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REVIEW ARTICLE

The Impact of Anabolic Androgenic Steroids and Exercise on Cognitive Functions

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ABSTRACT

Background: Anabolic-androgenic steroids (AAS) have been used by millions of people worldwide to increase muscle mass or enhance sports performance. According to recent in vitro research, supraphysiologic AAS dosages may induce neuronal cell death. These results suggest that high-dose AAS users may eventually experience cognitive impairments, a potential that has reportedly not been investigated. Over the past ten years, scientific evidence based on neuroimaging techniques has shown how effective physical activity is at enhancing cognitive health across the human lifespan. Aerobic fitness improves the functionality of higher order brain areas involved in cognition regulation and prevents age-related brain tissue loss. People with higher levels of fitness or activity can focus more of their attention on their surroundings and process information faster. According to these findings, aerobic fitness improves cognitive processes that allow one to adapt to challenges more successfully and accomplish tasks more effectively.

Conclusions: Cognitive impairments, particularly in visuospatial memory, may result after prolonged high-dose AAS exposure. Exercise seems to be a safe and efficient way to combat neurological and cognitive conditions.

Keywords: Anabolic Androgenic Steroids, Cognition, Exercise

INTRODUCTION

The term "cognition" describes the mental operations that go into understanding and learning new information. To put it another way, cognition is the mental process of learning and comprehending through experience, thought, and the senses. It includes every facet of cognitive processes and functioning [1]. To assess it simply and practically, cognitive functions have been broken down into more specialized psychological skills, such as perception, attention, working memory, decision-making, processing speed, planning, inhibition, cognitive flexibility, language comprehension and production, etc [2].

The cognitive skills that allow us to retain information in working memory, Executive function includes controlling highly automatic responses to stimuli and focusing attention on related but distinct aspects of a task or problem [3]. Coordinated, well-organized, and focused behaviors are the result of executive function [2]. Additionally, it represents the cognitive processes that govern behavior, such as memory, cognitive flexibility, and selective attention. **[4].**

The process of neuroplasticity, sometimes referred to as neural plasticity or brain plasticity, includes adaptive structural and functional alterations in the brain. By rearranging its connections, functions, or structure, the nervous system's ability to alter its activity in response to internal or external inputs makes sense [5]. neural networks, synaptic and neural connections, the formation of new neurons, and other neurobiochemical changes brought on by human experiences are examples of plastic modifications [6].

Evidence indicates a relatively recent kind of brain plasticity in many species, including humans, is adult hippocampus neurogenesis. Proliferation, neuronal migration, neuronal

destiny specification, and synaptic integration are all dynamic processes that the neural stem cells in the subgranular zone of the hippocampus dentate gyrus (DG) go through [7]. While stress-induced anxiety and depressive-like behaviors are linked to impaired adult hippocampal neurogenesis [9], these freshly produced neurons in the DG help with memory acquisition and spatial pattern separation [8].

Assessment of cognitive status:

The Montreal Cognitive Assessment, Addenbrooke's Cognitive Examination, the Mini Mental State Examination (MMSE), Clock Drawing Test, and Mini-Cog test are the most widely used assessments for evaluating various aspects of human cognition [10]. The Japanese language version of the MMSE is the one that is most frequently used for screening for cognitive impairment and evaluating cognitive performance. Lower scores indicate weaker cognitive performance on the MMSE, which has a range of 0 to 30 [11].

A significant area of behavioral neuroscience is examining cognitive functions in mouse illness models. It is crucial to understand that no behavioral test is tailored to a particular area of cognition. The majority of commonly used memory tasks can be affected by a variety of noncognitive factors. In order to rule these out, a battery of tests should be used, which should include assessments for anxiety, spontaneous activity, and motor functions in addition to cognitive components [12].

Anabolic steroids and cognitive functions (figure 1):

Because AAS users are exceptionally secretive about their use of steroids and are reluctant to tell doctors about it, research on AAS in humans is severely limited [13]. Randomized controlled human trials are also not possible since it is immoral to give volunteers the high dosages of AAS that are relevant to human users. Animal research, on the other hand, can investigate the effects of AAS in an experimental setting where athletic ability and attractiveness are unimportant. In order to explicitly address androgen effects on health and behavior, Additionally, animal research exclude possible confounding variables such past behavioral patterns and polydrug abuse [14].

Visuospatial memory is worse in human AAS users than in non-users, and the impairment gets worse the longer an individual uses AAS [14]. There have also been reports of issues with working memory, focus, processing speed, and problem-solving abilities [15]. While there is a loss in connection with cortical brain regions involved in cognitive regulation, AAS users also exhibit an increase in amygdala volume [16]. Similarly, AAS users report impairments in executive function and both prospective and retrospective memory in non-laboratory contexts [17].

The amygdala, hippocampus, and dorsal anterior cingulate cortex (dACC) are among the brain regions that are impacted by long-term use of anabolic androgenic steroids [16].The amygdala is responsible for processing threats and aggression [18]. Androgen injection to male rats causes amygdala neurogenesis and neuronal soma, as well as a rise in the complexity and volume of astrocytes [20]. Additionally, the rat amygdala is susceptible to androgens [19].

Amygdala reaction to angry or scared faces is positively correlated with endogenous AAS testosterone levels, according to functional MRI studies in healthy males [21]. Similarly, giving testosterone to healthy males caused their amygdala to become markedly more reactive to furious faces [22]. All of these results point to the possibility that AAS may enhance amygdala volume and facilitate aggressive behaviors.

AAS may decrease hippocampal volume, this may be the reason for the spatial memory impairments linked to AAS shown in both human and animal studies. AAS induces apoptosis in the hippocampus of rats [23] and inhibits hippocampal neurogenesis [24]. As previously mentioned, human AAS users have aberrant attentional processes [25], which are mediated by the dACC, a cognitive control region [26]. Visuospatial failure in AAS users may be linked to dACC dysfunction, as seen by

the aberrant dACC activation seen after individuals with alcohol dependence finished a spatial working memory fMRI test. [27].

Additionally, AAS causes aggressive behaviors in both adult and adolescent rodents, This may be related to increased N-methyl-d-aspartate (NMDA) receptor activation and decreased glutamate absorption **[28].**

There are two different ways that anabolic steroids cause pharmacological effects in the central nervous system: either directly by changing their intracellular receptors or indirectly by releasing neuropeptides or changing the binding location at the neurotransmitter receptor [29]. These behaviors can impact the expression of neurotransmitter receptors, including dopamine, glutamate, serotonin, and gamma-aminobutyric acid, which are widely expressed in brain regions linked to different behavioral patterns **[30].**

Effect of different types of exercise on cognition (figure 2):

It has long been known that maintaining one's physical, mental, and emotional health throughout one's life requires physical activity [31]. Numerous studies have shown that exercise can alter the structure and function of the brain. Through angiogenesis, aerobic exercise increases blood flow to the brain, particularly the hippocampus [32]. Conversely, strength training enhances cognitive functioning and develops functional capacities, preventing dependence in daily living activities. Aerobic training is known to promote neurophysiological effects, the results of which may resemble those seen following antidepressant drug treatments [33].

Although there are connections between neurogenesis, exercise, and memory, it is yet unknown what processes underlie exercise-induced neurogenesis. It has been proposed that substances like as BDNF, IGF-1, and Vascular Endothelial Growth Factor (VEGF) facilitate exercise-induced neurogenesis [34].

- **BDNF:**

In reaction to contraction, the neurological system and peripheral organs, including skeletal muscle, generate the protein BDNF, which promotes fat burning [35]. BDNF has a major effect on synaptic transmission and plasticity, neurogenesis, and neuronal survival [36]. In the barrel cortex, treadmill activity, which is regarded as aerobic training, increases BDNF expression, eliminates the spine clearance rate, and prevents memory impairment in mice [37]. Lower cognitive scores are linked to lower blood BDNF levels [38]. Additionally, exercise seems to make the human blood-brain barrier more permeable [39].

- **VEGF:**

Myocytes are the primary source of VEGF, a strong angiogenic agent that permeates the peripheral circulatory system [40]. Exercise-induced VEGF has been shown in studies to have an impact on hippocampal neurogenesis and angiogenesis [41]. It has been demonstrated that exercise-induced hippocampus neurogenesis is inhibited by anti-VEGF antibodies administered to the peripheral circulatory system, suggesting that muscle-derived VEGF functions as a somatic regulator of hippocampus neurogenesis [42]. Additionally, VEGF can penetrate the blood-brain barrier **[43].**

- **IGF-1:**

IGF-1 may mediate the benefits of exercise on brain health by influencing BDNF and VEGF [44], preventing brain damage and improving cognitive functions linked to memory and spatial learning [45]. Humans respond to physical activity by rapidly increasing peripheral IGF-1 levels [46]. As a potential mediator of exercise-induced BDNF and cognitive function, this increase appears to be crucial for exercise-induced neurogenesis and memory enhancement **[47].**

The biological impacts of exercise linked to "neuroplasticity" are especially important. The ability of the brain system to adjust to experience is known as neuroplasticity. PE may therefore be seen as an environmental element that encourages neuroplasticity [49]. Exercise has been demonstrated to activate the mechanistic target of rapamycin (mTOR) pathway, which is crucial for synaptogenesis,

neuronal activation, and axonal myelination and aids in improving motor learning [50].

Both people and rodents were able to increase their spatial learning and memory by aerobic and resistance training [36]. It was shown that increased cardiovascular conditioning from aerobic exercise enhanced short-term spatial memory. These outcomes were linked to a left hippocampal enlargement that was proportionate to the cognitive performance [51].

Exercise has been shown to increase cognitive performance, with executive function playing a significant role [52]. Working memory, cognitive flexibility, and inhibition are three commonly recognized subfunctions of executive function [53].

Conclusions:

Cognitive impairments, particularly in visuospatial memory, may result after prolonged high-dose AAS exposure. Exercise seems to be a safe and efficient way to combat neurological and cognitive conditions.

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Consent for publication

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Competing interests

The authors declare that they have no competing interest.

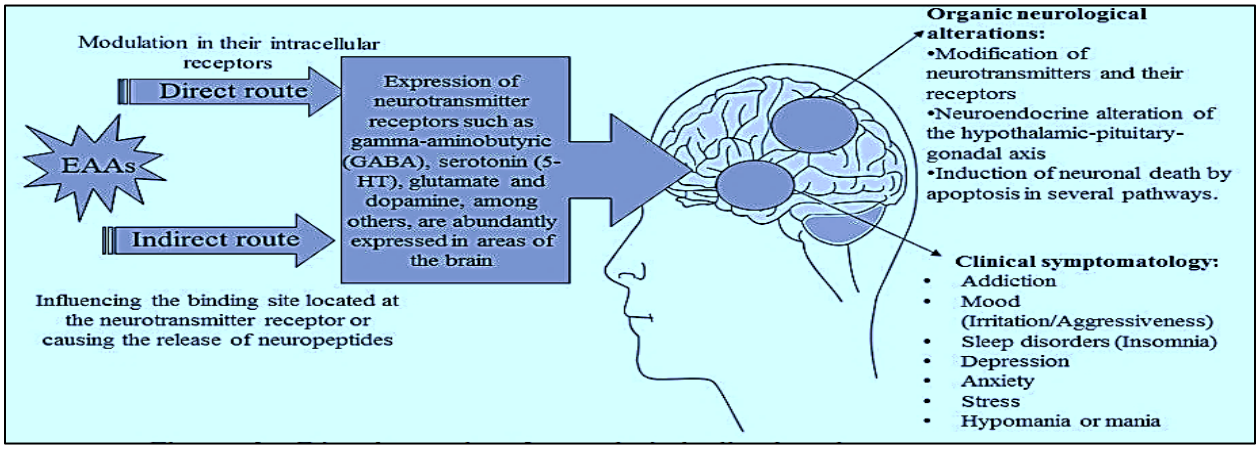

Fig 1: Anabolic-androgenic steroids' pharmacological effects in the central nervous system cause the etiopathogenesis of neurological diseases [29].

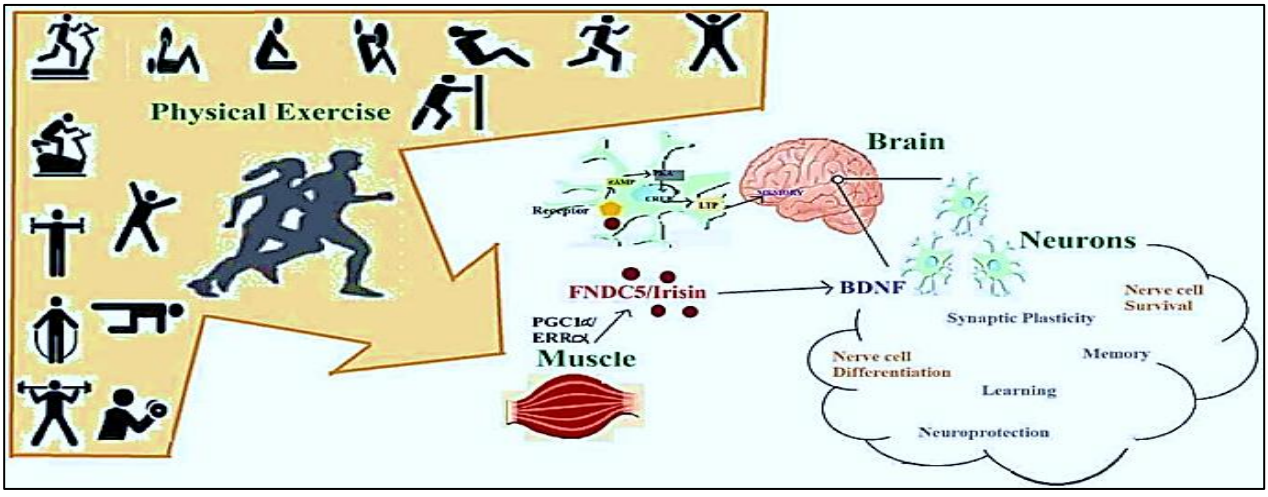

Fig 2: Exercise's effects on the brain [48].

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