Neurophysiology of Exercise: Current State of Learning

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1. Introduction

Exercise neurophysiology refers to learning on crucial role of central nervous mechanisms in determining physical/mental performance and health. There is awareness that exercise helps physical outcomes. There is much less awareness of mental health outcomes. Least awareness apparently prevails in respect of ability to translate the duel awareness in to clinically relevant exercise action. The physical-mental evolution of man specializes him as slow endurance runner, capable of outdoing most other species in making long distances. The adaptation implies characteristic asset of brain-mind-exercise. Interest of basic sciences is growing in mechanisms of positive exercise effects of on brain function and agility in health as well as infirmity. Approaches to scientific investigation of the perspects and certain important neuro-physiological revelations are briefly, reviewed.
2. Approach to study designs

Study of exercise neurophysiology includes study of mechanisms for positive effects of long term exercise on cognitive function, mood, sleep and fatigue related consequences; motivational determinants of nervous activities for effort and central and peripheral mechanisms promoting voluntary physical activity; the endocrine or humoral afferent signals from peripheral tissues to brain and their roles, impact of body mass and perceived work stress and the structural consequences relating growth and repair. There is major reliance on animal experiments to elaborate upon above stated perspectives. Techniques and inferences are ridden with cautions for different evolutionary status in structure and function of nervous system and behaviours among animals and men (Carruthers et al 2014). The biology and behaviour of animals, mostly rodents, differ regarding specific exercise. Artificial isolation by force is necessary for keeping non-exercising controls which must viciate findings. Elements of volition or compulsion, affect and behaviour are not simply translated from animals to humans. These issues remain crucial in studies of exercise effects on brain.

There have to be continuous brain-storming toward exploring opportunities for studies of nervous system in human’s e.g. by employing in vivo neuro-imaging (Marks and Katz 2012). Neuro-imaging is non-invasive means of evaluating brain structure and function and basis for cognitive dysfunction. Neuro-imaging can readily assess beneficial outcome of exercise interventions. Neuro-imaging may be indispensable for deciding optimal moment for clinical intervention and monitoring application. Structural imaging can involve gray and white matter volume determination, and integrity of cerebral white matter. It can also investigate cerebral blood vessels. MRI can focus on changes in discrete brain regions of interest. The findings can be readily examined for an association with executive function, long term memory and intelligence. Age and gender independently impact brain volume and cognition, (Madden et al 2009), requiring due discounting and control for right conclusions. Opportunities for autopsy studies, whenever feasible can make vital research tool supplementing neuro-imaging.

The type of exercise, its intensity, the timing and duration of single session and frequency of sessions, have all to be elaborated for impact on the defined nervous outcomes. Durability of such impacts and any revealing priming effects of previous exercise on consequent performance, also need elaboration. The consequences of different sex, age and probable status of health on the findings need be discerned. Potential mechanisms need elaboration for observed effects on behaviour, cognition, mood, stress resistance etc. New understanding of specific neuro-circuitries awaits due application in design of appropriate animal models to study unique perspectives, including personality and morbid traits.

Different paradigms of exercise training, cognitive training and dietary interventions should be evaluated for similarities and differences in mechanisms as well as their interactions of influencing brain function. Physiological, behavioural and mental processes are under intricate control of the brain and brain function is subject to control of genes. Social, developmental and environmental factors affect gene expression. Physical activity and exercise influences form and function of central and peripheral nervous system in such advanced context of knowledge. Finally, genes regulating physical activity and those expressed consequent to physical activity with their positive or negative impacts on metabolic regulation require elaboration. Specific neuro-physiological findings narrated in following paras, must be integrated in wider context of discussed perspectives, for practical clinical relevance.
3. Current neuro-chemical and functional understanding

Experimental and clinical studies have revealed information’s that may be considered in reference to broad perspectives of organism physiology.

i). Stress response and mediators:


ii). Neuroprotection:

Neurotrophic impact of long persisting exercise through increased expression of brain growth factors is prominently revealed (Neeper et al 1995). The neuro-protective and regenerative potential has shown to benefit against ischemic neuronal damage and neurotoxic chemicals (Ding et al 2004; Li et al 2003; 2004; Stummer et al 1994). Treadmill exercise training in rats also reduced brain infarcts induced by occlusion of middle cerebral arteries (Li et al 2004). Such effect accompanies increase in expression of BDNF and NGF (Nerve growth factor) genes (Neeper et al 1995; Ang et al 2003). Protection by same mechanisms is seen in traumatic brain concussion and chemical induced experimental neurotoxicity (Stummer et al 1994; Smith & Zigmond 2003).

iii). Energetics:

Physical exercise influences central nervous system through several neuro-chemical and metabolic pathways in brain, spinal cord and skeletal muscles. Both short term high intensity and prolonged low intensity exercises increase pyruvate dehydrogenase-4 kinase transcription in active skeletal muscle (Pileguard et al 2000). Entry of carbohydrate derived fuel for mitochondrial oxidation is inhibited and glucose use as fuel in skeletal muscle is limited. This helps meeting increased metabolic needs of brain during and after exercise. Study by Hara et al (2014), synergizes with recent discoveries revealing key role of mitochondria regulating synaptic transmission, brain function and cognition in aging. Relationship between mitochondrial shape and age related cognitive function is demonstrated. Deformed, donut shaped neuronal mitochondria are hall mark of mitochondrial stress associated with diminished synapses. Functional state of mitochondria at synapse, modulate synaptic strength and transmission function.

Acute strenuous treadmill exercise in rat induces temporary increase in cerebral local use of glucose (Vissing et al 1996). Neural input from motor centres and feedback from active muscles are both important for glucose production and lipolysis during exercise (Kjaer et al 1996). The central motor
command for attempting muscle contraction can independently exert control without need for sensory inputs, as perceived efforts increase even in paralysed individuals (Gandevia et.al 1993). Prolonged exercise in humans releases cytokine interleukin-6 from brain, and from skeletal muscles (Nybo et.al 2002), where it restricts glucose utilization (Pedersen et.al 2003). This indicates role of interleukin-6 in modulation of energy balance between expenditure and intake by the central nervous system.

Exercise affects key elements of energy metabolism (Vaynman et.al 2006; Vissing et.al 1996), which modulate substrates of synaptic plasticity, underlying learning and memory. Exercise induces compensatory changes in central neuro-peptide systems involved in regulation of energy homeostasis (Levin & DunnMyrnell 2004). Protective function of exercise on the brain appears mediated through similar molecular changes as seen in regulation of BDNF signalling system (Wu et.al 2004). Exercise therefore exhibits long term effect of enhancing cognition. Precisely, exercise significantly boosts level of mitochondrial uncoupling protein-2. This protein is involved in calcium regulation, ATP production and regulation of free radical profiles. It is major modulator of BDNF (Brain derived Neurotrophic factor) production and its downstream signalling function (Vaynman et.al 2006), crucially implicated in learning and memory. Exercise is shown to benefit learning and memory in transgenic mouse model of Alzheimer’s disease, with accompanied reduction in toxic amyloid β protein and its precursors (Vissing et.al 1996; Adlard et.al 2005).

iv). Psycho-physiological impact:

Single bouts of moderately intense aerobic exercise have positive impact on neurocognitive function and inhibitory control in children with attention deficit hyperactivity disorder. Exercise improves their behavioural, cognitive and scholastic performance (Pontifex et.al 2013). The anti-stress impact of qigong exercise is demonstrated in improving depression in elderly. The psychologic functioning improves through possible down regulation of hyperactive hypothalamo-pituitary-adrenal axis (Tsang et.al 2013). Epidemiological studies reveal that physically active people are less depressed than inactive people (Blumenthal et.al 2007). Exercise is important both in treating depression and in preventing relapse (Hoffman et.al 2011). It is suggested that adding exercise to treatment plan of depressed relapse is prudent (Otto et.al 2006). Panic reaction is less likely to strike anxiety sensitive people indulging in high physical activity than those who will low physical activity (Smit et.al 2011). The mentally enriching environment and exercise act to buffer response of brain to future stressors (Lehmann & Herkenham 2011).

Regular exercise has favourable, while vigorous exercise has negative impact on immunological function. Acute exercise effects on immune function are mediated through increased secretion of cortisol, catecholamines and neuropeptides. This is seen when bout of exercise raises maximal oxygen consumption by 60% and more. Regular moderate exercise also raises immunoglobulin profile, as protection against infection (Karacabey et.al 2005).

v). Neuro-Cognitive function:

Robust aerobic exercise improves cognitive tasks involving attention, processing speed and executive functioning. Aerobic exercise also promotes structural and functional adaptation of brain. There is thus, greater activation, blood flow, connectivity and cellularity in hippocampal, frontal and parietal cortex. Increased epinephrine and BDNF (brain derived neurotrophic factor) concentration during exercise facilitate memory consolidation and learning (Roig et.al 2012). Spirduso et.al (2005), suggested that exercise may support cognitive function by directly improving risk factors of cognitive decline e.g., stress, sleep disorder,
cardiovascular disease, insulin resistance, hypertension, inflammatory states and amyloid plaque. Exercise induced molecular cascades affecting neuronal plasticity, may play a role especially, for short term exercise effects (Lista & Sorrentino 2010).

Aerobic exercise upregulates expression of BDNF (Neeper et.al 1995). The resistance exercise stimulates IGF.1 (insulin like growth factor 1) production (Cassilhas et.al 2007). Both neurotrophins facilitate different plasticity mechanisms viz neurogenesis, synaptogenesis, and angiogenesis via partly interacting pathways (Cotman et.al 2007). Even moderate levels of persisting physical activity, in combination with rich sensorimotor and cognitive engagement (e.g. dancing), may ameliorate wide spectrum of age related decline of white and grey matter in frontal, temporal and parietal cortex, associated to executive functions (Colcombe et.al 2004). Cognitive performance is positively correlated with EEG alpha activity. The whole body exercise training induces cognitive improvement with increased frontal alpha coherence (Buzanova & Vermon 2013).

Aerobic exercise may attenuate progression of neurodegenerative processes and age related loss of synapses and neuropil. These effects may be direct on neuro-degeneration mechanisms or may be exerted indirectly through facilitation of neuro-protective/trophic factors and neuro-plasticity (Eric-Ahlskog et.al 2011). Long term memory is based on structural-functional changes in particular synaptic connections between neurons in brain, that depends on process of translation and transcription (Nikitin 2007). Exercise training increases task relevant cortical network, encompassing sensorimotor regions and areas of dorsal stream (Bezzola et.al 2011).

vi). Motor function and skill

Fatigue is exercise induced decline in capacity to generate muscle force. It results from changes both at peripheral and central levels. Brain activities related to preparing for and execution of a movement (movement related cortical potential MRCP), occur before the actual movement. These are related to perception of effort. Increase in prefrontal cortex positive activity depends on the effort perception and not peripheral fatigue (Berchicci et.al 2013). Probable brain mechanisms of impaired voluntary activation of motor neurons during prolonged strenuous exercise include, decrease in supra-spinal motor drive (Gandevia 2001), linked to increased serotonergic activity in brain, increased ammonia activity, depletion in brain glycogen content, decreased striatal dopamine and inhibitory feedback from exercising muscles (Nybo & Secher 2004).

Motor activity is essential for basal neuro-trophin function and neuro-plasticity in the spinal cord, as normal response to exercise. This involves release of growth hormone like trophic factor from the pituitary (Gomez et.al 2004). The spinal cord level, task specific learning involves two major inhibitory neurotransmitter systems, glycine and GABA. There release is exaggerated in spinal injury but restored back to normal by exercise training (Edgerton et.al 2004). Vanderwolf (1969) reported that voluntary exercises activate a persistent firing pattern, the THETA rhythm in rat hippocampus, vide cholinergic and GABAergic neurons. Such theta bursts lead to secretion of BDNF in hippocampus (Corro et.al 2000). Low intensity treadmill exercise also upregulates hippocampal BDNF levels, facilitating motor recovery following stroke. Higher exercise intensity causes stress, corticosteron release with counterproductive outcome (Ke et.al 2011).

Musculo-tendinous junction and tapotement massage as well as stretching exercise decrease spinal excitability and improve coherent motor function (Behm et.al 2013). Motor performance of healthy people improves with 30 minute co-contraction training, accompanied with decreased H
reflex. Long term treadmill exercise training in spinal cord injured patients similarly, improves motor performance, and indicates exercise induced increase in corticospinal connectivity. Reflex modulation may also improve gait in spastic patients. Children with bilateral cerebral palsy exhibit large H reflex during a gait. Treadmill exercise training for even brief period improves their walking ability through decreasing H reflex (Meunier et.al 2007).

4. The Practice and Study Perspectives

Exercise is universally believed to improve fitness and the physical fitness associates with mental agility. Performance enhancement in competitive sports requires enhanced physical and mental competencies in the participant. Exercise training aims to meet such requirement. A long term exercise intervention consists of implementing regular exercise, lasting from few weeks up to one year, and measuring different aspects of health and cognition. Studies employing this paradigm demonstrate that long term exercise can increase general cognitive functioning across the lifespan and decrease risk of dementia in older adults (Kramer & Erickson 2007; Voss et.al 2010).

Based on brains ability to adapt to new environmental challenges by phasic reorganization of the cortex, greater advantage may be reaped by combined physical and cognitive exercises. Presumably, physical exercise increases the potential for neurogenesis and synaptogenesis, while cognitive exercise guides it to induce positive plastic change (Fissler et.al 2013). Further research should examine modulatory potential of additional social, psychological and physical constitutional variables (Hotting & Roder 2013).

Acute outcome studies can state how exercise stresses the brain on an immediate basis. Only longitudinal outcome studies will be able to define more definitive exercise dosing and guide monitoring of exercise programme toward improving brain health over time. There is need for population and gender specific recommendations in context of specified physical activity. It is long before global physical activity/exercise guidelines would emerge for cognition disorders, as now available for cardiovascular disorders. Exercising safety of individual and the risk of dropout have to be successfully addressed without compromising efficacy of the intervention in consistence with the scientific evidence base. This is the obvious “art” of practical application. Inhered biological basis should amply convince in design of exercise recipe in its type, frequency, duration, intensity and rate of progression to the level optimum.

5. Conflict of interest statement

There is no conflict of interests present.

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