MOOD, ANXIETY, AND SERUM IGF-1 IN ELDERLY MEN GIVEN 24 WEEKS OF HIGH RESISTANCE EXERCISE ¹

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As aging advances there are mood and anxiety changes may show greater risk of mood disorders (anxiety and depression). Resistance exercise reduces anxiety and lessens risk of depression in elderly, but little is known of the mechanisms involved. Was hypothesized that IGF-1 is an important growth factor in improving mood and anxiety for elderly participants given resistance training. 43 elderly men age 65 to 75 years, were randomly assigned to two groups, control (n=23) and high resistance exercise (n=20). After 24 weeks, the High Resistance Exercise Group showed improved muscular strength and higher IGF-1 serum levels than the Control Group, as mean better scores on a visual analogue mood scale and the trait-state anxiety inventory. One may conclude that intensive resistance training was efficacious in improving mood, anxiety, and IGF-1 serum concentration of in elderly individuals free of mood disorders.
Elderly people tend to present mood changes and are at greater risk of developing mood disorders and anxiety (van Gool, Kempen, Bosma, van Boxtel, Jolles, & van Eijk, 2007). Some 20% of the elderly population are affected by a mental health problem, dementia and depression being among the most prevalent (Abbott, White, Ross, Masaki, Curb, & Petrovitch, 2004). The U.S. National Comorbidity Survey Replication Sample (Kessler, Berglund, Demler, Jin, Koretz, Merikangas, et al., 2003) reported 16% prevalence of depression in the US man. Depression in this age group is often associated with cognitive and functional decline, lower quality of life, change in body mass, negative attitudes, and low adherence to pharmaceutical intervention, and also, becomes more severe when associated with a sedentary lifestyle (van Gool, Kempen, Penninx, Deeg, Beekman, & van Eijk, 2003).

However, some researchers have found an inverse association between the engagement in physical exercise and depression. Absence of depression in participants engaged in more than 30 minutes of physical exercise everyday was reported (van Gool, Kempen, Bosma, van Boxtel, Jolles, & van Eijk, 2007). The American College of Sports Medicine, (2006) recognized in their guidelines, also there was less anxiety and depression in older individuals engaged in physical exercise. Our own group has also researched the relation between physical activity with changes in mood profile and quality of life. Antunes, Stella, Santos, Bueno, & de Mello, (2005) assigned elderly participants men to moderate aerobic exercise over 24 week period. After the intervention, the group improved quality of life and lower scores on anxiety and depression than a Control Group, which remained sedentary during the intervention. Previous studies corroborate these findings (North, McCullagh, & Tran, 1990; Netz & Lidor, 2003).
Since exercise has a positive relationship with improved mood and
depression symptoms, it has gained increasing importance as an alternative
treatment, especially for depression (Thachil, Mohan, & Bhugra, 2007). Aerobic and
resistance exercise has stood out among the different types of exercise, since
depressed elderly patients in randomized clinical trials showed significant
improvement in depression (Singh, Clements, & Fiatarone, 1997; Blumenthal,
Babyak, Moore, Craighead, Herman, Khatri, et al., 1999). Singh, Stavrinos, Scarbek,
Galambos, Liber, & Fiatarone Singh, (2005) recently investigated the effect of eight
weeks of resistance training at two levels (low and high) of intensity on depression in
an elderly group. After intervention, 61% of patients who trained at high-intensity
showed more improvement than 29% the low-intensity group. Therefore high-
intensity training is apparently more efficacious than low-intensity resistance exercise
in treating older patients with depression. Moreover, previous studies indicated that
this form of high intensity exercise had a similar beneficial effect when compared
with traditional pharmacological intervention using antidepressants, thereby justifying
use exercise as antidepressant treatment (Singh, Clements, & Fiatarone, 1997;

In a recent study, McLafferty, Jr., Wetzstein, & Hunter, (2004) evaluated mood
profiles in elderly participants of both sexes, all free of mood disorders, and found
improvement on these aspects after 24 weeks of resistance exercise. One limitation
of their study was the absence of a Control Group to evaluate social interaction so
the reach of its conclusions is limiting.

Despite significant evidence that resistance exercise improves mood in elderly
participants with or without mood disorder, there are as yet no findings clarifying
mechanisms through which these changes operate. In addition to socialization and
attention paid to these participants, it appears there are biological factors associated
with the antidepressant effect, merit further attention. Resistance training may obtain
an antidepressant effect through direct and indirect mechanisms, including
neurotrofines and growth factors such as insulin-like growth factor (IGF-1). IGF-1 is a
major factor in signaling cascades of muscle hypertrophy via resistance training
(Roubenoff, 2000) and also is essential in neural events related to improved
cognitive functioning (Ding, Vaynman, Akhavan, Ying, & Gomez-Pinilla, 2006;
Cassilhas, Viana, Grassmann, Santos, Santos, Tufik, et al., 2007). Hoshaw,
Malberg, & Lucki, (2005) reported cerebral administration of IGF-1 had
antidepressant effects in rodents. A year earlier, Khawaja, Xu, Liang, & Barrett,
(2004) found that 2 weeks with fluoxetine (a selective serotonin reuptake inhibitor)
and venlafaxine (a dual serotonin and norepinephrine reuptake inhibitor) raised
hippocampal IGF-1 concentration; the hippocampus, as well as the prefrontal cortex
are important neuroanatomical structures involved in the etiology of clinical
depression (Nestler, Barrot, DiLeone, Eisch, Gold, & Monteggia, 2002).

It was hypothesized that IGF-1 is an important growth factor in improving
mood and anxiety of elderly persons given resistance training. Study IGF-1
concentration and mood in elderly participants given high-intensity resistance
training is needed. Also, a Control Group in which the confounding effects of
socialization of the elderly population may be diminished is highly desirable, so in
this study, mood, anxiety, and IGF-1 serum concentration were measured in elderly
men who were free of mood disorders after 24 weeks of high-intensity resistance
training.

METHOD

Participants
In this study, previously approved by the Research Ethics Committee of the Federal University of Sao Paulo (number 95/03), and published (Cassilhas, Viana, Grassmann, Santos, Santos, Tufik, et al., 2007) was composed by 43 sedentary elderly men age 65 to 75 years. All read and signed their Informed consent. They were randomly assigned to two groups, Control and High Resistance Exercise. The exclusion/ inclusion criteria were the presence of cardiovascular pathologies, pre-existing or diagnosed by clinical evaluation, psychiatric conditions (mood or anxiety disorders), use of psychotropic drugs, and those who attended less than 75% (54 training sessions) of 24 weeks of training (72 training sessions). In addition, the Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975) was administrated to exclude individuals with suspected dementia who scored 23 points or less (Almeida, 1998). These criteria were used to obtain a homogeneous sample and ensure the health and well being of these volunteers with respect to the intervention. Moreover, no exclusion or inclusion criteria were applied to the volunteers recruited.

Training procedure

Training consisted of 24 weeks of resistance training at the Psychobiology and Exercise Research Center, in an environment at 23°C±2 and air humidity 60%±2. The training model followed American College of Sports Medicine guidelines in relation to prescription and evaluation of resistance training for the elderly (American College of Sports Medicine, 2006).

Training sessions and tests were held at the same time of day (morning period), and exercises included covered the major muscle groups used in activities of daily living. Six exercises (chest press, leg press, vertical traction, abdominal crunch, leg curl and lower back) were on specific apparatus made by (Technogym®).
Two volunteers were assigned to each machine, so that they could train in
twos to ensure spotting and motivation. For safety reasons, the blood pressure of all
participants was measured at the beginning and end of all sessions. In addition, all
sessions were supervised by the principal researcher the study and other highly
specialized auxiliary professionals.

The Control Group was not subjected to overload training during the
intervention period; however, this group attended the research center once a week.
Its members were restricted to exercise without overloading, warm-up or stretching,
the same exercise procedure for the High Resistance Exercise Group (six alternating
exercise models followed by two sets of eight repetitions, with the same rest breaks).
This Control Group was justified by the aim of reducing the bias introduced by the
factors neuromotor learning and socialization, which may mask a real effect of
resistance training on the variables studied.

Training for the High Resistance Exercise Group consisted of three one hour
sessions per week on alternate days. At the beginning of each session, the group
was submitted to a brief warm-up of 10 minutes followed by stretching exercises.
Training overload was 80% of one repetition maximum (1RM), and the model used
alternated with two series of eight repetitions each, with rests for 1 minute and 30
seconds between them and 3 minutes between different equipments. During the
intervention, three 1RM tests were conducted to adjust suitable training overload at
Weeks 15, 18 and 21.

**Evaluation procedure**

**1RM test**

To measure muscle strength and obtain training overload, the 1RM test
recommendations proposed by Kraemer, Ratamess, Fry, & French, (2006) and Weir,
Wagner, & Housh, (1994) for all six apparatus, and 1RM tests were performed at the same time of day as training sessions but never during or after a training session. Before the first 1RM test and during the evaluation period (pre-intervention), the two groups (Control and High Resistance Exercise) were given three sessions to acquire familiarity with the six machines without overload. This was done to measure maximum strength each participant and eliminate learning of the test on each apparatus. For details of 1RM protocol, see (Cassilhas, Viana, Grassmann, Santos, Santos, Tufik, et al., 2007).

Mood and Anxiety Measurements

Mood and anxiety measurements were evaluated on four rating scales: (1) a visual analogue mood scale, developed by Norris, (1971) and used with Brazilian samples several times (Monteiro-dos-Santos, Graeff, dos-Santos, Ribeiro, Guimaraes, & Zuardi, 2000; Del Ben, Vilela, Hetem, Guimaraes, Graeff, & Zuardi, 2001; Silva, Hetem, Guimaraes, & Graeff, 2001). Consisted of 16 analogue items composed of two adjectives with opposite feelings, separated by a 10-cm line on which the subject has to mark the point which best described his feelings at the time. These items were combined into four factors (Anxiety: calm/excited, relaxed/tense, tranquil/troubled; Physical sedation: quick-witted/mentally-slow, proficient/incompetent, energetic/lethargic, clear-headed/muzzy, gregarious/withdrawn, well-coordinated/clumsy, strong/feeble; Mental sedation: alert/drowsy, attentive/dreamy; Other feelings and attitudes: interested/bored, amicable/antagonistic, happy/sad, contented/discontented) according to a factorial analysis performed on a Brazilian sample (Zuardi, Cosme, Graeff, & Guimaraes, 1993). (2) State-trait anxiety inventory (Spielberger, Gorsuch, & Lushene, 1970), provided operational measures of intensity of anxiety at a particular moment state
and of anxiety as a relatively stable personality trait. Each scale contains 20 items with 4 points. The rating scales were administered by a single professional between 8 h and 10 h for both the initial and post intervention evaluations.

**IGF-1 Measurement**

Volunteers fasted for 8h overnight, and a sample of preprandial venous blood was collected in the morning (8 to 8:30 a.m.). IGF-1 serum concentration was assigned using an immunoradiometric assay kit (DSL-5600) manufactured by (Diagnostics Systems Laboratories – DSL®), and a Gamma Counter, model C12, manufactured by (Diagnostic Products Corporation – DPC®) for the quantitative analysis of gamma radioactivity.

**Statistical Analysis**

The Statistica program for Windows® was applied for analysis of the variables. One-way ANOVA with Duncan *post hoc* test was used to evaluate homogeneity of variables for the groups prior to the intervention period. One-way analysis of variance was used for repeated measures (2 times x 2 groups) to estimate the effect of intervention periods, using a Duncan *post hoc* test. The minimum significance level was set at 5% (CI=95%), and data were presented as mean and standard deviation (SD). The Effect Size (ES) was defined as small, ES = 0.2 to 0.49; medium, ES = 0.5 to 0.79; and large, ES = 0.8 to 2.0 (Cohen, 1988).

**RESULTS**

Training session attendance was above 75% for 43 participants, and no one dropped out. No significant differences were detected across groups for the variables prior to the intervention period. In Table 1 are the initial data, which indicate the groups were statistically similar at the beginning of the study.
Compared to the Control Group, the High Resistance Exercise Group showed increased muscular strength on all six machines. The means are presented, respectively for Control Group and High Resistance Exercise Group, (chest press, 90.87, 95% CI, and 121, 95% CI; P<0.05; ES=1.52), (leg press, 246.09, 95% CI, and 356, 95% CI; P<0.05; ES=1.29), (vertical traction, 141.30, 95% CI, and 203, 95% CI; P<0.05; ES=1.03), (abdominal crunch, 60.65, 95% CI, and 94, 95% CI; P<0.05; ES=1.06), (leg curl, 88.91, 95% CI, and 131.50, 95% CI; P<0.05; ES=1.40), and (lower back, 102.39, 95% CI, and 147, 95% CI; P<0.05; ES=1.38) (Table 2).

Table 3 show the visual analogue mood scale scores for Anxiety, Physical Sedation, Mental Sedation and Other Feelings and Attitudes. After training, the High Resistance Exercise Group gave lower mean ratings than on to the initial measurements. This decrease in ratings by the High Resistance Exercise Group was more pronounced than those in the Control Group, which remained unchanged in (Anxiety: 61.08, 95% CI for Control Group and 56.18, 95% for High Resistance Exercise Group; P<0.05; ES=1.24), (Physical Sedation: 55.76, 95% CI for Control Group and 52.42, 95% for High Resistance Exercise Group; P<0.001; ES=1.08), (Mental Sedation: 54.95, 95% CI for Control Group and 53.13, 95% for High Resistance Exercise Group; P<0.001; ES=1.00), (Other Feelings and Attitudes: 54.28, 95% CI for Control Group and 52.89, 95% for High Resistance Exercise Group; P<0.001; ES=0.60).

At the end of the intervention, compared with the initial period, the High Resistance Exercise Group had lower means on State and Trait Anxiety Inventory. Compared with the Control Group, the mean decrease for the High Resistance Exercise Group held for both Trait and State Anxiety, (Trait Anxiety: 35.91, 95% CI for Control Group and 31, 95% for High Resistance Exercise Group; P<0.05;
ES=0.92), (State Anxiety: 35.17, 95% CI for Control Group and 28.95, 95% for High Resistance Exercise Group; P<0.05; ES=0.91) (Table 3). The IGF-1 serum concentration is in Table 3. The Exercise Group showed higher concentration after resistance training, and also when compared with values for the Control Group (IGF-1: 216.78, 95% CI for Control Group and 313.29, 95% for High Resistance Exercise Group; P<0.05; ES=0.68).

**DISCUSSION**

Resistance training has gained major importance for the scientific community over recent decades in light of its major benefits for health. Both young and elderly persons given resistance exercise have improved muscle strength and reported other positive changes in the muscle system (Fiatarone, Marks, Ryan, Meredith, Lipsitz, & Evans, 1990). Corroborating these classic studies, the present also showed an improvement in muscle strength for High Resistance Exercise Group on all machine exercises compared with the Control Group.

A number of other improvements are currently being attributed to resistance training for elderly. Tsutsumi, Don, Zaichkowsky, Takenaka, Oka, & Ohno, (1998) selected 36 sedentary older women ages 60 to 86 years and divided them into three groups: Control (n=12), Moderate Intensity Resistance Exercise (n=12), and High Intensity Resistance Exercise (n=12). The Exercise Groups had 12 weeks of resistance training in order to compare the effects of different training intensities on mood parameters. The Control Group was not engaged in training but was limited to their daily life activities. Researchers reported both Exercise Groups showed improved mood and anxiety in relation to Controls after intervention. In a recent study, McLafferty, Jr., Wetzstein, & Hunter, (2004) tested 28 sedentary elderly given resistance training at three times a week for 24 weeks, and evaluated their mood
profiles. One group trained at 80% of 1RM intensity and the other group trained at varying (50, 65 or 80%) of 1RM. After the intervention there was overall improvement in mood for the two Exercise Groups compared with the Control Group.

However, both studies have some important limitations, the most serious is not being Control Group for social interaction. In the present study, these limitations were addressed and the protocol used with the Control Group diminished the masking effect of socialization on the variables studied. After 24 weeks of intervention, the High Resistance Exercise Group showed improvement in mood as seen in lower means scores on all four analogue measures (Anxiety, Physical sedation, Mental Sedation and Other feelings and attitudes) compared with the pretraining means. In addition to this overall improved mood, the High Resistance Exercise Group was also less anxious after training than the Control Group and had lower means on Trait and State Inventory. This reflects an improvement in their anxiety profiles after 24 weeks of resistance training. Results similar to those found in studies conducted by Tsutsumi, Don, Zaichkowsky, Takenaka, Oka, & Ohno, (1998) and McLafferty, Jr., Wetzstein, & Hunter, (2004).

In elderly patients with clinical depression, Singh, Stavrinos, Scarbek, Galambos, Liber, & Fiatarone Singh, (2005) conducted an elegant randomized study submitting subjects to high-intensity (80% of 1RM) or low-intensity (20% of 1RM) resistance training for 8 weeks. After this period, there was an improvement in 61% of patients in the high-intensity training group compared with only 29% of patients in the low-intensity group. These results for elderly patients with depression match findings for the elderly persons who were free of mood disorders in the present study. High-intensity resistance training may have positive effects on mood and anxiety of elderly persons with or without clinical depression.
Despite the significant evidence that high-intensity resistance training improves the mood and anxiety of elderly people with or without mood disorders, the mechanisms through which these changes take place are as yet unknown. Two factors (socialization and attention paid to participants) were considered in this study by adding a Control Group. Therefore, the findings of improved mood and less anxiety cannot be attributed to these socialization factors alone. Perhaps there are biological factors associated with antidepressant effects through which exercise (in this case resistance training) improves mood and decreases anxiety. Perhaps resistance training achieves antidepressant action through mechanisms directly or indirectly related to IGF-1. The present study showed this growth factor was increased in High Resistance Exercise Group and this increased was significantly larger than the Control Group. To explain the association between IGF-1 and antidepressant effects, may consider data from Hoshaw, Malberg, & Lucki, (2005) who showed that cerebral administration of IGF-1 in rodents lead to antidepressant effects similar to those observed by antidepressant medications in humans. Moreover, Khawaja, Xu, Liang, & Barrett, (2004) found that chronic administration of fluoxetine and venlafaxine raised hippocampal IGF-1 concentration.

It seems resistance training for elderly participants free of mood disorders raises IGF-1 concentration peripherally and perhaps in the central nervous system (CNS); this IGF-1 serum is transported to the brain via blood-brain barrier and cephalic fluid (Trejo, Carro, & Torres-Aleman, 2001). Involvement of serotonin and noradrenergic systems were add to central IGF-1, these may signal or be modulated by various molecules, such as brain-derived neurotrophic factor (BDNF) and boost neurogenesis in anatomical structures related to these disorders (Trejo, Carro, & Torres-Aleman, 2001; Cotman & Berchtold, 2002; Kramer & Willis, 2002), thereby
improving symptoms of depression and anxiety or mood disorders which may have similar mechanisms. In a review wrote by Agid, Buzsaki, Diamond, Frackowiak, Giedd, Girault, et al., (2007), there is a profound discussion concerning the possible pharmacological and biochemical mechanisms of several types of drugs, antidepressant – selective serotonin reuptake inhibitors (SSRIs) and antipsychotics, which activation of IGF-1 and BDNF pathways seem to the therapeutically effects. But, addition to IGF-1 involvement in the neurobiology of depression, there are other possible biological pathways, such as hormonal involvement, neurotransmitter levels and balance between sympathetic and parasympathetic central activity.

Present results provide some pointers for research on mechanisms underlying the effect of exercise on depression and other disorders with similar mechanisms, but socialization and attention do not appear to be the mechanisms for improved mood and anxiety through resistance exercise or at least not the principal factors. In addition to improving mood and anxiety, high-intensity resistance training provides other benefits such as improved quality of life, quality of sleep, and muscular mass. This spectrum of benefits is more extensive than those attributed to standard treatment and should be taken into consideration, especially for elderly persons presenting not only clinical depression but also physical weakness or sarcopenia.

In conclusion, 24 weeks of high intensity resistance training seems efficacious in improving mood, reducing anxiety, and boosting IGF-1 serum concentration in elderly men who were free of mood disorders.

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REFERENCES


older patients with major depression. *Archives of Internal Medicine, 159*(19), 2349-2356.


Table 1. Initial means and standard deviation for Control Group and High Resistance Exercise Group: Age, Body Mass, Height and Body Mass Index (BMI). (n=43).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (n=23)</th>
<th>High Resistance Exercise (n=20)</th>
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<tr>
<td></td>
<td>M</td>
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</tr>
<tr>
<td>Age (yr)</td>
<td>67.04</td>
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<tr>
<td>Height (m)</td>
<td>1.68</td>
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<tr>
<td>Total body mass (Kg)</td>
<td>76.44</td>
<td>2.81</td>
</tr>
<tr>
<td>BMI (Kg/m)</td>
<td>26.83</td>
<td>0.70</td>
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</tbody>
</table>

Table 2. One Maximum Repetition test (1RM) for Control Group and High Resistance Exercise Group. (n=43).

<table>
<thead>
<tr>
<th>Variable (lb)</th>
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<th>After</th>
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<td></td>
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<td>SD</td>
<td>M</td>
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<td>CHEST PRESS</td>
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<tr>
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<td>89.78</td>
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<td>89.25</td>
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<td>260.00</td>
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<td>229.00</td>
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<td>VERTICAL TRACTION</td>
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<td>Control</td>
<td>167.17</td>
<td>81.60</td>
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<td>153.00</td>
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<td>70.87</td>
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<tr>
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<td>LEG CURL</td>
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<tr>
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<td>91.30</td>
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<tr>
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<td>96.75</td>
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<tr>
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<td>99.35</td>
<td>24.79</td>
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<td>High Resistance Exercise</td>
<td>107.25</td>
<td>20.42</td>
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Data of Control and High Resistance Exercise Groups (before and after 24 week period). Values expressed as Mean (M), Standard Deviation (SD) and Effect Size (ES). ANOVA for repeated measurements, Duncan’s post hoc test.

* Difference between groups (Control and High Resistance Exercise), p<0.05.
* Difference between groups (Control and High Resistance Exercise), p<0.001.
* Difference in relation to baseline condition for the same group, p<0.05.
* Difference in relation to baseline condition for the same group, p<0.001.
Table 3. Mood profile, anxiety profile and serum concentration of IGF-1 for Control Group and High Resistance Exercise Group. (n=43).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before</th>
<th>After</th>
<th>ES</th>
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<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
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<tr>
<td>Control</td>
<td>62.18</td>
<td>2.34</td>
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<tr>
<td>Anxiety High Resistance Exercise</td>
<td>62.91</td>
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<td>Control</td>
<td>56.73</td>
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<td>ANALOGUE Mental Sedation</td>
<td>High Resistance Exercise</td>
<td>56.85</td>
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<td>SCALE Other Feelings and Attitudes</td>
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<td>Control</td>
<td>37.22</td>
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<td>STAI-STATE ANXIETY</td>
<td>High Resistance Exercise</td>
<td>38.45</td>
<td>4.15</td>
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<tr>
<td>Control</td>
<td>36.00</td>
<td>7.69</td>
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<td>IGF-1 (ng/mL)</td>
<td>High Resistance Exercise</td>
<td>35.85</td>
<td>3.80</td>
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<tr>
<td>Control</td>
<td>242.13</td>
<td>95.40</td>
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<td>High Resistance Exercise</td>
<td>232.56</td>
<td>92.20</td>
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Data of Control and High Resistance Exercise Groups (before and after 24 week period). Values expressed as Median (M), Standard Deviation (SD) and Effect Size (ES). ANOVA for repeated measurements, Duncan’s post hoc test.

* Difference between groups (Control and High Resistance Exercise), p<0.05.

* Difference between groups (Control and High Resistance Exercise), p<0.001.

* Difference in relation to baseline condition for the same group, p<0.05.

* Difference in relation to baseline condition for the same group, p<0.001.