Training is Not “Exercising”

The term “training” does not have the same meaning as the terms “exercise” or “exercise training”, which are used by various health organizations, and it is also not the same as the term “chronic exercise” which is widely used in research.

True, “training” is what researchers call “progressive training,” and if the training is done with weights, it is called progressive resistance training (PRT). This definition is correct because of the use of the term “progress.” Training is the process of progressing from an “untrained” state to a “trained from X, to a level of Y.” This training happens intentionally, is controlled by measurable variables (like volume, intensity, and frequency), and is quantified by direct measurement of the progress that was achieved [1].

The correct definition of “training” is particularly important when dealing with older adults. The term “well-being” (mainly meaning a positive and comfortable feeling) is a central concept in the caregiving and treatment of the elderly in both private and state day care centers [2]. This term includes the word “being,” which means in this context “to be now.” Accordingly, when physical activities are used with the elderly in these institutions they are usually performed with the intention of making the elderly feel good now (“exercise”), and not as a part of a plan to enhance their future physical abilities in a systemic and measurable way (“training”).

The “being” part of the “well-being” concept has far-reaching negative consequences for the elderly. It is a fact that training – a prolonged, strenuous, planned effort in order to achieve a physical improvement over time – can help old people achieve physical independence and produce drastic cognitive improvements. The “being” concept – feeling good temporarily – is the opposite of the “training” concept, and the time incorrectly invested in it misses the opportunity to improve the quality of life.

Progressive Training for Brain and Cognition Improvements in Seniors

Both progressive resistance and aerobic training have a proven and measurable ability to slow the deterioration of the aging brain [3]. In seniors, progressive training can improve cognition considerably
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[4], and alleviate some of the mental disorders that are typical of this demographic, like major depressive disorder [5, 6].

For example, progressive resistance training was found effective in stopping and even reversing cognitive decline in older adults with mild cognitive impairment (MCI), through mechanisms that preserve brain tissue [7]. Seniors doing PRT showed a 0.01 millimeter yearly increase in their brain cortex thickness, while non-training control groups had a 0.05 average decrease over the same period [8] (the change was measured in the cingulate cortex that spreads along the cleavage between the two hemispheres and processes sensory, movement and emotional information).

And in seniors doing progressive aerobic training it was found that their hippocampus volume increased about 2% every year, while non-trainers hippocampus volume decreased 1.4%/year [9].

In general, properly-prescribed progressive physical training can be a major factor in facilitating cognitive improvement in seniors of all ages and in any cognitive situation [10].

Why Resistance Training?

There is a considerable body of evidence that shows that resistance training and aerobic training are both important for cognitive and brain health in the elderly. While progressive resistance training is better at increasing anabolic hormone levels and relieving oxidative stress, aerobic training is more significant than PRT in other aspects, such as raising certain nerve growth factor levels. Both training modules increase brain volume and improve cardiovascular effects considerably.

Recent studies recommend doing both for best cognitive long-term health.

But there is a hierarchy here: except for the direct benefits of resistance training for brain, cognition, and daily function, PRT is also the key for the therapeutic use of aerobic training, for two reasons: first, very old adults are often too weak and/or frail to engage in any considerable aerobic training, and PRT is essential to prepare them for it; and second, it is an empirical finding that the benefits of aerobic training for brain and cognition are amplified considerably when combined with PRT [11, 12].

The Biology of Brain Degeneration with Age

Aging and chronic inflammation

Aging is usually accompanied by a physical state of chronic inflammation. This state resembles acute inflammation (that occurs in response to damage), but it lasts longer and it usually has more diffuse symptoms.

Chronic inflammation starts a chain of phenomena that can end in the death of the tissues involved. It is a major cause for old-age death [13], and it takes part in the development of diseases like type-2 diabetes, Alzheimer's disease (and dementia in general), heart and blood vessel diseases, frailty, sarcopenia, osteoporosis, and cancer [14].

An outline of the development of chronic inflammation in the CNS could be as follows [15]:

1. The innate immune system discovers molecules that it regards as harmful.
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2. Microglia cells, which support neurons and destroy pathogens, activate protein complexes (like NF-kB, a DNA coder) and enzymes (like MAPK, cell activity regulators), and initiate the production of cytokines (communication units between immune system cells and other cells) of the kinds that encourage inflammation (like IFN-γ, TNF, IL-1β, IL-17, and TGF-β). This is a local immune reaction, which only affects the surroundings of the suspect substance or where damage had occurred.

3. Cytokines get into the blood stream, which turns the local immune reaction into a systemic reaction that involves other parts of the body.

4. If the inflamed tissues do not heal, or in reaction to constant stimulation, the inflammation becomes chronic and affects surrounding tissues. These tissues get into a cycle of damage and healing that can last for months or even years.

5. The increased production of inflammatory cytokines causes a decrease in the secretion of anabolic agents such as insulin, IGF-1, and erythropoietin (a hormone that prevents neuron death) [16].

The main reasons for the increase in chronic inflammation with age include the prolonged accumulation of molecules and cells that are identified by the innate immune system as dangerous (some of them products of oral or gut microbiota that leaked into tissues and blood), cell senescence (the aging and eventually death of cells) because of damage or stress, and increased activation of the blood coagulation system (blood clotting) [17]. Genetics also have a role in determining the extent of the inflammation that will eventually develop [13].

Aging and Brain Blood-Flow Decrease

A sufficient blood supply to the brain is essential for proper neuronal activity, and cerebral blood perfusion (the volume of blood that passes through a given brain-volume in a given time) is an important indicator of the brain's health [18].

Cerebral blood perfusion (CBP) is reduced with aging. There is a 28-50% reduction of CBP between the ages of 30 to 70 [9], with a yearly whole-cortex reduction rate of an average 0.38% in healthy brains, and probably faster in older people [18, 19].

Reduced CBP is related to cerebral small vessel disease (CSVD), which is the cause of an estimated 20% of the strokes and 40% of the diagnosed dementia cases [20]. A typical result of CSVD is brain white matter lesions [21], which are observed in most people at ages over 60 [22], and are also related to cognitive decline and dementia.

Aging and CNS-Degenerative Diseases

CNS-degenerative diseases like Alzheimer's Disease (AD) are related also to the aging of the general population, and some of their symptoms can be found, to some extent (and more with aging), in those that are not strictly defined as affected [22]. The mechanism of AD can serve as an example for a typical CNS-degenerative disease.

In the neuronal membranes in the brain there is a protein called APP (amyloid precursor protein). In healthy brains, scavenged APP is dissected in a specific manner that leaves the cut segments soluble, and they are removed. In the brain of AD patients, APP is cut differently and the segments
that are produced (which are called beta-amyloid, “Aβ”) are insoluble, and they accumulate outside the neurons in clumps (called amyloid plaques) [23].

Amyloid plaques can disturb neuron action, start an immune reaction, and cause inflammation [24]. They can also settle around brain blood vessels, weaken these vessels, and cause rupture and blood loss.

APP and Aβ themselves can apparently penetrate the mitochondrion, disrupt its function and the function of the neurons, and even cause neuron death by initiating controlled self-destruction (apoptosis) [25].

Another characteristic of AD is the formation of insoluble fibrous tangles within the neurons. In the healthy brain, a protein called “tau” stabilizes the small tube-like “microtubules” that support the neuron structure and help with transferring materials within it. Accumulation of Aβ outside the neurons causes changes within the neuron, which cause a change in the structure of tau. Damaged tau can no longer support microtubules, and it sticks to other damaged tau fragments and forms neurofibrillary tangles within the neuron. Like amyloid plaques, neurofibrillary tangles interrupt neuron function and can cause neuron death [26].

A similar mechanism of neuron degeneration is the accumulation within the neurons of Lewy bodies, which are made of another brain-abundant protein called Alpha-synuclein. Lewy bodies cause Parkinson’s disease, Lewy body dementia, and brain atrophy.

Aging and Oxidative Stress

Oxidative stress is caused by oxygen species (molecules that have an oxygen atom in them) which are free radicals (i.e., they have an unpaired electron) and therefore react readily with other substances. The most abundant radicals in our body are hydroxyl (OH•), superoxide (O2–•), and nitrogen monoxide (•NO). Other substances, like hydrogen peroxide (H2O2), peroxynitrite (ONOO-) and even the Aβ protein [27] also contribute to oxidative stress indirectly, because their reactions with other substances produce free radicals.

Small amounts of free radicals are produced as a part of regular metabolism, and are essential for body function. When free radicals’ levels are above the body’s ability to control, a stress develops, and radicals start to oxidize essential cell building blocks like fat, protein and DNA [28]. The cell and its control mechanisms are damaged [29], and the cell's function deteriorates – sometimes ending in apoptosis.

Oxidative stress increases with age [22, 30] and is related to aging processes, and especially to brain aging. The brain’s vulnerability to oxygenation is a result of its high oxygen demand, its high polyunsaturated (and thus easily oxidized) fatty acid content, its relatively high metal content (mainly copper, zinc and iron) which increases free radical production [31, 32], and the abundance of neurotransmitters and amino acids (like glutamate) whose own metabolism produce free radicals.

Measurable Results of Brain Aging

As a result of neuronal volume loss and death, total brain volume decreases. Volume decrease (atrophy) can be local and affect functions that are operated by the atrophied part of the brain, or they can be general and affect most aspects of human function. Brain atrophy is typical to brain degenerative diseases [33] but it occurs to some extent in regular aging brains too, with an estimated 5% volume decrease in every decade after the age of 40, and at a higher rate at older ages [34].
Dementia is another measurable phenomenon, and it is related to brain atrophy. Dementia is the most prevalent chronic disease in the elderly, and its prevalence rises almost exponentially with age. It is found in 20-30% of the octogenarians and in about 40% of the nonagenarians [35]. Its symptoms include deteriorating memory, thinking and learning abilities, and a difficulty in daily function [36]. And 40% to 70% of all dementia cases are related to AD, with about 15% of the cases related to Lewi body disease.

The Effects of Progressive Training on the Brain

Progressive Resistance Training and IGF-1

Insulin-like growth factor 1 (IGF-1) is an anabolic (tissue synthesis-promoting) hormone, similar in its structure to insulin, and is one of the main growth and metabolic hormones in the body [37]. In the nervous system and in the brain, IGF-1 has critical tasks: it promotes nerve cell development, affects the creation of the myelin layer that electrically insulates the axons, stimulates the connection of denervated muscle fibers to existing axons (sprouting), and induces the repair of damaged axons, among others [38]. An optimal (not too low and not too high [39]) amount of IGF-1 in the body is essential for proper cognitive function.

The anabolic effect of IGF-1 on the brain is achieved mainly through the inhibition of an enzyme called GSK3. This inhibition enhances glucose use and protein synthesis in neurons [40].

IGF-1 is especially important for seniors because of its ability to prevent the formation and the accumulation of amyloid plaques and neurofibrillary tangles. It does so by preventing the phosphorylation of the tau protein (the change that deactivates tau and enables it to form tangles), and by making the blood-brain barrier more penetrable to albumin, which bonds to Aβ and leaves the brain along with the blood stream.

The amount of IGF-1 in the body decreases with age [41], and this decrease is correlated with a decrease in neuron volume, dendrite length, and synapse number – and generally with brain volume decrease.

Progressive resistance training is quite unique in its ability to considerably and significantly raise IGF-1 levels in seniors [42–47], compared to a small or insignificant change in these levels due to aerobic or endurance training [48, 49]. The chronic IGF-1 increase is gradual, and its extent depends on the training program variables [50] – which can include, among others: the muscles that are trained, training intensity, training frequency, and the structure of the training session (i.e., the number of exercise sets and the number of repetitions in every set).

Progressive Resistance Training and the Immune System

Any kind of progressive training (resistance or aerobic, or even training modules that induce totally different adaptations like flexibility training or martial arts [51]) increases immune activity, and induces anti-inflammatory processes. A suggested anti-inflammatory mechanism that is activated by PRT done by seniors is presented in the following model [52]:

1. During a resistance training session with a sufficient load, the blood concentration of inflammation-inducing cytokines like interlekyne-6 rise sharply (100-fold of baseline). Right after training, IL-6 level starts a 24-hour decline back to baseline level.
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2. The sharp rise in IL-6 causes increased secretion of anti-inflammatory cytokines (IL-1Ra, IL-10, sTNF-R) that prevent the formation of more pro-inflammatory agents (like IL-1α, IL-1β, TNF-α, CXCL8).

3. The total product of the two reactions – inflammation right after the training session, and a strong anti-inflammatory reaction following it – is a net anti-inflammatory effect.

4. With time, the repeating exposure to sufficient loads cause a considerable decrease in the baseline levels of the pro-inflammatory agents (like IL-6). This reduces the extent and the intensity of chronic inflammation, and of the damages that it causes to tissues.

Progressive Training and Nerve Growth Factors

Nerve growth factors are proteins that encourage and participate in neuronal self-repair processes, in the creation of new synapses [53], and in the formation of new neurons in adults from neuronal stem-cells [54].

The first-discovered and most researched group of nerve growth factors are the neurotrophins (NT), that include NGF (nerve growth factor), BDNF (brain-derived neurotrophic factor), NT-3 (neurotrophin-3), and NT4/5 (neurotrophin-4/5) [55]. Of the NT, the most prevalent growth factor in the CNS is BDNF, and it is considered to have a central role in nerve growth. Most of the BDNF (70-80%) is produced in the brain, but it is also produced in endothelial cells, in lymphocytes and monocytes, and in skeletal muscles. In the brain, BDNF is active in the hippocampus, the cortex, and in the basal forebrain – regions that take part in learning, memory, and thinking [56].

The amount of BDNF decreases with age, and its decline is correlated with an increase in depression, degenerative nerve diseases, and frailty.

Physical training increases BDNF concentration in older adults. This effect is both acute (during and immediately after the training session) and chronic, and its size depends on the specifics of the training session, the training program, and the trainee’s medical condition. Resistance training [57], aerobic training [58] and mixed training [59] all have the ability to raise BDNF concentration.

Training and Cardiovascular Effects

Aerobic training improves cerebral blood perfusion [60]. It induces the formation of new blood vessels in the cortex [61], and improves the blood’s rheology (the blood’s ability to flow freely) [62]. These effects allow for better distribution of nutrients in the brain cells [63]. It is possible that resistance training causes similar adaptations, but it seems that to date there isn’t much comparative research about this subject.

Both aerobic and resistance training are effective in reducing blood pressure [64]. But older adults that practiced PRT had a 3.4% decrease in white matter lesions in the right periventricular area, compared to non-trainers that suffered a 3%/year increase in these lesions [8].

The cardiovascular effects of progressive training are optimized when the training module combines resistance training with aerobic training [65].

PRT and Oxidative Stress

As stated earlier, oxidative stress is closely related to aging, and it plays a big role in the age-related damage that accumulates in the brain. Oxidative stress is also a by-product of aerobic training due to the obviously higher volumes of oxygen processed.
Conversely, PRT lowers oxidative substance concentrations in the body. This makes PRT a unique protective measure against oxidative stress in the elderly in general [66], and it makes it a cross-protection measure against the oxidative stress produced by aerobic training [67].

Physical Training to Heal and Protect the Aging Brain: General Outlines of the Medical Prescription

A certain amount of time and effort is already being invested in older adults with the intention of strengthening their bodies and minds. Progressive physical training is the best way to use this time productively and cost-effectively, and should be considered as preventive therapeutic treatment.

General Physical Training Prescription

Physical training for cognitive improvement of the elderly (in any cognitive state) should include regular physical exercise within a structured program that is intended to improve physical abilities in a measurable way. The most suitable training modules are resistance or aerobic training, and preferably a combination of both. Other exercise modules (like martial arts or flexibility) can also be useful and should be added if time (and the trainees’ situation) permits. Training intensity should be moderate to high, and every training session should be at least 45 minutes long. Training frequency should be as high as recovery permits [10, 68].

PRT Prescription

The heavier the weights an older person can lift, the bigger the cognitive benefits of resistance training [69]. In light of that, a therapeutic strength training program for seniors should be planned, executed, and corrected during execution in a way that will achieve the biggest improvement in intensity (i.e., the heaviest weights) possible, within the constraints of age, health situation, recovery capacity, and genetics.

Building such a training plan, adjusting it for older trainees, and coaching it are not trivial concerns for the average gym instructor. A therapeutic training program for the elderly is target-oriented and must be personally designed for each trainee. In this respect, such a program resembles the training of a professional athlete more than that of the average gym goer’s (if he has one). Accordingly, such a program should be built and carried out by those who have experienced building and delivering such programs to seniors, and who would know how to manage all the program variables (the specific
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Exercises, the number of repetitions for each exercise, the weights used, and the training frequency, and the intra-session variables (like technique, speed, and rest times) in order to achieve the specific trainee's best results.

It should be noted that an integral part of training (and especially resistance training) is consumption of adequate amounts of nutrients (mainly protein, energy and water [70]), together with adequate rest. These are essential for sufficient recovery from the training stress [71], for the construction of new muscle, bone and nerve tissue, and for obtaining the largest immune and hormonal gains from the training program [72].

References

33. NCBI – NIH – Cerebral Atrophy Information Page (https://www.ninds.nih.gov/Disorders/All-Disorders/Cerebral-Atrophy-Information-Page)
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