability with gait-disorder) would affect the intervention focus. Further consideration of work status, home situation and personal preferences for exercise would further shape the intervention strategy. Additional research to understand disease-specific issues, including understanding of comorbidities, impact of cognitive dysfunction and strategies to address lack of motivation and apathy is needed.[40]

Aerobic and strengthening exercise interventions

In contrast to physical activity interventions, which aim to increase general levels of activity across a range of activity intensities, exercise interventions evaluate programs with a defined prescription of mode, intensity, frequency and duration. Exercise research in dementias[16,15], Parkinson disease[21], multiple sclerosis[10], Alzheimer disease[14], mild cognitive impairment[46] and Huntington disease[12,13] has received considerable attention and yielded positive outcomes in terms of motor symptoms, behavior and quality of life. Importantly, exercise appears to have significant impact on cognitive function as well. In a recent meta-analysis, Groot et al[15] reported that aerobic exercise, but not non-aerobic exercise, positively influenced cognitive function, and this effect was independent of the clinical diagnosis (e.g. AD versus non-AD dementia) and the frequency of exercise.

Preliminary research has further indicated that exercise, particularly aerobic exercise, has the potential to drive neuroplasticity changes.[47] In PD, for example, studies have suggested that targeted exercise can increase levels of corticomotor excitability,[48] weaken the overactive indirect striatal pathway DA-D2R expression levels of brain[49] as well as increase levels of brain derived neurotrophic factor.[50] Interest in exercise-induced neuroplasticity has largely been driven by animal research. Studies in HD mouse models,[6] for example, have demonstrated that sustained wheel running reduced gross anatomical neuropathology associated motor and cognitive decline, and wheel running from an early age delayed the onset of specific motor symptoms.[51,52] Continued research to further elucidate the potential mechanisms by which exercise exerts its effects will promote a better understanding of exercise response and inform future trials, which can ultimately promote personalized approaches to management of neurodegenerative diseases.

Intensive motor training

Intensive motor training and targeted, task-specific therapeutic exercise interventions present an exciting, transformative area of research in neurodegenerative diseases.[21] This is particularly relevant for those individuals in the early stages of the disease when neuronal dysfunction and other neurobiological abnormalities may still be to some extent reversible.[53] Addressing motor impairments in neurodegeneration may provide a long-term beneficial effect in delaying disease progression and maximizing functional abilities over a longer period. Directed motor training paradigms have been successfully implemented in patients with PD.[54] Frazzitta et al[54–56] conducted a randomized controlled trial to evaluate an inpatient, intensive rehabilitation program in patients with early stage PD, who were also being treated with rasagiline monotherapy. The authors reported a 14% increase in BDNF serum levels, improvements in all secondary outcomes (including Timed Up and Go and 6 minute walk test), and a delay in the need for increasing drug treatment across the course of the disease. Such intensive interventions, provided in the early stages of neurodegenerative diseases, have the potential to be used in combination with disease-modifying drugs, cell replacement therapy or genetic manipulations, when available, to maximize the functional benefits of these interventions by facilitating adaptive neuroplasticity.[57,58]

A model for secondary prevention in neurological conditions: a paradigm shift

The mounting evidence in support of exercise as a powerful neuroprotective tool in neurological diseases and disorders offers an exciting opportunity for physical therapists to utilize their unique skills to facilitate exercise adherence and uptake throughout the course of a lifespan of an individual with a neurologic disease. With our indepth knowledge of both disease pathophysiology, directed motor training and exercise prescription, physical therapists are uniquely qualified to be in the forefront of delivering exercise and physical activity interventions.

In adult neurologic populations, particularly in neurodegenerative diseases such as PD, HD, and MS, a secondary prevention management strategy is needed to facilitate exercise uptake and adherence from the very earliest time period. Exercise interventions have the potential to delay the onset or slow the progression of disease by specifically targeting neuroprotective mechanisms within the central nervous system, including facilitating synaptogenosis, neurogenesis and neurotransmitter synthesis (e.g. dopamine)[21,30,59] (see Figure 2). As such, the traditional role of rehabilitation services to provide an episode of care roughly 6-8 weeks, discharging with a home exercise program and re-evaluating only if there is a significant change or decline in function must be reconsidered.

A model of rehabilitation that emphasizes secondary prevention in neurodegenerative diseases, such as that proposed in PD and MS[60], is urgently needed. Indeed many therapists already work in such a way intuitively, particularly those who are part of interdisciplinary clinics, however it is not being implemented consistently. Such a model would provide a framework for management over the lifespan of neurodegenerative diseases, starting first with assessment upon diagnosis to establish baseline status and identify key impairments and activity limitations. Therapists would provide ongoing consultation with follow-up visits scheduled regularly, similar to doctor's visits, to facilitate exercise adherence, identify changes in functional abilities and collaborate on setting new goals as needed.[60] Therapists may take on a more coaching and advisory role over the course of the disease, importantly incorporating behavioural interventions to facilitate exercise adherence and uptake.

Health promotion and secondary prevention in pediatric neurologic populations

Reduced physical activity levels in youth with neurologic disease (ND) can lead to a cycle of deconditioning, further inactivity, diminished physical function, and reduction in overall health status.[61-64] In addition, obesity rates in youth with disabilities are 38% higher compared to age-matched children who are not disabled.[65] Overweight and obese youth are also more likely to become obese adults[66] and excessive weight gain in young people with

ND can increase cardiovascular and metabolic disease risk and lead to a number of secondary conditions, including mobility limitations, fatigue, pain depression, and social isolation.[67-75] Because physical activity tracks from childhood and adolescence into adulthood at moderate to high levels,[76] young people with ND should be encouraged to develop, engage in, and maintain active living behaviors and limit participation in sedentary behaviors. Efforts to identify the presence of ‘exercise deficit disorder’[77] in youth with ND and reduce the onset and progression of early-stage lifestyle disease by creating opportunities to engage in health-producing physical activity should be aggressively promoted to positively impact future health outcomes.

Physical Activity Levels in Youth with ND

Indirect (e.g., surveys, questionnaires) and direct (e.g., StepWatch Activity Monitor (SAM), ActiGraph and RT3 accelerometers, SenseWear Armband, doubly-labelled water) methods of quantifying physical activity have consistently shown that youth with ND are not as physically active as typically-developing peers. Quantitative assessment of physical activity levels and patterns has revealed that children and adolescents with cerebral palsy (CP) and other neuromuscular impairments take fewer daily steps in free-living settings, spend a lower percentage of time being active, engage in a higher percentage of time in low-intensity activity and a lower absolute and percentage of time in moderate-to-vigorous physical activity (MVPA), exhibit a lower relative total energy expenditure, perceive themselves to be less fit, and report a greater number of perceived limitations in the types or amount of physical activities they can perform compared to young people without ND.[78-91]

A review of electronic databases indicates that children and adolescents with CP are 13% to 53% less active than their peers and physical activity levels are approximately 30% lower compared to existing guidelines.[92] In addition, findings from a systematic review demonstrated that in children with CP, increased habitual physical activity is positively associated with higher motor capacity as reflected by Gross Motor Function Classification Scale (GMFCS) levels.[93] Results from a limited number of studies have also shown that in youth with CP, (1) fundamental movement skill is positively related to time spent in MVPA, (2) boys are more active than girls, (3) activity levels are higher on weekdays than weekends, and (4) a minimum of six (GMFCS I), five (GMFCS II), and four (GMFCS III) days of activity monitoring is sufficient to acquire reliable step count data, as measured by the SAM. [84-85,87,94]

Sedentary Behavior

Sedentary behavior, defined as any waking activity characterized by very low levels of energy expenditure (< 1.5 METS) and performed in a sitting or reclining position,[95-96] tracks during childhood and adolescence and into adulthood at moderate levels similar to, or slightly larger than, those observed for physical activity.[97] Excessive sedentary behavior, and especially screen-based sedentary activity, is independently associated with adiposity and cardiometabolic disease risk in children and youth.[98] No evidence-based guidelines have been established for limiting general sedentary activity, but current recommendations suggest that young people should avoid extended periods (> 2 hours) of screen time.[99]

A paucity of research exists describing sedentary behavior in youth with ND.[64] Analysis of survey and questionnaire data have produced conflicting findings, with one study indicating that adolescents with physical disabilities are two times more likely to watch television and play video and computer games for extended periods on school days[80] and another reporting little difference in weekly recreational screen time between youth with CP and typically-developing peers and no association between sedentary activity and gross motor function, age, and activity level.[81] In contrast, data from studies employing accelerometry revealed that when compared to able-bodied peers, absolute and relative sedentary time is greater in children with CP and adolescents with CP accumulate more sedentary time and display fewer interruptions in sedentary behaviors.[87,100]

Health-Related Fitness

Health-related fitness (HRF) is comprised of cardiorespiratory, muscular, morphological, metabolic, and motor components.[101] Based on plausible causal pathways, a bidirectional association exists between physical activity and HRF.[101] Compared to typically-developing children, clusters of cardiorespiratory (CR), metabolic and biomechanical (MB), and neuromuscular (NM) variables measured in youth with CP (GMFCS I - II) were 25% to 60% below values for age- and sex-matched peers.[102] A comprehensive review of published studies indicates that cardiorespiratory endurance, muscle strength, and anaerobic fitness are lower in children with CP (GMFCS I-III) compared to typically-developing youth and responsive to various training regimens featuring different activity modes and dosages, although the extent to which fitness improvements are sustained following training is less clear.[103] In an 8-month randomized controlled trial (RCT) of sequential aerobic and anaerobic training in youth with CP (GMFCS I-II), increases of 20% to 38% occurred in aerobic (20%) and anaerobic (25%) capacity, lower-extremity muscle strength (20-23%), and agility (15%), and these gains in HRF were maintained, to some extent, four months after training ended.[104]

The use of various modes, types, and combinations of activity interventions has led to generally positive effects on HRF in youth with CP.[103] In an 8-week RCT, internet-based lifestyle activity intervention for adolescents with CP (GMFCS I-III), a non-significant trend for improvement in physical activity was noted[105] and a 6-month physical activity stimulation program consisting of counseling, fitness training, and home-based physiotherapy did not alter physical activity, mobility capacity, walking capacity and functional muscle strength, or fitness in children with CP (GMFCS I-III).[106] In contrast, a 6-month lifestyle intervention featuring supervised physical fitness training and counseling sessions was effective in improving cardiopulmonary fitness and body composition in adolescents and young adults with CP (GMFCS I-IV)[107] and a 9-week functional circuit training program increased aerobic endurance, walking distance, and ambulation in children with CP (GMFCS I-II).[108] Better arm-cranking metabolic economy, higher maximal aerobic power, and increased GMFM scores in youth with spastic diplegia were also detected after 12 weeks of combined aerobic interval and strength training[109] and a recent systematic review found that whole-body vibration resulted in better standing function, greater femur bone density, and increased gait speed in children with CP (GMFCS I-IV).[110]

Data from a trio of studies featuring young and very young children with CP (GMFCS I-IV) have shown that prolonged, moderate-to-intense, land-based treadmill training, performed with or without body support, lasting four to seven weeks, and occurring in either clinic- or home-based settings, produced gains in mobility, gross motor function, and accelerated the onset of walking skills while reducing support needed during walking.[111-113] A 10-week RCT featuring underwater treadmill training in youth with CP (GMFCS I-II) also led to faster preferred and maximal walking speeds and more distance covered during a 5-minute overground walk.[114]

Future Directions

As the use of accelerometers becomes an increasingly common method of quantifying childhood physical activity, it is essential that youth-specific calibration equations and associated cutpoint thresholds for sedentary, light, moderate, and vigorous physical activity are validated against criterion assessments of energy expenditure or activity assessment for the population being evaluated.[115-116] This is especially important when using published accelerometer equations and cutpoint values to quantify physical activity behavior in young people with CP, because their increased locomotor energy demands compared to typically-developing youth[117-118] may lead to an underestimation of MVPA.[93,115] In this regard, recent studies involving ambulatory youth with CP (GMFCS I – III) have demonstrated good concurrent validity between accelerometry data and indirect calorimetry while performing standardized physical activities of varying intensity[119] and shown that GMFCS-specific intensity-based cutpoint thresholds produce more accurate assessments of MVPA levels compared to previously published cutpoint values.[120]

One limitation of using accelerometry to document physical activity levels is that accelerometer-derived energy expenditure values obtained during non step-based activity (e.g., cycling, weight-training, swimming) may be inaccurate.[121] Another limitation of accelerometers is their inability to identify the types of activities being performed and the location and context of physical activity participation. One alternative to relying solely on accelerometry to measure physical activity levels is to combine the use of accelerometers with direct observation systems (e.g., SOPLAY, SOPARC, ORSAC)[122] or global positioning system devices[123] to provide a richer and fuller description of physical activity and enable interventions to be customized to specific domains and related subdomains of childhood activity participation.[123]

Given the link between fundamental movement skills and physical activity in children with CP,[87] efforts should be undertaken to develop motor skill ability and proficiency in rehabilitation and school physical education programs. Longitudinal research examining the influence of age, sex, and GMFCS levels on the natural history of physical activity during childhood and adolescence should also be conducted and greater attention should be focused on measuring physical activity and promoting physical activity participation in preschoolers with ND, especially in light of current trends signaling a higher prevalence of overweight and obesity in children aged 2 to 5 years.[66]

More studies featuring accelerometry-based monitoring are needed to better characterize habitual sedentary activity of young people with ND, define what is meant by excessive sedentary time, determine the effects of reducing sedentary behaviors on HRF, and describe the physiological and health effects of prolonged sitting. From a measurement perspective, research should be conducted to identify the types of sedentary behavior that children are engaged in and quantify the amount of time spent in sedentary activities, frequency of breaks in daily sedentary behavior, and within- and between-day variability in sedentary behaviors. The impact of substituting light physical activity (e.g., standing[124]) for sedentary behaviors and the combined influence of reducing sedentary activity and increasing physical activity on HRF in youth with ND is another issue worth exploring.

While cardiorespiratory endurance and muscle strength can be improved in youth with CP, relatively little is known regarding the trainability of anaerobic fitness, a key factor limiting motor ability in youth with this neurological condition.[125] Continued emphasis should be placed on documenting the effectiveness of new and innovative exercise interventions on HRF and exploring ways of combining training modes and intervention approaches that are age-appropriate and suitable for children and adolescents with differing levels of gross motor function. In addition, concerted efforts should be made to translate physical activity and exercise interventions which have proven successful in laboratory settings for use by therapists in clinical and community settings. Ongoing evaluation of the clinimetric properties of laboratory- and field-based fitness tests in youth with physical disabilities[126] is a high priority that has the potential to lead to standardized testing and evaluation of the impact of activity and exercise on participation in daily life. Further work should also be performed to assess (1) the unique and combined influence of aerobic exercise and strength training on reducing excess body weight and preventing unhealthy changes in body composition, (2) the extent to which HRF tracks from childhood into adolescence and from adolescence into adulthood, and (3) the nature of the dose-response relationship between volume of physical activity and specific HRF components and how this relationship is moderated by factors such as age, sex, and biological maturation.

Summary

Regular engagement in physical activity can serve as a powerful strategy to promote health and well-being in adults and youth with neurologic disease. Accurate and reliable measurement of physical activity and ongoing monitoring, improvement, and maintenance of health-related fitness can help individuals with physical disabilities achieve optimal physical function. Physical therapists must play a key role in promoting fitness and wellness by encouraging active living, providing early diagnosis of disease, and prescribing targeted activity interventions to improve fitness and participation, connecting individuals to community-based activity programs and resources, and helping persons of all ages overcome personal and environmental barriers to a physically-active lifestyle.

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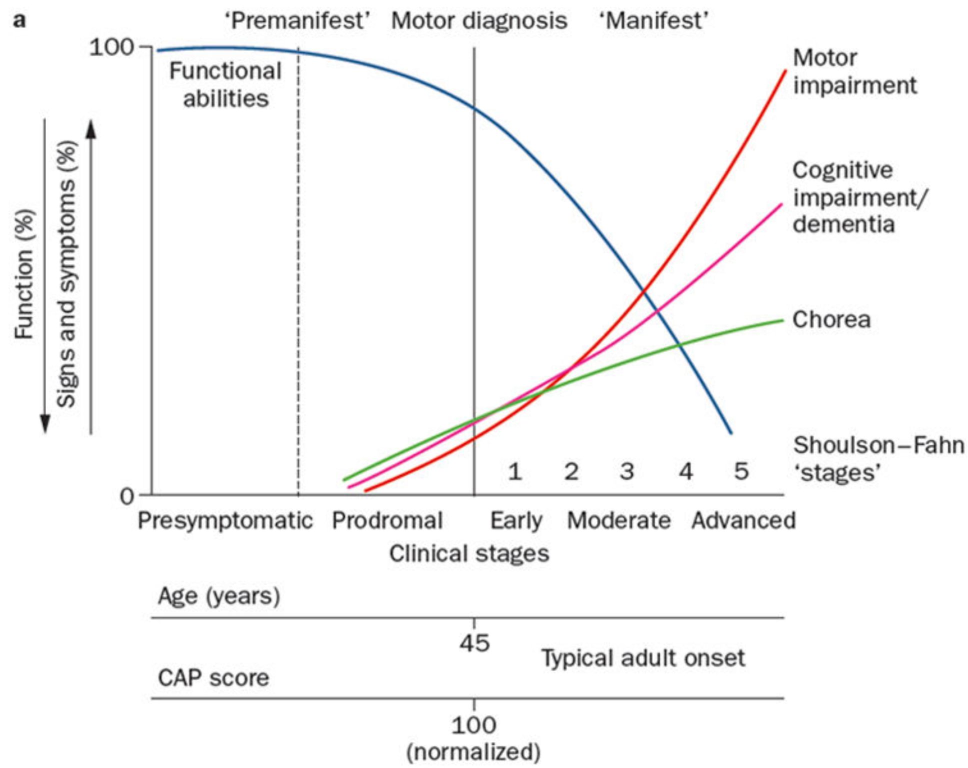

Figure 1.

Progression of symptoms of Huntington's disease across the clinical stages of presyptomatic, prodromal (just prior to motor diagnosis), and early, moderate and advanced disease stages. Ross et al. Nat Rev Neurol. 2014;10(4):204-16

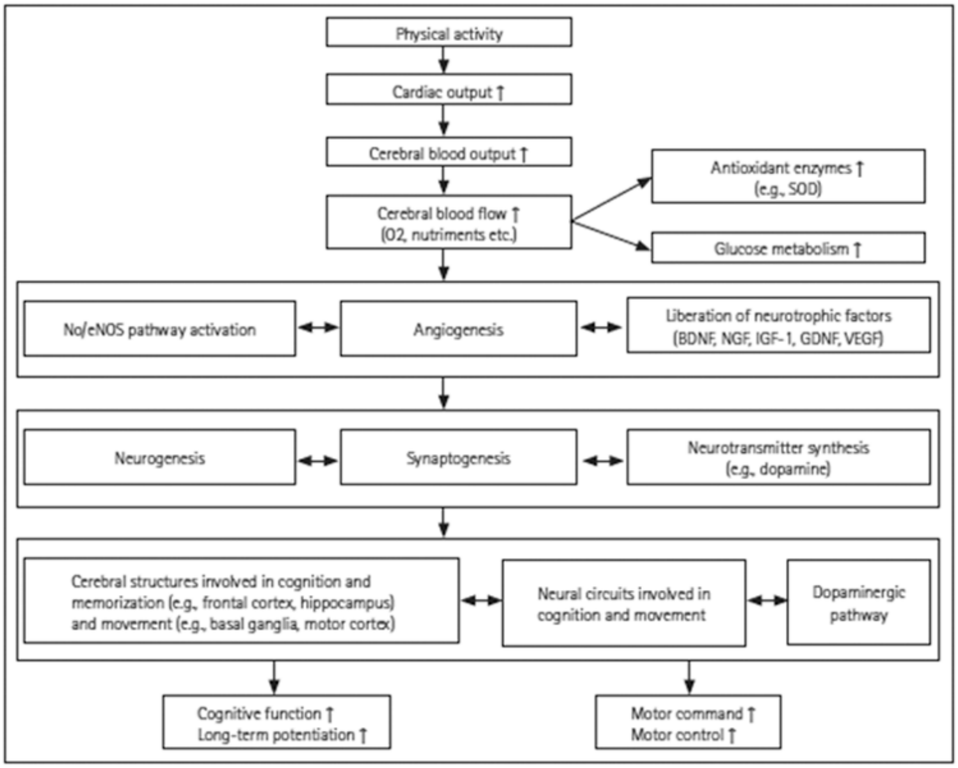

Figure 2.

Preventive and neuroprotective mechanisms induced by regular physical exercise on the cognitive and motor functions. BDNF: brain-derived neurotrophic factors, eNOS: endothelial nitric oxide synthases, GDNF: glial cell line-derived neurotrophic factors, IGF-1: insulin-like growth factors, NGF: nerve growth factors, NO: nitric oxide, SOD: superoxide dismutase, VEGF: vascular endothelial growth factor. Reprinted from: Paillard T, Rolland Y, de Souto Barreto P. Protective effects of physical exercise in Alzheimer's disease and Parkinson's disease: a narrative review. J Clin Neurol. 2015;11:212-219.