

Sellami, Maha, Bragazzi, Nicola Luigi, Slimani, Maamer, Hayes, Lawrence, Jabbour, Georges, De Giorgio, Andrea and Dugue, Benoit (2019) The effect of exercise on glucoregulatory hormones: a countermeasure to human aging: insights from a comprehensive review of the literature. *International Journal of Environmental Research and Public Health*, 16 (10). e1709.

Downloaded from: <http://insight.cumbria.ac.uk/id/eprint/4768/>

Usage of any items from the University of Cumbria's institutional repository 'Insight' must conform to the following fair usage guidelines.

Any item and its associated metadata held in the University of Cumbria's institutional repository Insight (unless stated otherwise on the metadata record) may be copied, displayed or performed, and stored in line with the JISC fair dealing guidelines (available [here](#)) for educational and not-for-profit activities

provided that

- the authors, title and full bibliographic details of the item are cited clearly when any part of the work is referred to verbally or in the written form
- a hyperlink/URL to the original Insight record of that item is included in any citations of the work
- the content is not changed in any way
- all files required for usage of the item are kept together with the main item file.

You may not

- sell any part of an item
- refer to any part of an item without citation
- amend any item or contextualise it in a way that will impugn the creator's reputation
- remove or alter the copyright statement on an item.

The full policy can be found [here](#).

Alternatively contact the University of Cumbria Repository Editor by emailing insight@cumbria.ac.uk.



1 *Review*

2 **The Effect of Exercise on Glucoregulatory Hormones:** 3 **A Countermeasure to Human Ageing: Insights from a** 4 **Comprehensive Review of the Literature**

5 **Maha Sellami** ¹, **Nicola Luigi Bragazzi** ^{2,*}, **Maamer Slimani** ², **Lawrence Hayes** ³, **Georges Jabbour**
6 **¹, Andrea De Giorgio** ⁴ and **Benoit Dugué** ⁵

7 ¹ Sport Science Program, College of Arts and Sciences (QU-CAS), University of Qatar, Doha 2713, Qatar.
8 maha.sellami@gmail.com (M.S.); georges.jabbour.qu@gmail.com (G.J.)

9 ² Postgraduate School of Public Health, Department of Health Sciences (DISSAL), University of Genoa,
10 Genoa 16132, Italy; robertobragazzi@gmail.com (N.L.B.); maamer2011@hotmail.fr (M.S.)

11 ³ Active Ageing Research Group, Department of Medical and Sport Sciences, University of Cumbria,
12 Bowerham Road, Lancaster, UK; lawrence.hayes@cumbria.ac.uk

13 ⁴ eCampus University, Novedrate, Italy; andrea.degiorgio@uniecampus.it

14 ⁵ Laboratory of Mobility, Aging and Exercise (MOVE) - EA 6314, Poitiers, France

15 * Correspondence: robertobragazzi@gmail.com

16 Received: date; Accepted: date; Published: date

17 **Abstract:** Hormones are secreted in a circadian rhythm, but also follow larger-scale timetables,
18 such as monthly (hormones of the menstrual cycle), seasonal (i.e. winter, summer), and, ultimately,
19 lifespan-related patterns. Several contexts modulate their secretion, such as genetics, lifestyle,
20 environment, diet, and exercise. They play significant roles in human physiology, influencing
21 growth of muscle, bone, and regulating metabolism. Exercise training alters hormone secretion,
22 depending on the frequency, duration, intensity, and mode of training which has an impact on the
23 magnitude of the secretion. However, there remains ambiguity over the effects of exercise training
24 on certain hormones such as glucoregulatory hormones in aging adults. With advancing age, there
25 are many alterations with the endocrine system, which may ultimately alter human physiology.
26 Some recent studies have reported an anti-aging effect of exercise training on the endocrine system
27 and especially testosterone, cortisol, growth hormone and insulin. As such, this review examines
28 the effects of endurance, interval, resistance and combined training on hormones (i.e., at rest and
29 after) exercise in older individuals. We summarize the influence of age on relevant hormones, the
30 influence of exercise training, and where possible, examine masters' athletes' endocrinological
31 profile.

32 **Keywords:** glucose; insulin; cortisol; growth hormone; physical activity; advanced age and
33 senescence

35 1. Introduction

36 The ageing process is accompanied by one or more changes in biological functions (affecting
37 nervous system, cardiovascular and respiratory systems, or renal function, amongst others), often
38 associated with an increasing susceptibility to co-morbidities and mortality [1,2].

39 According to the World Health Organization (WHO), three categories of population can be
40 distinguished: "young old" (65-74 years old), "middle aged" (75-84) and the oldest (85+). Generally,
41 ageing leads to an overall loss of tissue vitality through a myriad of signaling mechanisms [3].

42 The anatomical and physiological changes associated with ageing start several years before the
43 appearance of external signs. Many of these alterations gradually manifest in the third decade and
44 continue until death. These changes are also accompanied by a gradual decline in physical fitness

45 and physical activity. This alteration of the cardiovascular and respiratory systems during the
46 ageing process can be mainly explained by a decline in maximum oxygen uptake (~10% per decade)
47 starting from the age of 20 [4-7].

48 Advancing age is also associated with a decline in anaerobic performance, which can be mainly
49 explained by changes involving the neuromuscular system and a major loss in type II fibers. Indeed,
50 advanced age is accompanied by muscular wasting, a decrease in the rate of contraction, and
51 maximum force.

52 According to Korhonen et al. [8], the first decline in muscle strength and volume (consider
53 using mass instead of volume) occurs around the age of 30 and the loss is around 15% *per* decade
54 from the age of 50 to 30% at the age of 70. Moreover, literature suggests that starting from the 4th
55 decade of life both skeletal muscle mass and strength decline in a linear fashion and within the 8th
56 decade of life the 50% of mass will be lost [9]. Since the muscle mass amount to 60% of body mass, its
57 pathologic changes can have deep consequences in elderly.

58 One hypothesis for the reduction in physical performance and muscle weakness associated
59 with age is an alteration of the endocrine system [10-14]. In particular, the glucoregulatory system
60 that is characterized by important molecules such as L-glucose, glucagon, and insulin is critical to
61 maintain the constancy of glucose in the internal milieu. It is clear that exercise training improves
62 fitness and physical capacity in older adults [15-19], whether exercise can improve hormonal profiles
63 of older adults remains contentious [20-27].

64 Therefore, this review will summarize the existing literature concerning the influence of age,
65 and the influence of each mode of exercise (endurance, sprint, and resistance training) on relevant
66 (basal) hormones, especially those belonging to the glucoregulatory system.

67 Where possible, we will provide evidence from masters athletes involving the influence of
68 lifelong exercise on these hormones, but also report findings from intervention studies providing
69 information on the training effect on these hormones.

70 2. Materials and Methods

71 The present review was designed as a comprehensive review of the literature. Search strategy
72 adopted in the present review is summarized in Table 1.

73 **Table 1.** Search strategy adopted in the present comprehensive review of the literature for retrieving
74 studies investigating the effects of physical activity and exercise on glucoregulatory hormones in
75 elderly subjects.

Search strategy item	Details
Search string	(old OR elderly OR effect of age OR ageing OR aging) AND (physical activity OR sport OR exercise OR training) AND (insulin OR glucagon OR growth hormone OR IGF-1 OR glucoregulatory hormones OR cortisol OR catecholamines)
Searched databases	PubMed/MEDLINE, Scopus, ISI/Web of Science
Inclusion criteria	P: older subjects in good health I: exposure to physical activity interventions C: young subjects (both trained and untrained) and old untrained subjects O: changes in glucoregulatory hormones levels S: original, primary research article
Exclusion criteria	P: young subjects; old frail subjects or with diseases (diabetes, obesity) I: not exposed to physical activity / sports /exercise interventions or exposed to combined interventions (dietary intervention, supplementation, pharmacological treatment or other forms of manipulation) from which it

	was not possible to dissect the effect of training only
	C: absence of comparisons between age groups
	O: changes in glucoregulatory hormone levels not reported in detail or not clear
	S: not original study
Time filter	None applied (from inception)
Language filter	None applied (any language)

76

77 3. Insulin, Ageing and Physical Activity

78 Insulin plays a key role in glucose uptake by muscle, fat, and liver cells. Moreover, insulin
79 inhibits both the liver glucose production and its secretion in blood.

80 Recent reports suggest that the insulin/insulin-like growth factor-1 (IGF-1) signaling pathways
81 and signaling cascades have an important, evolutionarily conserved influence over rate of aging
82 and, thus, longevity [28]. The most important effects of advancing age on this hormone are the
83 increase of fasting insulin and decrease in insulin sensitivity [29,30].

84 Many studies examined the effect of different training modes, volumes and intensities on
85 insulin levels in older adults. From the available investigations, it appears that short-term (2 weeks)
86 training was unable to reduce fasting insulin level in a group of 28 healthy middle-aged (40-55 years)
87 sedentary men, as shown by Heiskanen and coauthors [31]. More in detail, a program of six
88 supervised cycle ergometer training sessions, characterized either by high-intensity (n = 14; 4-6 × 30 s
89 all-out cycling/4-min recovery) or moderate-intensity continuous (n = 14; 40-60 min at 60% peak O₂
90 uptake) training did not affect fasting insulin concentration.

91 In contrast, Kirwan et al. [32] reported that 9 months of endurance training reduced fasting
92 insulin and improved insulin action. Seals and colleagues [33] (12 months of endurance training
93 program), Kahn and coworkers [34] (6 months of intensive endurance exercise program), Evans and
94 coauthors [35] (10-12 months of endurance training program) reported similar results. Therefore, it
95 appears that an intervention with longer duration (e.g., from 6 up to 9-12 months) is required to
96 observe significant changes in fasting insulin in older adults. On the other hand, some studies
97 investigating the effects of 6/9-month training programs, such as the investigation by Goulet et al.
98 [36], Dipietro and coworkers [37] or Ihalainen and collaborators [38] failed to report beneficial
99 changes in insulin concentration.

100 The length of the training program seems to have an impact on insulin (in terms of levels or
101 activity) depending on the age group in which the intervention is carried out. Herbert et al. [23]
102 reported a moderate decrease in basal insulin following 6 weeks of high-intensity interval training
103 (HIIT) in sedentary older males, suggesting that sprint training can reduce fasting insulin in older
104 adults. Guezennec et al. [39,40] had investigated the impact of 4 months of weight lifting in athletes
105 aged ~35 years old. After maximal sessions, the level of insulin did not change significantly.

106 Other studies examined the effect of resistance training in insulin sensitivity in elderly subjects
107 and reported that strength training induced improvement in insulin-stimulated glucose uptake
108 promoted by glucose transporter type 4 (GLUT-4) in elderly [41]. Further studies investigated the
109 influence of 12 weeks of high resistance training (weight lifting program) in the elderly and observed
110 decreased insulin response [42].

111 Furthermore, when comparing young and middle-aged men, Sellami et al. [43] investigated the
112 impact of 13 weeks of combined sprint and strength training on insulin concentration in blood. They
113 reported a significant decrease in fasting insulin in both groups. Interestingly, the effect of age that
114 was evident at baseline was no longer present post-training, suggesting that combined sprint and
115 strength training can prevent the negative effects of aging in trained men [43].

116 From a molecular standpoint, it seems that lifelong regular physical activity leads to epigenetic
117 mechanisms in terms of global DNA methylation patterns positively impacting on skeletal muscles'
118 functioning in aged healthy individuals. One study has recently found that DNA methylation was
119 statistically significantly lower in 714 promoters of genes involved in glycogen metabolism,

glycolysis, oxidative stress resistance and muscle contraction activity and myogenesis, whereas methylation of introns, exons and CpG islands was apparently independent of physical activity practice [38]. Other cellular mechanisms that can explain how exercise can mitigate the mandatory age-related change in insulin levels include GLUT expression and translocation, skeletal muscle capillarization, improving insulin activity and sensitivity and favoring glucose uptake [42,44-52].

Even if short-term training cannot effect insulin levels, it seems to be sufficient in improving or at least preserving insulin secretion pattern and response to oral glucose load. Some studies have, indeed, shown that a single bout of high intensity intermittent exercise [53], a couple of bouts of exercise [54,55] or light-/moderate-intensity physical activity [56-60] can be sufficient in preserving insulin activity and response to oral glucose tolerance test (OGTT).

In other studies, the physical activity level (trained versus untrained) was self-reported and assessed through the administration of questionnaires [61-65] or *via* quantitative measurements, such as accelerometer [59]. Some studies included in the present comprehensive review were high-quality randomized or pseudo-randomized studies [66-68].

Summarizing (Table 2), based on the available studies, it appears that ageing is associated with an increase of insulin level, a major part of this improvement can be counteracted by exercise training. Exercise is, indeed, a full mediator of the relationship between inactivity time sedentary behaviors and insulin resistance [69]. Exercise, especially long-term (i.e., 12-24 weeks and not less than 8-10 weeks) [70-72] endurance, resistance and multimodal/combined training [73,74] or short-term (i.e., bouts or 6 weeks of HIIT) [75-77] training program, can positively impact on insulin levels [78], even though existing scholarly findings are not so clear-cut and warrant further investigations.

Table 2. Studies investigating the effects of physical activity and exercise on insulin in elderly subjects.

Authors	Stud y Year	Sample Size	Age	Gender	Intervention	Main findings
Seals et al. [33]	1984	11	63 ± 1 y	Male and female	12-mo endurance training (low- versus high-intensity program)	Improved insulin sensitivity and reduction in total AUC for insulin by 8-23% (by 8% after the low-intensity training program and by 23% after the high-intensity training program)
Seals et al. [61]	1984	12	62 ± 1 y	Male	Self-reported physical activity	Lean older subjects had similar insulin levels when compared to younger subjects and statistically lower than the

Hollenbeck et al. [62]	1985	20 (13 inactive versus 7 active subjects)	60-75 y	Male	Self-reported physical activity level	older untrained individuals Better insulin resistance profile in older trained subjects
Craig et al. [42]	1989	9 (cases versus 6 young controls)	62.8 ± 0.7 y	Male	12 w of progressive high resistance training (weight lifting program with a three set, six-eight repetition protocol: 45-- 60 min of isotonic weight-conditioning exercise on Nautilus equipment and leg press, leg extension, leg curl, torso extension, bench press, pull down, pull over and horizontal arm adduction)	Reduction in insulin levels (from 381.18 ± 56.1 to 257.0 ± 32.3)
Tonino [70]	1989	11	60-80 y	Male	12 w of physical training	Decrease in peripheral insulin resistance
Kahn et al. [34]	1990	13	61-82 y	Male	6 mo of intensive endurance exercise training	Decrease of insulin levels (from 61 ± 6 to 48 ± 6 pM, p <0.01) Increase of insulin sensitivity by 36% from 3.47 ± 0.41 to 4.71 ± 0.42 10 ⁻⁵ min ⁻¹ /pM (p = 0.01)
Broughton et al. [63]	1991	13 (cases versus 14 young controls)	60 y and older	Male	Self-reported physical activity level	No significant differences
Poehlman and Danforth [71]	1991	19	64 ± 1.6 y	Male	8-w endurance training program (cycling exercise)	No changes in insulin levels
Kirwan et al. [32]	1993	12	65 ± 1 y [60-70 y]	Male	9 mo of endurance training	Reduction in fasting insulin (from 36 ± 6 μU/mL to 26 ± 5 μU/mL) Improved insulin activity

Cononie et al. [75]	1994	9	60-80 y	Male	Seven days of 50 minutes of exercise at 70% VO _{2max}	Fasting plasma insulin levels and plasma insulin responses to an oral glucose challenge were reduced by 15% and 20%
DiPietro et al. [60]	1998	16 (7 of which serving as controls)	73 ± 1 y	Male and female	Moderate-intensity aerobic training, 4 times a w for 60-min sessions	Improvement in insulin resistance and glucose tolerance
Chadan et al. [54]	1999	7	62-69 y	Female	Four bouts of physical activity on separate occasions at either a low (heart rate = 100 bpm) or moderate intensity (heart rate = 120 bpm) for either 25 or 50 min	Decrease by 35% in all experimental conditions
Evans et al. [35]	2005	10	80.3 ± 2.5 y, 77-87 y	Male (n = 8) and female (n = 2)	10-12 mo program (for a total of 108 exercise sessions) consisting in a supervised endurance exercise training comprising of 2.5 sessions/w (SD 0.2), 58 min/session (SD 6), at an intensity of 83% (SD 5) of peak heart rate	Improvement in insulin activity
Goulet et al. [36]	2005	8 versus 14 younger controls	62.3 ± 4.7 y	Female	Aerobic training (25-60 min sessions of running at 60-95% of maximal heart rate) 3 d per w during 6 mo, with insulin resistance measured 3-5 d after the last training bout	No improvement in insulin resistance
DiPietro et al. [66]	2006	25	73 ± 10 y	Female	Random allocation to high-intensity [80% peak aerobic capacity (VO _{2peak})] aerobic training, moderate-intensity (65% VO _{2peak}) aerobic training, and low-intensity (stretching) placebo control (50% VO _{2peak}) groups	Significant improvements only in the high-intensity training group
Bassami	2007	13	60 y	Male	Three 30 min trials on a	No significant

et al. [76]			and older	cycle ergometer at 50, 60 and 70% VO_{2max} and two other trials at 60 and 70% VO_{2max} in which the total energy expenditure was equal to that for 30 min at 50% VO_{2max}	differences between groups	
Fujita et al. [55]	2007	13	70 ± 2 y	Male (n = 10) and female (n = 3)	Bout of aerobic exercise (45-min treadmill walk, 70% heart rate max)	Improvement in insulin resistance
Kodama et al. [56]	2007	56	64 ± 6 y	Male (n = 14) and female (n = 42)	Low-intensity and low-volume exercise training (12-w exercise program, comprising aerobic training and resistance training)	Decrease in insulin resistance by 21%
Dipietro et al. [37]	2008	20	74 ± 5 y	Female	Random allocation into a high-volume, moderate-intensity aerobic (n = 12) and a lower-intensity resistance training (n = 8) groups 4 times per week for 45- to 60-min sessions over 9 months.	Not statistically significant changes in insulin levels in both groups (in the low-intensity exercise group decrease in basal insulin from 9.8 ± 4.5 to 8.1 ± 4.9 $\mu\text{U/mL}$, decrease in total insulin AUC from 8.3 ± 1.6 to 7.2 ± 2.4 $[(\mu\text{U/mL})/180 \text{ min}] \cdot 10^3$; in the moderate-intensity aerobic exercise group decrease in basal insulin from 9.3 ± 6.3 to 8.5 ± 5.5 $\mu\text{U/mL}$, increase in total insulin AUC from 7.3 ± 3.1 to 8.4 ± 3.0 $[(\mu\text{U/mL})/180 \text{ min}] \cdot 10^3$)

Dela et al. [72]	2011	60 y and older		Male and female	12 w of of alpine ski training	Decrease in insulin concentration, decreased insulin resistance
Lira et al. [57]	2011	70.32 ± 0.72 y		Male	Moderate training for 60 min/d, 3 d/w for 24 w at a work rate equivalent to the ventilatory aerobic threshold	Improvement in insulin concentration and insulin resistance
Mikkelsen et al. [64]	2013	27 versus 22 young controls		Male	Self-reported physical activity (n = 15 trained, n = 12 untrained)	Better insulin profile in trained subjects
Gando et al. [59]	2014	807		Male and female	Physical activity was measured using a triaxial accelerometer worn for 28 days and summarized as light intensity (1.1-2.9 METs) or moderate to vigorous intensity (≥ 3.0 METs)	Light physical activity inversely associated with insulin resistance
Hwang et al. [67]	2016	51 (16 of which serving as controls)	65 ± 1 y		Randomly allocated to high-intensity interval training (n = 17) or to moderate intensity continuous training (n = 18)	Insulin resistance decreased by 26% only in the high-intensity interval training group
Chen et al. [68]	2017	26	60-76 y	Male	Random allocation to the eccentric training or concentric training group (n = 13 per group), performing 30-60 eccentric or concentric contractions of knee extensors once a w. The intensity of the training program was progressively increased over a period of 12 w from 10% to 100% of maximal concentric strength for eccentric training and from 50% to 100% for the concentric training program	Statistically significant improvement of insulin sensitivity only after eccentric training
Herbert et al. [23]	2017	22 (cases) versus 17 (controls)	62 ± 2 y	Male	6 w of high-intensity interval training	Moderate reduction in insulin levels

Robinson et al. [73]	2017	26	60 y and older	Male (53.8%)	12 w of high-intensity aerobic interval, resistance, and combined exercise training	Increased insulin activity and sensitivity, with effects more marked in the high-intensity aerobic interval group
Banitalebi et al. [74]	2018	40 (12 of which serving as controls)	67.35 ± 1.40 y	Female	Random allocation to a resistance followed by endurance training program (n = 12), endurance training followed by resistance training (n = 12, interval resistance-endurance training (n = 12)	No differences among the groups and no difference between before and after the intervention
Lithgow and Leggate [53]	2018	14	64 ± 2 y		Single bout of high intensity intermittent exercise	Insulin concentration during an OGTT elevated at 60 min when compared to the control trial
McGregor et al. [58]	2018	1,454	65-79 y		Light-intensity physical activity and moderate-to-vigorous-intensity physical activity assessed during the Canadian Health Measures Survey	2,000 steps/day can be sufficient to preserve insulin activity and sensitivity
Park et al. [65]	2018	2,325	60-74 y	Male (n = 862) and female (n = 1,463)	Self-reported physical activity level	OR of developing insulin resistance 0.55 [95%CI 0.34-0.87] in men and 0.68 [95%CI 0.47-0.98] in women
Søgaard et al. [77]	2018	22	63 ± 1 y	Male (n = 11) and female (n = 11)	High-intensity interval training three times/w for 6 w on a bicycle ergometer	Statistically significant improved insulin sensitivity
Ihalainen et al. [38]	2019	92 randomly assigned to a group performing strength training one-, two-, or	65-75 y	Male and female	Whole-body strength training using 2-5 sets and 4-12 repetitions per exercise and 7-9 exercises per session for	No differences between groups and between before and after the intervention

three-times-per-week and a non-training control group

6 mo

Abbreviations: AUC (area under the curve); d (day); MET (metabolic equivalent task); min (minute); mo (month); OGTT (oral glucose tolerance test); SD (standard deviation); w (week); y (years).

3. IGF-1, Ageing and Physical Activity

The IGF1 gene is situated on the long arm of chromosome 12. IGF-I is an endocrine and autocrine/paracrine growth factor expressed by multiple cell types. It plays a key role in the growth of cells, muscle, cartilage, bone, skin, and controls cell growth. The concentration of IGF-1 in blood peaks around adolescence and then declines after middle-age. This reduction in anabolic hormones has been termed the 'somatopause', and is suggested as a mechanism for the process of aging.

Importantly, IGF-1 is implicated in skeletal and muscle function, which deteriorates with age. Eight weeks' endurance training increased systemic IGF-1 in ~66-year-old males by ~19% [79].

However, other studies failed to observe any change in IGF-I following six months' endurance training in ~67-year-old males. Herbert et al. [23] investigated the difference between endurance-trained master athletes (~60 years) and lifelong sedentary older adults (~62 years) and observed greater serum IGF-1 concentration in the trained compared to the sedentary subjects (~18.4 vs. ~13.1 ug/dl, respectively). Moreover, when inducting the sedentary individuals onto an endurance training program of 150 min/week, there was a small, non-significant increase in IGF-1 (~8% increase).

In addition, few studies explored the influence of sprint training on IGF-1 in older adults. Herbert et al. [23] observed that old (~62 years) sedentary subjects experienced a large increase in IGF-1 following 12 weeks' preconditioning and HIIT (~13.1 to ~16.9 ug/dl). Although 6 weeks' preconditioning of 150 min/week accounted for 8% of the change in IGF-1, HIIT was responsible for a further 21% increase (28% greater than baseline). Findings from the same study suggest a trivial change in IGF-1 post-HIIT in age-matched master athletes. Therefore, post-HIIT, the sedentary individuals and master athletes have IGF-1 concentrations that were not significantly different.

Furthermore, when looking the alteration of IGF-1 after resistance training in older adults, Parkhouse et al. [80] observed an increase in ~68 year old females circulating IGF-1. However, a recent investigation reported decreased systemic IGF-1 following 12 weeks' resistance training in older adults (74 ± 6 years) with an increase in lean mass [81].

As such, Arnason et al. [81] hypothesized that IGF-I was redistributed from circulation into tissue during periods of anabolism. As a result of the ambiguity in findings, the role of IGF-I in the adaptive process to exercise during middle and older age remains unclear. The majority of studies report that resistance training increases the concentration of IGF-1 in blood and increases muscle mass and function [82-97]. Yet, more longitudinal studies are needed to explore the influence of resistance training on IGF-1 in older adults, given also the presence of discrepancy among the findings.

In a recent study, Sellami et al. [43] investigated the influence of age on somatotrophic hormones. They observed that young males had greater serum IGF-1 concentration than middle-aged men. Moreover, Sellami et al. [43] reported that 13 weeks' combined sprint and resistance training increased circulating IGF-1 in middle-aged participants. Furthermore, the effect of age that was apparent at study commencement was abrogated post-training, suggesting exercise can counteract the effect of age on IGF-1 in middle-aged men.

Taken together (Table 3), these data suggest that HIIT, resistance and combined may be a countermeasure to the age- and lifestyle-related reduction in IGF-1 with advanced age, activating some gene pathways and protein cascades [98,99].

Table 3. Studies investigating the effects of physical activity and exercise on IGF-1 in elderly subjects.

Authors	Study Year	Sample Size	Age	Gender	Intervention	Main findings
Hagberg et al. [82]	1985	10 (cases versus 11 young trained subjects, 13 young sedentary subjects and 11 old trained subjects)	60-70 y	Male	Progressive VO _{2max} test and modified Balke protocol	No changes
Poehlman and Copeland [83]	1990	26 (cases versus 42 young controls)	59-76	Male	Self-reported physical activity level	IGF-1 level correlating with leisure time physical activity (r = 0.45; p < 0.01)
Poehlman et al. [84]	1994	18	66.1 ± 1.4 y	Male (n = 10) and female (n = 8)	8 w of endurance training	Increase in IGF-1 level by 14% from 76 ± 4.8 to 86 ± 5.6 n
Vitiello et al. [85]	1997	67	60 y and older	Male (n = 46) and female (n = 21)	Randomized allocation to 3 d/w, 6-mo endurance, stretching/flexibility groups and to 5 d/w, 6-mo endurance protocol	No differences among the different experimental groups and between before and after the exercise interventions
Bermon et al. [86]	1999	32	67-80 y	Male (n = 16) and female (n = 16)	Randomly allocated to habitual physical activity or to an 8-w strength training program	Increase in total and free IGF-1 levels immediately after exercise (by 17.7% and 93.8%) and at 6 hours after exercise (by 7.5% and +31.2%)
Bonnefoy et al. [87]	1999	39	66-84 y	Male (n = 14) and female (n = 25)	Acute and chronic exercise (in a period of 6 mo) evaluated using a self-administered questionnaire	IGF-1 levels correlated with sports activity
Chadan et al.	1999	7	62-69	Female	Four bouts of	No differences

[54]			y		physical activity on separate occasions at either a low (heart rate = 100 bpm) or moderate intensity (heart rate = 120 bpm) for either 25 or 50 min	among the different experimental conditions
Ravaglia et al. [88]	2001	48	60 y and older	Male	Self-reported physical activity: active (n = 24) and inactive (n = 24)	Higher IGF-1 levels in active men
Borst et al. [89]	2002	62	68.1 y	Male and female	Randomly allocated to 6-mo, 3-d/w program of low-intensity or high-intensity resistance training programs	No changes
Dennis et al. [90]	2008	16 versus 15 young controls	72 ± 5 y	Male	Acute resistance exercise	Higher levels of IGF-1 and IGFBP5 in younger subjects, especially after acute resistance exercise
Tsai et al. [91]	2015	48 (24 of which serving as controls)	71.40 ± 3.79 y (65-79 y)	Male	Long-term resistance exercise	Increase in IGF-1 levels
Maass et al. [92]	2016	40	60-77	Male	Pseudo-random allocation to aerobic exercise group (indoor treadmill, n=21) or to a control group (indoor progressive-muscle relaxation/stretching, n=19)	No changes
de Gonzalo-Calvo et al. [93]	2012	26 (active, n = 13, inactive, n = 13)	65 y and older	Male	49 ± 8 y of long-life training	Increase in IGF-1 concentration correlating with physical activity
Arnarson et al. [81]	2015	235	73.7 ± 5.7 y	Male (41.8%) and female (58.2%)	12-w resistance exercise program (3 times/w; 3 sets, 6-8 repetitions at 75-80% of the 1-repetition maximum)	Decrease in IGF-1 levels (from 112.1 ± 35.6 to 106.1 ± 35.2 µg/L)

Herbert et al. [23]	2017	22 (cases) versus 17 (controls)	62 ± 2 y	Male	12 w of preconditioning and 6 w of high-intensity training	Increase compared to baseline, from 13.1 ± 4.7 mg/dl to 16.9 ± 4.4 (29% increase; p = 0.002, Cohen's d = 0.85) and compared to preconditioning (21% increase; 14.2 ± 6.0 mg/dl [p = 0.005, Cohen's d = 0.51]) Preconditioning accounted for 8% of the increase from baseline (p = 0.376, Cohen's d = 0.22)
Negaresh et al. [94]	2017	15 versus 16 younger controls	60 y and older	Male	8 w of resistance training	No change in IGF-1 levels after training
Yoon et al. [95]	2017	21	65-75 y	Female	Randomly allocated a low-intensity resistance training with heating sheet group (n = 8), a moderate-intensity resistance training (n = 6), and a heating sheet group (n = 7), over 12 weeks	Increased IGF-1 level
Banitalebi et al. [74]	2018	40	67.35 ± 1.40 y	Female	Randomized allocated to a resistance followed by endurance training (n = 12), endurance training followed by resistance training (n = 12, interval resistance-endurance training (n = 12) and a control (n = 12) groups	No differences among the groups and no difference between before and after the intervention
Cunha et al. [96]	2018	62 (21 of which serving as controls)	60 y and older	Female	Random allocation to a single set resistance training (n = 21) or multiple set resistance training (n = 20) programs, for 12 w using 8 exercises of	Increase in IGF-1 levels (by 7.1% in the single set resistance training group and by 10.1% in the multiple set

					10-15 repetitions maximum for each exercise	resistance training group)
Negaresh et al. [97]	2019	15	55-70 y	Male	Whole-body progressive resistance training program 3 days/week for 8 weeks (24 sessions	Increase in IGF-1 levels from 130.15 ± 22.23 to 138.11 ± 16.41

190 Abbreviations: mo (month); w (week); y (years).

191 **4. Growth Hormone, Ageing and Physical Activity**

192 Growth hormone (GH) secretion decreases with age, resulting in a downstream reduction in
 193 IGF-1 levels. This change, termed the somatopause, is associated with loss of vitality, muscle mass,
 194 physical function, and an increase risk of frailty, cardiovascular disease, and adiposity, amongst
 195 others [100].

196 Veldhuis et al. [101] showed that GH secretion during puberty varied between 1-1.5 mg/day,
 197 while elderly people can produce only 50 µg/day. Several factors may be responsible for this decline,
 198 such as physical inactivity, poor nutrition, and subsequent changes in body composition. Moreover,
 199 Khan et al. [102] found that GH pulse decreased, and this decline was related to the alteration of
 200 hypothalamic and somatostatin hormones.

201 Moreover, GH has a beneficial neuroprotective effect [103] mainly due to the activation of
 202 anti-apoptotic pathway [104], this one particularly studied in literature. GH is also able to act on
 203 BDNF and neurotrophin-3 (NT3) [103] which, in turn, are particularly sensitive to physical activity.

204 Till to date, there are no studies that have explored the impact of endurance training on GH in
 205 older adults. Deuschle et al. [105] studied 11 elderly male marathon runners compared to 10
 206 age-matched male sedentary people (control), in order to study plasma concentration of GH, total
 207 and free IGF-I/II and IGF-binding protein-1, 2, and 3 and insulin. In particular, authors did not found
 208 any differences between runner vs controls, except for IGF-binding protein-1 and 2 increased in
 209 runners.

210 Moreover, Vanhelder al. [106] found similar results with a group of men aged 24 – 54 yr who
 211 participated in resistance training for 1 year. The program was composed of 2 exercises (exercise
 212 protocol 1: vertical leg lifts at 85% of the subjects seven repetition maximum (SRM)/ exercise protocol
 213 2: vertical leg lifts with one third of the previously used load). The results showed that GH increased
 214 immediately after 5, 10, 25 min of exercise protocol 1. However, there was no significant increase
 215 after exercise protocol 2. These findings suggest that the frequency, duration of exercise play an
 216 important role in the regulation of GH secretion. Generally, the studies showed that the frequency
 217 and intensity of resistance training are important factors in the regulation of GH secretion.

218 Recently, Sellami et al. [43] reported that younger adults had greater GH at rest and in response
 219 to sprint exercise than middle-aged participants. However, 13 weeks of combined sprint and
 220 resistance training abrogated this age effect and increased GH at rest and post-exercise in both
 221 young and middle-aged participants.

222 Summarizing (Table 4), very few studies have investigated the effect of physical activity and
 223 training on GH levels in elderly subjects [74,107,108], generally reporting negative findings. Further
 224 studies are needed to elucidate the mechanism of exercise on GH.

225 **Table 4.** Studies investigating the effects of physical activities on growth hormone in elderly subjects.

Authors	Study Year	Sample Size	Age	Gender	Intervention	Main findings
Pyka et al. [107]	1992	11 versus 12	72 0.8 y	Male (n = 6) and female (n	3 sets of 8 repetitions for each of the 12 exercises, at 70% of	GH response to resistance exercise abolished/diminished

		younger controls		= 5)	1RM values	in elderly subjects
Cearlock and Nuzzo [108]	2001	9 versus 16 younger controls	60-85 y	Female	4 w exercise program followed by 1 w of no exercise	No changes
Banitalebi et al. [74]	2018	40 (12 of which serving as controls)	67.35 ± 1.40 y	Female	Random allocation to a resistance followed by endurance training program (n = 12), endurance training followed by resistance training (n = 12, interval resistance-endurance training (n = 12)	No changes

226

Abbreviations: w (week); y (years).

227

5. Glucagon, Glucagon-Like Peptide-1, Fetuin-A, Ageing and Physical Activity

228

Glucagon is a peptide hormone, belonging to the secretin family of hormones, produced and released by the alpha cells of the pancreas. Being the major catabolic hormone of the human body, it increases blood glucose and fatty acids concentration, differently from insulin [109].

229

230

231

232

233

Of note, no studies investigated the effect of physical activity on glucagon concentration in elderly subjects, with the exception of Hagberg and coworkers [82], who found no changes in trained older subjects, whereas untrained individuals reported increases in glucagon levels.

234

6. Cortisol, Ageing and Physical Activity

235

236

237

238

239

240

241

Cortisol, the primary stress hormone, is a steroid belonging to the glucocorticoid family, produced and released by the zona fasciculata of the adrenal cortex. This hormone plays a key role in controlling blood glucose and metabolism in general. Studies exploring the impact of age on cortisol have shown that cortisol increases with human aging. Seaton [110] reported that there was an elevation of nighttime cortisol levels in elderly individuals and this increase could be caused by stressful factors such as insomnia. Our laboratory has demonstrated that middle-aged men have higher basal cortisol concentrations than young men [111].

242

243

244

245

246

247

248

249

There are only few studies which have examined the effect of exercise training on cortisol in elderly subjects. Herbert et al. [23] investigated the difference between lifelong sedentary and endurance-trained master athletes and observed no difference in basal cortisol. Moreover, when inducting the sedentary individuals onto an endurance training program of 150 min/week, there was no alteration to basal cortisol. Similarly, De Souza Vale et al. [112] investigated the effect of three months' water aerobics training in elderly women and reported no alteration to basal cortisol. However, an increase in cortisol following 6 weeks' HIIT in master athletes has been observed, with a concomitant increase in peak power output [23].

250

251

252

253

254

255

256

257

258

In middle-aged men, we have previously observed no alteration to basal cortisol following combined sprint and resistance training, however the acute cortisol response to a supramaximal sprint was elevated post-training [111].

Regarding the aging-related changes in the effect of exercise training on cortisol level, Kraemer et al. [113] compared the level of cortisol in young and older men after heavy resistance training 3 times per week for 10 weeks. Results showed a decline in resting cortisol at 3 and 10 weeks in the older group. However, Häkkinen et al. [114] reported that elderly subjects and middle-aged subjects did not experience any change in cortisol after six months' progressive resistance training. Similarly, Izquierdo et al. [115] investigated the effect of 16 weeks' progressive resistance training in older and

259 middle-aged participants and observed no change in cortisol in the middle-aged group, but a
260 decrease in the elderly group.

261 Summarizing, given the ambiguity of cortisol adaptation to resistance training, more research is
262 required to determine the effect of training variables (duration, intensity, volume, frequency) and
263 participant characteristics (age, training status, sex) on cortisol level.

264 7. Catecholamines, Ageing and Physical Activity

265 Catecholamine levels have been found to be different between young (20 years old) and
266 middle-aged men (40 years old), with plasma noradrenaline concentrations being significantly lower
267 ($p < 0.05$) in the young group when compared to the aged group. However, the precise
268 neurobiological mechanisms leading to this difference in concentration levels are not very
269 well-known and conflicting findings have been reported in the literature.

270 For instance, Hoeldtke et al. [116] showed that basal plasma noradrenaline concentration was
271 greater in the elderly due to age-affected sympathetic nervous activity or sensitivity to
272 sympatho-adrenal stimulation, without any difference in noradrenaline clearance. On the other
273 hand, other authors found that clearance of noradrenaline tends to diminish with advancing age,
274 which may contribute to the increased plasma concentrations observed.

275 Of note, no study has examined the effects of exercise training on catecholamines in older
276 adults. In fact, the majority of studies investigated the impact of different types of training (sprint,
277 endurance, resistance training) on catecholamine in young individuals [117–123]. Results were
278 found to be at variance, and most of the time it was concluded that duration, intensity and type of
279 training (aerobic and anaerobic) are the principal factors that induce alteration in catecholamine
280 responses.

281 A notable exception was the investigation carried out by Poehlman and Danforth [71], who
282 assessed the effects of 8 weeks of an endurance training program on norepinephrine kinetics in a
283 sample of 19 older persons aged 64 ± 1.6 yr. Resting concentrations of norepinephrine were found to
284 be increased by 24% after cycling exercise due to a 21% increase in norepinephrine appearance rate,
285 whereas no change in norepinephrine clearance could be detected.

286 As such, future studies are needed to determine the effect of different exercise training modes
287 and moderator variables on catecholamine secretion and catecholamine circulating concentration in
288 older adults.

289 8. Discussion and Future Prospects

290 There is an increased interest in exercise training as a therapeutic lifestyle strategy to attenuate
291 hallmarks of aging and improve health. Exercise training attenuates many markers of biological
292 aging and one of the underlying mechanisms may be through the promotion of a more 'youthful'
293 endocrine profile. *In vitro* experiments suggest that cells treated with plasma isolated from younger
294 individuals are healthier or more 'youthful' than those treated with plasma from their older peers.
295 Therefore, *in situ* cells exposed to a youthful systemic environment will likely have improved
296 functioning compared to those exposed to an older systemic environment. Evidence cited in this
297 review suggests that it is possible that exercise can act as a countermeasure to endocrinological
298 aging.

299 Regarding this last point, it is necessary to keep in mind that exist both similarities and
300 differences in aging between/within genders.

301 However, despite such increasing body of interest, the physiological effects of physical activity
302 and exercise on glucoregulatory hormones in elderly subjects is relatively understudied. Evidence of
303 the impact of training is generally circumstantial and randomized studies, carried out with high
304 methodological rigor and quality are few or lacking for some hormones. Whereas insulin has
305 captured the attention of scholars, there is a relative dearth of data and information for other
306 hormones.

307 Given the importance of the topic of counter-aging effect of sports and physical activity and
308 considering the epidemiological and clinical burden of aging and age-related disorders, more
309 attention in the field is needed. Longitudinal studies employing large sample sizes are warranted.

310 **Funding:** This research received no external funding.

311 **Conflicts of Interest:** The authors declare no conflict of interest.

312 References

- 313 1. Watad, A.; Bragazzi, N.L.; Adawi, M.; Amital, H.; Toubi, E.; Porat, B.S.; Shoenfeld, Y. Autoimmunity in the
314 Elderly: Insights from Basic Science and Clinics - A Mini-Review. *Gerontology* **2017**, *63*, 515-523.
- 315 2. Harman, S.M.; Metter, E.J.; Tobin, J.D.; Pearson, J.; Blackman, M.R. Longitudinal effects of aging on serum
316 total and free testosterone levels in healthy men. *J Clin Endocrinol Metab* **2001**, *86*, 724-731.
- 317 3. López-Otín, C.; Blasco, M.A.; Partridge, L.; Serrano, M.; Kroemer, G. The hallmarks of aging. *Cell* **2013**, *153*,
318 1194-217.
- 319 4. Fleg, J.L.; Lakatta, E.G. Role of muscle loss in the age-associated reduction in VO₂max. *J Appl Physiol* **1988**,
320 *65*, 1147-1151.
- 321 5. Frontera, W.R.; Hughes, V.A.; Lutz, K.J.; Evans, W.J. A cross-sectional study of muscle strength and mass
322 in 45- to 78-yr-old men and women. *J Appl Physiol* **1991**, *71*, 644-50.
- 323 6. Gaitanos, G.C.; Williams, C.; Boobis, L.H.; Brooks S. Human muscle metabolism during intermittent
324 maximal exercise. *J Appl Physiol* **1993**, *75*, 712-719.
- 325 7. Evans, W.J. Effects of exercise on body composition and functional capacity of the elderly. *J Gerontol A Biol*
326 *Sci Med Sci* **1995**, *50*, 147-150.
- 327 8. Korhonen, M.T.; Cristea, A.; Alén, M.; Hakkinen, K.; Sipilä, S.; Mero, A.; Viitasalo, J.T.; Larsson, L.;
328 Suominen, H. Aging, muscle fiber type, and contractile function in sprint-trained athletes. *J Appl Physiol*
329 **2006**, *101*, 906-17.
- 330 9. Metter, E.J.; Conwit, R.; Tobin, J.; Fozard, J.L. Age-associated loss of power and strength in the upper
331 extremities in women and men. *J Gerontol A Biol Sci Med Sci* **1997**, *52*, B267-B276.
- 332 10. Augustin, H.; Adcott, J.; Elliott, C.J.H.; Partridge, L. Complex roles of myoglianin in regulating adult
333 performance and lifespan. *Fly (Austin)* **2017**, *11*, 284-289.
- 334 11. Elliott, B.T.; Herbert, P.; Sculthorpe, N.; Grace, F.M.; Stratton, D.; Hayes, L.D. Lifelong exercise, but not
335 short-term high-intensity interval training, increases GDF11, a marker of successful aging: a preliminary
336 investigation. *Physiol Rep* **2017**, *5*.
- 337 12. Sakuma, K.; Yamaguchi, A. Sarcopenia and age-related endocrine function. *Int J Endocrinol* **2012**, *2012*,
338 127362.
- 339 13. Sipilä, S.; Narici, M.; Kjaer, M.; Pöllänen, E.; Atkinson, R.A.; Hansen, M.; Kovanen, V. Sex hormones and
340 skeletal muscle weakness. *Biogerontology* **2013**, *14*, 231-45.
- 341 14. Kalampouka, I.; van Bekhoven, A.; Elliott, B.T. Differing Effects of Younger and Older Human Plasma on
342 C2C12 Myocytes in Vitro. *Front Physiol* **2018**, *9*, 152.
- 343 15. Bean, J.F.; Vora, A.; Frontera, W.R. Benefits of exercise for community-dwelling older adults. *Arch Phys*
344 *Med Rehabil* **2004**, *85*, 31-42.
- 345 16. Covey, A.; Jokl, P. Qualitative Performance of the Aging Athlete. *J Med Sci Tennis* **2009**, *14*, 5-15.
- 346 17. Galloway, M.T.; Jokl, P. Aging successfully: the importance of physical activity in maintaining health and
347 function. *J Am Acad Orthop Surg* **2000**, *8*, 37-44.
- 348 18. Chu, C.H.; Chen, A.G.; Hung, T.M.; Wang, C.C.; Chang, Y.K. Exercise and fitness modulate cognitive
349 function in older adults. *Psychol Aging* **2015**, *30*, 842-8.
- 350 19. Slimani, M.; Ramirez-Campillo, R.; Paravlic, A.; Hayes, L.D.; Bragazzi, N.L.; Sellami, M. The Effects of
351 Physical Training on Quality of Life, Aerobic Capacity, and Cardiac Function in Older Patients With Heart
352 Failure: A Meta-Analysis. *Front Physiol* **2018**, *9*, 1564.
- 353 20. Galbo, H. Endocrinology and metabolism in exercise. *Int J Sports Med* **1981**, *2*, 203-211.
- 354 21. Hayes, L.D.; Herbert, P.; Sculthorpe, N.F.; Grace, F.M. Exercise training improves free testosterone in
355 lifelong sedentary aging men. *Endocr Connect* **2017**, *6*, 306-310.
- 356 22. Morganti, C.M.; Nelson, M.E.; Fiatarone, M.A.; Dallal, G.E.; Economos, C.D.; Crawford, B.M.; Evans, W.J.
357 Strength improvements with 1 year of progressive resistance training in older women. *Med Sci Exerc* **1995**,
358 *27*, 906-12.

- 359 23. Herbert, P.; Hayes, L.D.; Sculthorpe, N.; Grace, F.M. High-intensity interval training (HIIT) increases
360 insulin-like growth factor-I (IGF-I) in sedentary aging men but not masters' athletes: an observational
361 study. *Aging Male* **2017**, *20*, 54-59.
- 362 24. Sellami, M.; Ben Abderrahman, A.; Kebsi, W.; De Sousa, M.V.; Zouhal, H. Effect of sprint and strength
363 training on glucoregulatory hormones: Effect of advanced age. *Experimental Biology and Medicine* **2017**, *242*,
364 113-123.
- 365 25. Hagberg, J.M.; Seals, D.R.; Yerg, J.E.; Gavin, J.; Gingerich, R.; Premachandra, B.; Holloszy, J.O. Metabolic
366 responses to exercise in young and older athletes and sedentary men. *J Appl Physiol* **1988**, *165*, 900-908.
- 367 26. Ronkainen, H.; Vakkuri, O.; Kauppila, A. Effects of physical exercise on the serum concentration of
368 melatonin in female runners. *Acta obstetricia et gynecologica Scandinavica* **1986**, *65*, 827-829.
- 369 27. Benelli, P.; Ditroilo, M.; Forte, R.; De Vito, G.; Stocchi, V. Assessment of post-competition peak blood
370 lactate in male and female master swimmers aged 40-79 years and its relationship with swimming
371 performance. *European Journal of Applied Physiology* **2007**, *99*, 685-693.
- 372 28. Morris, B.J.; Donlon, T.A.; He, Q.; Grove, J.S.; Masaki, K.H.; Elliott, A.; Willcox, D.C.; Willcox, B.J.
373 Association analyses of insulin signaling pathway gene polymorphisms with healthy aging and longevity
374 in Americans of Japanese ancestry. *J Gerontol A Biol Sci Med Sci* **2014**, *69*, 270-3.
- 375 29. Kusy, K.; Zieliński, J. Aging, aerobic capacity and insulin sensitivity in masters athletes: endurance and
376 speed-power training benefits. *Trends in Sport Sciences* **2014**, *21*.
- 377 30. Chang, A.M.; Halter, J.B. Aging and insulin secretion. *American Journal of Physiology-Endocrinology And*
378 *Metabolism* **2003**, *284*, E7-E12.
- 379 31. Heiskanen, M.A.; Leskinen, T.; Heinonen, I.H.; Löyttyniemi, E.; Eskelinen, J.J.; Virtanen, K.; Hannukainen,
380 J.C.; Kalliokoski, K.K. Right ventricular metabolic adaptations to high-intensity interval and
381 moderate-intensity continuous training in healthy middle-aged men. *Am J Physiol Heart Circ Physiol* **2016**,
382 *311*, H667-75.
- 383 32. Kirwan, J.P.; Kohrt, W.M.; Wojta, D.M.; Bourey, R.E.; Holloszy, J.O. Endurance exercise training reduces
384 glucose-stimulated insulin levels in 60-to 70-year-old men and women. *J Gerontol* **1993**, *48*, M84-M90.
- 385 33. Seals, D.R.; Hagberg, J.M.; Hurley, B.F.; Ehsani, A.A.; Holloszy, J.O. Effects of endurance training on
386 glucose tolerance and plasma lipid levels in older men and women. *JAMA* **1984**, *252*, 645-9.
- 387 34. Kahn, S.E.; Larson, V.G.; Beard, J.C.; Cain, K.C.; Fellingham, G.W.; Schwartz, R.S.; Veith, R.C.; Stratton,
388 J.R.; Cerqueira, M.D.; Abrass, I.B. Effect of exercise on insulin action, glucose tolerance, and insulin
389 secretion in aging. *Am. J. Physiol.* **1990**, *258*, E937-43.
- 390 35. Evans, E.M.; Racette, S.B.; Peterson, L.R.; Villareal, D.T.; Greiwe, J.S.; Holloszy, J.O. Aerobic power and
391 insulin action improve in response to endurance exercise training in healthy 77-87 yr olds. *J. Appl. Physiol.*
392 **2005**, *98*, 40-5.
- 393 36. Goulet, E.D.; Mélançon, M.O.; Aubertin-Leheudre, M.; Dionne, I.J. Aerobic training improves insulin
394 sensitivity 72-120 h after the last exercise session in younger but not in older women. *Eur. J. Appl. Physiol.*
395 **2005**, *95*, 146-52.
- 396 37. Dipietro, L.; Yeckel, C.W.; Dziura, J. Progressive improvement in glucose tolerance following
397 lower-intensity resistance versus moderate-intensity aerobic training in older women. *J. Phys. Act. Health*
398 **2008**, *5*, 854-69.
- 399 38. Ihalainen, J.K.; Inglis, A.; Mäkinen, T.; Newton, R.U.; Kainulainen, H.; Kyröläinen, H.; Walker, S. Strength
400 Training Improves Metabolic Health Markers in Older Individual Regardless of Training Frequency. *Front*
401 *.Physiol.* **2019**, *10*, 32.
- 402 39. Guezennec, C.Y.; Giaoui, M.; Voignier, J.P.; Legrand, H.; Fournier, E. Evolution of plasma levels of LDH
403 (lactate dehydrogenase), CPK (creatine phosphokinase) and myoglobin at the end of a 100 km race and a
404 triathlon. *Science and Sports* **1986**, *1*, 255-63.
- 405 40. Guezennec, Y.; Leger, L.; Lhoste, F.; Aymonod, M.; Pesquies, P.C. Hormone and metabolite response to
406 weight-lifting training sessions. *Int J Sports Med* **1986**, *7*, 100-105.
- 407 41. Holten, M.K.; Zacho, M.; Gaster, M.; Juel, C.; Wojtaszewski, J.F.; Dela, F. Strength training increases
408 insulin-mediated glucose uptake, GLUT4 content, and insulin signaling in skeletal muscle in patients with
409 type 2 diabetes. *Diabetes* **2004**, *53*, 294-305.
- 410 42. Craig, B.W.; Everhart, J.; Brown, R. The influence of high-resistance training on glucose tolerance in young
411 and elderly subjects. *Mechanisms of aging and development* **1989**, *49*, 147-157.

- 412 43. Sellami, M.; Dhahbi, W.; Hayes, L.D.; Padulo, J.; Rhibi, F.; Djemail, H.; Chaouachi, A. Combined sprint and
413 resistance training abrogates age differences in somatotrophic hormones. *PLoS One* **2017**, *12*, e0183184.
- 414 44. Sailani, M.R.; Halling, J.F.; Møller, H.D.; Lee, H.; Plomgaard, P.; Pilegaard, H.; Snyder, M.P.; Regenberg, B.
415 Lifelong physical activity is associated with promoter hypomethylation of genes involved in metabolism,
416 myogenesis, contractile properties and oxidative stress resistance in aged human skeletal muscle. *Sci. Rep.*
417 **2019**, *9*, 3272.
- 418 45. Sharples, A.P.; Stewart, C.E.; Seaborne, R.A. Does skeletal muscle have an 'epi'-memory? The role of
419 epigenetics in nutritional programming, metabolic disease, aging and exercise. *Aging Cell* **2016**, *15*, 603-16.
- 420 46. Prior, S.J.; Goldberg, A.P.; Ortmeyer, H.K.; Chin, E.R.; Chen, D.; Blumenthal, J.B.; Ryan, A.S. Increased
421 Skeletal Muscle Capillarization Independently Enhances Insulin Sensitivity in Older Adults After Exercise
422 Training and Detraining. *Diabetes* **2015**, *64*, 3386-95.
- 423 47. Hildebrandt, W.; Schwarzbach, H.; Pardun, A.; Hannemann, L.; Bogs, B.; König, A.M.; Mahnken, A.H.;
424 Hildebrandt, O.; Koehler, U.; Kinscherf, R. Age-related differences in skeletal muscle microvascular
425 response to exercise as detected by contrast-enhanced ultrasound (CEUS). *PLoS One* **2017**, *12*, e0172771.
- 426 48. Richter, E.A.; Hargreaves, M. Exercise, GLUT4, and skeletal muscle glucose uptake. *Physiol. Rev.* **2013**, *93*,
427 993-1017.
- 428 49. Distefano, G.; Goodpaster, B.H. Effects of Exercise and Aging on Skeletal Muscle. *Cold Spring Harb.*
429 *Perspect. Med.* **2018**, *8*.
- 430 50. Bayol, S.A.; Bruce, C.R.; Wadley, G.D. Growing healthy muscles to optimise metabolic health into adult
431 life. *J. Dev. Orig. Health Dis.* **2014**, *5*, 420-34.
- 432 51. Ryan, A.S. Insulin resistance with aging: effects of diet and exercise. *Sports Med.* **2000**, *30*, 327-46.
- 433 52. Santos-Parker, J.R.; Santos-Parker, K.S.; McQueen, M.B.; Martens, C.R.; Seals, D.R. Habitual aerobic
434 exercise and circulating proteomic patterns in healthy adults: relation to indicators of healthspan. *J. Appl.*
435 *Physiol.* **2018**, *125*, 1646-1659.
- 436 53. Lithgow, H.M.; Leggate, M. The Effect of a Single Bout of High Intensity Intermittent Exercise on Glucose
437 Tolerance in Non-diabetic Older Adults. *Int. J. Exerc. Sci.* **2018**, *11*, 95-105.
- 438 54. Chadan, S.G.; Dill, R.P.; Vanderhoek, K.; Parkhouse, W.S. Influence of physical activity on plasma
439 insulin-like growth factor-1 and insulin-like growth factor binding proteins in healthy older women. *Mech.*
440 *Ageing Dev.* **1999**, *109*, 21-34.
- 441 55. Fujita, S.; Rasmussen, B.B.; Cadenas, J.G.; Drummond, M.J.; Glynn, E.L.; Sattler, F.R.; Volpi, E. Aerobic
442 exercise overcomes the age-related insulin resistance of muscle protein metabolism by improving
443 endothelial function and Akt/mammalian target of rapamycin signaling. *Diabetes* **2007**, *56*, 1615-22.
- 444 56. Kodama, S.; Shu, M.; Saito, K.; Murakami, H.; Tanaka, K.; Kuno, S.; Ajisaka, R.; Sone, Y.; Onitake, F.;
445 Takahashi, A.; Shimano, H.; Kondo, K.; Yamada, N.; Sone, H. Even low-intensity and low-volume exercise
446 training may improve insulin resistance in the elderly. *Intern. Med.* **2007**, *46*, 1071-7.
- 447 57. Lira, F.S.; Pimentel, G.D.; Santos, R.V.; Oyama, L.M.; Damaso, A.R.; Oller do Nascimento, C.M.; Viana,
448 V.A.; Boscolo, R.A.; Grassmann, V.; Santana, M.G.; Esteves, A.M.; Tufik, S.; de Mello, M.T. Exercise
449 training improves sleep pattern and metabolic profile in elderly people in a time-dependent manner.
450 *Lipids Health Dis.* **2011**, *10*, 1-6.
- 451 58. McGregor, D.E.; Carson, V.; Palarea-Albaladejo, J.; Dall, P.M.; Tremblay, M.S.; Chastin, S.F.M.
452 Compositional Analysis of the Associations between 24-h Movement Behaviours and Health Indicators
453 among Adults and Older Adults from the Canadian Health Measure Survey. *Int. J. Environ. Res. Public*
454 *Health* **2018**, *15*.
- 455 59. Gando, Y.; Murakami, H.; Kawakami, R.; Tanaka, N.; Sanada, K.; Tabata, I.; Higuchi, M.; Miyachi, M.
456 Light-intensity physical activity is associated with insulin resistance in elderly Japanese women
457 independent of moderate-to vigorous-intensity physical activity. *J. Phys. Act. Health* **2014**, *11*, 266-71.
- 458 60. DiPietro, L.; Seeman, T.E.; Stachenfeld, N.S.; Katz, L.D.; Nadel, E.R. Moderate-intensity aerobic training
459 improves glucose tolerance in aging independent of abdominal adiposity. *J. Am. Geriatr. Soc.* **1998**, *46*,
460 875-9.
- 461 61. Seals, D.R.; Hagberg, J.M.; Allen, W.K.; Hurley, B.F.; Dalsky, G.P.; Ehsani, A.A.; Holloszy, J.O. Glucose
462 tolerance in young and older athletes and sedentary men. *J. Appl. Physiol. Respir. Environ. Exerc. Physiol.*
463 **1984**, *56*, 1521-5.
- 464 62. Hollenbeck, C.B.; Haskell, W.; Rosenthal, M.; Reaven, G.M. Effect of habitual physical activity on
465 regulation of insulin-stimulated glucose disposal in older males. *J. Am. Geriatr. Soc.* **1985**, *33*, 273-7.

- 466 63. Broughton, D.L.; James, O.W.; Alberti, K.G.; Taylor, R. Peripheral and hepatic insulin sensitivity in healthy
467 elderly human subjects. *Eur. J. Clin. Invest.* **1991**, *21*, 13-21.
- 468 64. Mikkelsen, U.R.; Couppe, C.; Karlsen, A.; Grosset, J.F.; Schjerling, P.; Mackey, A.L.; Klausen, H.H.;
469 Magnusson, S.P.; Kjær, M. Life-long endurance exercise in humans: circulating levels of inflammatory
470 markers and leg muscle size. *Mech. Ageing Dev.* **2013**, *134*, 531-40.
- 471 65. Park, J.M.; Dong, J.J.; Lee, J.W.; Shim, J.Y.; Lee, Y.J. The relationship between employment status and
472 insulin resistance in the Korean elderly population. *Aging Clin. Exp. Res.* **2018**, *30*, 1385-1390.
- 473 66. DiPietro, L.; Dziura, J.; Yeckel, C.W.; Neuffer, P.D. Exercise and improved insulin sensitivity in older
474 women: evidence of the enduring benefits of higher intensity training. *J. Appl. Physiol.* **2006**, *100*, 142-9.
- 475 67. Hwang, C.L.; Yoo, J.K.; Kim, H.K.; Hwang, M.H.; Handberg, E.M.; Petersen, J.W.; Christou, D.D. Novel
476 all-extremity high-intensity interval training improves aerobic fitness, cardiac function and insulin
477 resistance in healthy older adults. *Exp. Gerontol.* **2016**, *82*, 112-9.
- 478 68. Chen, T.C.; Tseng, W.C.; Huang, G.L.; Chen, H.L.; Tseng, K.W.; Nosaka, K. Superior Effects of Eccentric to
479 Concentric Knee Extensor Resistance Training on Physical Fitness, Insulin Sensitivity and Lipid Profiles of
480 Elderly Men. *Front. Physiol.* **2017**, *8*, 209.
- 481 69. García-Hermoso, A.; Martínez-Vizcaíno, V.; Sánchez-López, M.; Recio-Rodriguez, J.I.; Gómez-Marcos,
482 M.A.; García-Ortiz, L.; EVIDENT Group. Moderate-to-vigorous physical activity as a mediator between
483 sedentary behavior and cardiometabolic risk in Spanish healthy adults: a mediation analysis. *Int. J. Behav.*
484 *Nutr. Phys. Act.* **2015**, *12*, 78.
- 485 70. Tonino, R.P. Effect of physical training on the insulin resistance of aging. *Am. J. Physiol.* **1989**, *256*, E352-6.
- 486 71. Poehlman, E.T.; Danforth, E. Jr. Endurance training increases metabolic rate and norepinephrine
487 appearance rate in older individuals. *Am. J. Physiol.* **1991**, *261*, E233-9.
- 488 72. Dela, F.; Niederseer, D.; Patsch, W.; Pirich, C.; Müller, E.; Niebauer, J. Glucose homeostasis and
489 cardiovascular disease biomarkers in older alpine skiers. *Scand. J. Med. Sci. Sports* **2011**, *21* Suppl 1, 56-61.
- 490 73. Robinson, M.M.; Dasari, S.; Konopka, A.R.; Johnson, M.L.; Manjunatha, S.; Esponda, R.R.; Carter, R.E.;
491 Lanza, I.R.; Nair, K.S. Enhanced Protein Translation Underlies Improved Metabolic and Physical
492 Adaptations to Different Exercise Training Modes in Young and Old Humans. *Cell Metab.* **2017**, *25*,
493 581-592.
- 494 74. Banitalebi, E.; Faramarzi, M.; Bagheri, L.; Kazemi, A.R. Comparison of performing 12 weeks' resistance
495 training before, after and/or in between aerobic exercise on the hormonal status of aged women: a
496 randomized controlled trial. *Horm. Mol. Biol. Clin. Investig.* **2018**, *35*.
- 497 75. Cononie, C.C.; Goldberg, A.P.; Rogus, E.; Hagberg, J.M. Seven consecutive days of exercise lowers plasma
498 insulin responses to an oral glucose challenge in sedentary elderly. *J. Am. Geriatr. Soc.* **1994**, *42*, 394-8.
- 499 76. Bassami, M.; Ahmadizad, S.; Doran, D.; MacLaren, D.P. Effects of exercise intensity and duration on fat
500 metabolism in trained and untrained older males. *Eur. J. Appl. Physiol.* **2007**, *101*, 525-32.
- 501 77. Søgaard, D.; Lund, M.T.; Scheuer, C.M.; Dehlbaek, M.S.; Dideriksen, S.G.; Abildskov, C.V.; Christensen,
502 K.K.; Dohlmann, T.L.; Larsen, S.; Vigelsø, A.H.; Dela, F.; Helge, J.W. High-intensity interval training
503 improves insulin sensitivity in older individuals. *Acta Physiol.* **2018**, *222*, e13009.
- 504 78. Conn, V.S.; Koopman, R.J.; Ruppert, T.M.; Phillips, L.J.; Mehr, D.R.; Hafdahl, A.R. Insulin Sensitivity
505 Following Exercise Interventions: Systematic Review and Meta-Analysis of Outcomes Among Healthy
506 Adults. *J. Prim. Care Community Health* **2014**, *5*, 211-22.
- 507 79. Poehlman, E.T.; Dvorak, R.V.; DeNino, W.F.; Brochu, M.; Ades, P.A. Effects of resistance training and
508 endurance training on insulin sensitivity in nonobese, young women: a controlled randomized trial. *J Clin*
509 *Endocrinol Metab* **2000**, *85*, 2463-2468.
- 510 80. Parkhouse, W.S.; Coupland, D.C.; Li, C.; Vanderhoek, K.J. IGF-1 bioavailability is increased by resistance
511 training in older women with low bone mineral density. *Mechanisms of aging and development* **2000**, *113*,
512 75-83.
- 513 81. Arnarson, A.; Gudny Geirsdottir, O.; Ramel, A.; Jonsson, P.V.; Thorsdottir I. Insulin-Like Growth Factor-1
514 and Resistance Exercise in Community Dwelling Old Adults. *J Nutr Health Aging* **2015**, *19*, 856-60.
- 515 82. Hagberg, J.M.; Seals, D.R.; Yerg, J.E.; Gavin, J.; Gingerich, R.; Premachandra, B.; Holloszy, J.O. Metabolic
516 responses to exercise in young and older athletes and sedentary men. *J. Appl. Physiol.* **1988**, *65*, 900-8.
- 517 83. Poehlman, E.T.; Copeland, K.C. Influence of physical activity on insulin-like growth factor-I in healthy
518 younger and older men. *J. Clin. Endocrinol. Metab.* **1990**, *71*, 1468-73.

- 519 84. Poehlman, E.T.; Rosen, C.J.; Copeland, K.C. The influence of endurance training on insulin-like growth
520 factor-1 in older individuals. *Metabolism* **1994**, *43*, 1401-5.
- 521 85. Vitiello, M.V.; Wilkinson, C.W.; Merriam, G.R.; Moe, K.E.; Prinz, P.N.; Ralph, D.D.; Colasurdo, E.A.;
522 Schwartz, R.S. Successful 6-month endurance training does not alter insulin-like growth factor-I in healthy
523 older men and women. *J. Gerontol. A Biol. Sci. Med. Sci.* **1997**, *52*, M149-54.
- 524 86. Bermon, S.; Ferrari, P.; Bernard, P.; Altare, S.; Dolisi, C. Responses of total and free insulin-like growth
525 factor-I and insulin-like growth factor binding protein-3 after resistance exercise and training in elderly
526 subjects. *Acta Physiol. Scand.* **1999**, *165*, 51-6.
- 527 87. Bonnefoy, M.; Kostka, T.; Patricot, M.C.; Berthouze, S.E.; Mathian, B.; Lacour, J.R. Influence of acute and
528 chronic exercise on insulin-like growth factor-I in healthy active elderly men and women. *Aging* **1999**, *11*,
529 373-9.
- 530 88. Ravaglia, G.; Forti, P.; Maioli, F.; Pratelli, L.; Vettori, C.; Bastagli, L.; Mariani, E.; Facchini, A.; Cucinotta, D.
531 Regular moderate intensity physical activity and blood concentrations of endogenous anabolic hormones
532 and thyroid hormones in aging men. *Mech. Ageing Dev.* **2001**, *122*, 191-203.
- 533 89. Borst, S.E.; Vincent, K.R.; Lowenthal, D.T.; Braith, R.W. Effects of resistance training on insulin-like growth
534 factor and its binding proteins in men and women aged 60 to 85. *J. Am. Geriatr. Soc.* **2002**, *50*, 884-8.
- 535 90. Dennis, R.A.; Przybyla, B.; Gurley, C.; Kortebein, P.M.; Simpson, P.; Sullivan, D.H.; Peterson, C.A. Aging
536 alters gene expression of growth and remodeling factors in human skeletal muscle both at rest and in
537 response to acute resistance exercise. *Physiol. Genomics* **2008**, *32*, 393-400.
- 538 91. Tsai, C.L.; Wang, C.H.; Pan, C.Y.; Chen, F.C. The effects of long-term resistance exercise on the relationship
539 between neurocognitive performance and GH, IGF-1, and homocysteine levels in the elderly. *Front. Behav.*
540 *Neurosci.* **2015**, *9*, 23.
- 541 92. Maass, A.; Düzel, S.; Brigadski, T.; Goerke, M.; Becke, A.; Sobieray, U.; Neumann, K.; Lövdén, M.;
542 Lindenberger, U.; Bäckman, L.; Braun-Dullaeus, R.; Ahrens, D.; Heinze, H.J.; Müller, N.G.; Lessmann, V.;
543 Sendtner, M.; Düzel, E. Relationships of peripheral IGF-1, VEGF and BDNF levels to exercise-related
544 changes in memory, hippocampal perfusion and volumes in older adults. *Neuroimage* **2016**, *131*, 142-54.
- 545 93. de Gonzalo-Calvo, D.; Fernández-García, B.; de Luxán-Delgado, B.; Rodríguez-González, S.; García-Macia,
546 M.; Suárez, F.M.; Solano, J.J.; Rodríguez-Colunga, M.J.; Coto-Montes, A. Long-term training induces a
547 healthy inflammatory and endocrine emergent biomarker profile in elderly men. *Age* **2012**, *34*, 761-71.
- 548 94. Negaresh, R.; Ranjbar, R.; Habibi, A.; Mokhtarzade, M.; Fokin, A.; Gharibvand, M.M. The effect of
549 resistance training on quadriceps muscle volume and some growth factors in elderly and young men. *Adv.*
550 *Gerontol.* **2017**, *30*, 880-887.
- 551 95. Yoon, S.J.; Lee, M.J.; Lee, H.M.; Lee, J.S. Effect of low-intensity resistance training with heat stress on the
552 HSP72, anabolic hormones, muscle size, and strength in elderly women. *Aging Clin. Exp. Res.* **2017**, *29*,
553 977-984.
- 554 96. Cunha, P.M.; Nunes, J.P.; Tomeleri, C.M.; Nascimento, M.A.; Schoenfeld, B.J.; Antunes, M.; Gobbo, L.A.;
555 Teixeira, D.; Cyrino, E.S. Resistance Training Performed With Single and Multiple Sets Induces Similar
556 Improvements in Muscular Strength, Muscle Mass, Muscle Quality, and IGF-1 in Older Women: A
557 Randomized Controlled Trial. *J. Strength Cond. Res.* **2018**, in press.
- 558 97. Negaresh, R.; Ranjbar, R.; Baker, J.S.; Habibi, A.; Mokhtarzade, M.; Gharibvand, M.M.; Fokin, A. Skeletal
559 Muscle Hypertrophy, Insulin-like Growth Factor 1, Myostatin and Follistatin in Healthy and Sarcopenic
560 Elderly Men: The Effect of Whole-body Resistance Training. *Int. J. Prev. Med.* **2019**, *10*, 29.
- 561 98. Saghiv, M.S.; Sira, D.B.; Goldhammer, E.; Sagiv, M. The effects of aerobic and anaerobic exercises on
562 circulating soluble-Klotho and IGF-I in young and elderly adults and in CAD patients. *J. Circ. Biomark.*
563 **2017**, *6*, 1849454417733388.
- 564 99. Hand, B.D.; Kostek, M.C.; Ferrell, R.E.; Delmonico, M.J.; Douglass, L.W.; Roth, S.M.; Hagberg, J.M.;
565 Hurley, B.F. Influence of promoter region variants of insulin-like growth factor pathway genes on the
566 strength-training response of muscle phenotypes in older adults. *J. Appl. Physiol.* **2007**, *103*, 1678-87.
- 567 100. Sattler, F.R. Growth hormone in the aging male. *Best Pract Res Clin Endocrinol Metab* **2013**, *27*, 541-55.
- 568 101. Veldhuis, J.D.; Liem, A.Y.; South, S.; Weltman, A.; Weltman, J.; Clemmons, D.A.; Abbott, R.; Mulligan, T.;
569 Johnson, M.L.; Pincus, S. Differential impact of age, sex steroid hormones, and obesity on basal vs.
570 pulsatile growth hormone secretion in men as assessed in an ultrasensitive chemiluminescence assay. *J*
571 *Clin Endocrinol Metab* **1995**, *80*, 3209-3222.

- 572 102. Khan, A.S.; Sane, D.C.; Wannenburg, T.; Sonntag, W.E. Growth hormone, insulin-like growth factor-1 and
573 the aging cardiovascular system. *Cardiovascular Research* **2002**, *54*, 25-35.
- 574 103. Martinez-Moreno, C.G.; Fleming, T.; Carranza, M.; Ávila-Mendoza, J.; Luna, M.; Harvey, S.; Arámburo, C.
575 Growth hormone protects against kainate excitotoxicity and induces BDNF and NT3 expression in chicken
576 neuroretinal cells. *Exp Eye Res* **2018**, *166*, 1-12.
- 577 104. Sanders, E.J.; Parker, E.; Harvey, S. Growth hormone-mediated survival of embryonic retinal ganglion
578 cells: signaling mechanisms. *Gen Comp Endocrinol* **2008**, *156*, 613-621.
- 579 105. Deuschle, M.; Blum, W.F.; Frystyk, J.; Ørskov, H.; Schweiger, U.; Weber, B.; Körner, A.; Gotthardt, U.;
580 Schmider, J.; Standhardt, H.; Heuser, I. Endurance training and its effect upon the activity of the GH-IGFs
581 system in the elderly. *Int J Sports Med* **1998**, *19*, 250-254.
- 582 106. Vanhelder, W.; Radomski, M.W.; Goode, R.C. Growth hormone responses during intermittent weight
583 lifting exercise in men. *European journal of applied physiology and occupational physiology* **1984**, *53*, 31-34.
- 584 107. Pyka, G.; Wiswell, R.A.; Marcus, R. Age-dependent effect of resistance exercise on growth hormone
585 secretion in people. *J. Clin. Endocrinol. Metab.* **1992**, *75*, 404-7.
- 586 108. Cearlock, D.M.; Nuzzo, N.A. Effects of sustained moderate exercise on cholesterol, growth hormone and
587 cortisol blood levels in three age groups of women. *Clin. Lab. Sci.* **2001**, *14*, 108-11.
- 588 109. Jones, B.J.; Tan, T.; Bloom, S.R. Minireview: Glucagon in stress and energy homeostasis. *Endocrinology*
589 **2012**, *153*, 1049-54.
- 590 110. Seaton, K. Cortisol: the aging hormone, the stupid hormone. *Journal of the National Medical Association* **1995**,
591 *87*, 667.
- 592 111. Sellami, M.; Dhabbi, W.; Hayes, L.D.; Kuvacic, G.; Milic, M.; Padulo, J. The effect of acute and chronic
593 exercise on steroid hormone fluctuations in young and middle-aged men. *Steroids* **2018**, *132*, 18-24.
- 594 112. De Souza Vale, R.G.; de Oliveira, R.D.; Pernambuco, C.S.; da Silva Novaes, J.; de Andrade, A.D.F.D. Effects
595 of muscle strength and aerobic training on basal serum levels of IGF-1 and cortisol in elderly women.
596 *Archives of gerontology and geriatrics* **2009**, *49*, 343-347.
- 597 113. Kraemer, W.J.; Fleck, S.J.; Maresh, C.M.; Ratamess, N.A.; Gordon, S.E.; Goetz, K.L.; Harman, E.A.;
598 Frykman, P.N.; Volek, J.S.; Mazzetti, S.A.; Fry, A.C.; Marchitelli, L.J.; Patton, J.F. Acute hormonal
599 responses to a single bout of heavy resistance exercise in trained power lifters and untrained men.
600 *Canadian journal of applied physiology* **199**, *24*, 524-537.
- 601 114. Häkkinen, K.; Pakarinen, A.; Kraemer, W.J.; Newton, R.U.; Alen, M. Basal concentrations and acute
602 responses of serum hormones and strength development during heavy resistance training in middle-aged
603 and elderly men and women. *J. Gerontol. A Biol. Sci. Med. Sci.* **2000**, *55*, B95-105.
- 604 115. Izquierdo, M.; Häkkinen, K.; Ibañez, J.; Garrues, M.; Antón, A.; Zuñiga A.; Larrión, J.L.; Gorostiaga, E.M.
605 Effects of strength training on muscle power and serum hormones in middle-aged and older men. *J Appl*
606 *Physiol* **2001**, *90*, 1497-1507.
- 607 116. Hoeldtke, R.D.; Cilmi, K.M. (1985). Effects of aging on catecholamine metabolism. *J Clin Endocrinol Metab*
608 **1985**, *60*, 479-484.
- 609 117. Lacour, J.R.; Pequignot, J.M.; Geysant, A.; Coudert, J.; Peyrin, L. Effect of training on plasma levels of
610 catecholamines on the course of submaximal exercise. *J Physiol* **1983**, *78*, 838-842.
- 611 118. Winder, W.W.; Hagberg, J.M.; Hickson, R.C.; Ehsani, A.A.; McLane, J.A. Time course of sympathoadrenal
612 adaptation to endurance exercise training in man. *Journal of Applied Physiology* **1978**, *45*, 370-374.
- 613 119. Winder, W.W.; Hickson, R.C.; Hagberg, J.M.; Ehsani, A.A.; McLane, J.A. Training-induced changes in
614 hormonal and metabolic responses to submaximal exercise. *Journal of Applied Physiology* **1979**, *46*, 766-771.
- 615 120. Zouhal, H.; Jacob, C.; Delamarche, P.; Gratas-Delamarche, A. Catecholamines and the effects of exercise,
616 training and gender. *Sports Med* **2008**, *38*, 401-423.
- 617 121. Zouhal, H.; Jacob, C.; Rannou, F.; Gratas-Delamarche, A. Effect of training status on the sympathoadrenal
618 activity during a supramaximal exercise in human. *Journal of sports medicine and physical fitness* **2001**, *41*,
619 330.
- 620 122. Zouhal, H.; Gratas-Delamarche, A.; Rannou, F.; Granier, P.; Bentue-Ferrer, D.; Delamarche, P. Between 21
621 and 34 Years of Age, Aging Alters the Catecholamine Responses to Supramaximal Exercise in Endurance
622 Trained Athletes. *Int J Sports Med* **1999**, *20*, 343-8.
- 623 123. Zouhal, H.; Lemoine, S.; Mathieu, M.E.; Casazza, G.A.; Jabbour, G. Catecholamines and Obesity: Effects of
624 Exercise and Training. *Sports Med* **2013**, *43*, 591-600.



© 2019 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>).