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MOOD, ANXIETY, AND SERUM IGF-1 IN ELDERLY MEN GIVEN 24 WEEKS OF HIGH RESISTANCE EXERCISE[1, 2]

RICARDO C. CASSILHAS

Department of Psychobiology
Federal University of São Paulo

HANNA KAREN M. ANTUNES

Department of Health Science
Federal University of São Paulo

SÉRGIO TUFIK

Psychopharmacology Research
Support Association, Brazil

MARCO TÚLIO DE MELLO

Department of Psychobiology
Federal University of São Paulo

Summary.—As aging advances, changes in mood and anxiety may imply greater risk of mood disorders, particularly anxiety and depression. Resistance exercise reduces anxiety and lessens risk of depression in the elderly, but little is known of the mechanisms involved. It was hypothesized that the human growth factor (IGF-1) may improve mood and anxiety in elderly participants given resistance training. 43 elderly men ages 65 to 75 years were randomly assigned to two groups, Control ($n=23$) and high resistance Exercise ($n=20$). After 24 wk., the Exercise group showed improved muscular strength and higher IGF-1 serum levels than the Control group, as indicated by mean scores on a visual analogue mood scale and the State-Trait Anxiety Inventory. Intensive resistance training was efficacious in improving mood, anxiety, and IGF-1 serum concentration in elderly individuals free of clinical mood disorders.

Elderly people tend to present with 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 is 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 a 16% prevalence of depression in U.S. elderly men. Depression in this age group is often associated with cognitive and functional decline, lower quality of life, changes in body mass, negative attitudes, and low adherence to pharmaceutical interventions. Depression is more severe when associated with a sedentary lifestyle (van Gool, Kempen, Penninx, Deeg, Beekman, & van Eijk, 2003).

Researchers have found an inverse association between the engage-

[1]Address correspondence to Dr. Marco Túlio de Mello, Rua Marselhesa, 535, São Paulo, SP, Brasil 04020-060 or e-mail (tmello@psicobio.epm.br).

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ment in physical exercise and depression. Absence of depression in participants engaged in more than 30 min. of physical exercise every day has been reported (van Gool, *et al.*, 2007). The American College of Sports Medicine (2006) recognized less anxiety and depression in older individuals engaged in physical exercise. There is also a relation among physical activity and changes in mood profile and quality of life (North, McCullagh, & Tran, 1990; Netz & Lidor, 2003). Antunes, Stella, Santos, Bueno, and de Mello (2005) assigned elderly participants men to moderate aerobic exercise over a 24-wk. period. After the intervention, the group had improved ratings of quality of life and lower scores on anxiety and depression than a control group which remained sedentary during the intervention.

Since exercise improves mood and depression symptoms, it has gained increasing importance as an alternative treatment, especially for depression (Thachil, Mohan, & Bhugra, 2007). Aerobic and resistance exercise stands 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, and Fiatarone Singh (2005) recently investigated the effect of 8 wk. 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% who trained at low intensity. High intensity training is apparently more efficacious than low intensity resistance exercise in treating older patients with depression. Moreover, previous studies have indicated that this form of high intensity exercise had a similar beneficial effect when compared with traditional pharmacological intervention using antidepressants, thereby justifying use of resistance exercise as antidepressant treatment (Singh, *et al.*, 1997; Singh, Clements, & Singh, 2001). In a recent study, McLafferty, Wetzstein, and Hunter (2004) evaluated mood profiles in elderly participants of both sexes, all free of mood disorders, and found improvement on these aspects after 24 wk. of resistance exercise. One limitation of their study was the absence of a control group to evaluate social interactions, so conclusions may not be generalizable.

Despite significant evidence that resistance exercise improves mood in elderly participants with or without mood disorder, there are as yet no findings clarifying the 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 that merit further attention. Resistance training may obtain an antidepressant effect through direct and indirect mechanisms, including neurotrofines and growth factors such as the 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, and Lucki (2005) reported cerebral administration of IGF-1 had antidepressant effects in rodents. A year earlier, Khawaja, Xu, Liang, and Barrett (2004) found that 2 wk. of treatment with fluoxetine (a selective serotonin reuptake inhibitor) and venlafaxine (a dual serotonin and norepinephrine reuptake inhibitor) raised hippocampal IGF-1 concentration; the hippocampus and prefrontal cortex are important neuroanatomical structures involved in the etiology of clinical depression (Nestler, Barrot, DiLeone, Eisch, Gold, & Monteggia, 2002).

It was hypothesized that increasing IGF-1 would be an important mechanism in improving mood and anxiety of elderly persons given resistance training. Study of serum IGF-1 concentrations and mood in elderly participants taking part in high resistance training is needed. Also, a control group is highly desirable to reduce the confounding effects of socialization of the elderly population. In this study, mood, anxiety, and IGF-1 serum concentration were measured in elderly men (who were free of mood disorders after 24 wk. of high resistance training).

Method

Participants

This study was approved by the Research Ethics Committee of the Federal University of São Paulo (Grant Number 95/03). Results from the study have been published (Cassilhas, *et al.*, 2007), including data from neuropsychological tests and the Profile of Mood States in three groups. Here, data from the control and high intensity exercise groups only are reported, with the focus on anxiety and perceptions of mood.

The sample was composed of 43 sedentary elderly men ages 65 to 75 years. All read and signed informed consent. They were randomly assigned to two groups, Control ($n = 23$) and Exercise ($n = 20$); these were the control and high resistance exercise groups of Cassilhas, *et al.* (2007). The exclusion 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 the 24 wk. of training (72 training sessions). In addition, the Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975) was administered 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.

Training Procedure

Training consisted of 24 wk. of high resistance training at the Psychobiology and Exercise Research Center, in a controlled environment with temperature at 23°C and humidity 60%. 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), and exercises 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) used specific apparatus made by Technogym®. Two participants were assigned to each machine, so that they could train in pairs 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 and other highly specialized auxiliary professionals.

The Control group was not subjected to high resistance 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, using the same schedule as the Exercise group: six alternating exercises followed by two sets of eight repetitions, with the same rest breaks. The Control group was incorporated into the design with the aim of reducing the bias introduced by the neuromotor learning and socialization, which may mask a real effect of resistance training on the variables studied.

Training for the Exercise group consisted of three 1-hr. sessions per week on alternate days. At the beginning of each session, the group was submitted to a brief warm-up of 10 min. followed by stretching exercises. Training overload was 80% of the one repetition maximum (1RM), two sets of eight repetitions each, with rests for 1 min. 30 sec. between them and 3 min. between different weight machines. 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, and French (2006) and Weir, Wagner, and Housh (1994) were used 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 Exercise) were given three sessions to acquire familiarity with the six machines without overload. This was done both to measure maximum strength of each participant and to eliminate the effect of learning on each apparatus. For details of the 1RM protocol, see Cassilhas, *et al*. (2007).

Mood.—A visual analogue scale (VAS) of mood, 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). This scale consisted of 16 analogue items composed of two opposite adjectives, separated by a 10-cm line on which the participant 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 adult sample (Zuardi, Cosme, Graeff, & Guimaraes, 1993).

Anxiety.—The State-Trait Anxiety Inventory (Spielberger, Gorsuch, & Lushene, 1970) provided an operational measure of intensity of anxiety at a particular moment (State) and of relatively stable anxiety (Trait). State and Trait scales each comprise 20 items rated on a 4-point scale. The rating scales were administered by a single professional between 8:00 a.m. and 10:00 a.m. for both the initial and postintervention evaluations.

IGF-1.—Volunteers fasted for 8 hr. overnight, and a sample of preprandial venous blood was collected in the morning (between 8:00 and 8:30 a.m.). IGF-1 serum concentration was measured 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 analysis of variance (ANOVA) with Duncan *post hoc* test was used to evaluate homogeneity of variables for the groups prior to the intervention period. One-way ANOVA was used for repeated measures (2 time × 2 group) to estimate the effect of intervention period, using a Duncan *post hoc* test. The minimum significance level was set at 5% (95%CI), and data were presented as means and standard deviations. The effect size was defined as small, 0.2 to 0.49; medium, 0.5 to 0.79; and large, 0.8 to 2.0 (Cohen, 1988).

Results

Training session attendance was above 75% for all 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.

TABLE 1

Initial Characteristics of Control Group ($n = 23$) and High Resistance Exercise Group ($n = 20$): Age, Body Mass, Height, and Body Mass Index (BMI)

Variable	Control		Exercise	
	M	*SD*	*M*	*SD*
Age, yr.	67.04	0.54	68.40	0.67
Height, m	1.68	0.02	1.70	0.02
Total body mass, kg	76.44	2.81	76.61	2.12
BMI, kg/m	26.83	0.70	26.43	0.64

Compared to the Control group, the high resistance Exercise group showed increased muscular strength on all six machines. The means are presented in Table 2, respectively, for the Control and high resistance Exercise groups.

TABLE 2

One Maximum Repetition Test (1RM) in Pounds for Control Group ($n = 23$) and High Resistance Exercise Group ($n = 20$)

Exercise	Group	Before		After		ES_g	ES_t
		M	*SD*	*M*	*SD*		
Chest Press	Control	89.78	19.57	90.87	18.93		
	Exercise	89.25	13.40	121.00[ac]	15.53	1.52	1.84
Leg Press	Control	260.00	60.30	246.09	61.33		
	Exercise	229.00	27.13	356.00[ac]	69.77	1.29	1.90
Vertical Traction	Control	167.17	81.60	141.30[c]	33.72		
	Exercise	153.00	20.55	203.00[ac]	32.62	1.03	1.38
Abdominal Crunch	Control	70.87	14.19	60.65[c]	33.72		
	Exercise	64.00	17.29	94.00[ac]	21.86	1.06	1.28
Leg Curl	Control	91.30	14.16	88.91	19.88		
	Exercise	96.75	14.26	131.50[ac]	18.72	1.40	1.75
Lower Back	Control	99.35	24.79	102.39	24.16		
	Exercise	107.25	20.42	147.00[ac]	26.53	1.38	1.41

Note.—Effect Sizes are ES_g, the between-groups effect size, and ES_t, the within-groups effect size between measurements (before and after treatment), from ANOVA for repeated measurements with Duncan's *post hoc* tests. Superscripts on means indicate statistically significant differences between: groups, $^a p < .05$ and $^b p < .001$; measurement times, $^c p < .05$ and $^d p < .001$.

Table 3 shows the VAS mood scores for Anxiety, Physical Sedation, Mental Sedation, and Other Feelings and Attitudes. After training, the Exercise Group had statistically significantly lower mean ratings than in the initial measurements. This decrease in ratings by the Exercise group was not observed for the Control group, for which mean ratings remained unchanged on all mood scales.

At the end of the intervention, compared with the initial measurement, mean scores on both State and Trait Anxiety were lowered statistically significantly in the Exercise group. The changes in mean State and Trait Anxiety for the Control group were not statistically significant.

The IGF-1 serum concentration in the Exercise group was higher after the 24 wk. of high resistance training, and also when compared with concentrations in the Control group. There was no significant change in IGF-1 serum concentration for the Control group from initial to final measurements.

TABLE 3

Mood Profile, Anxiety Profile, and Serum Concentration of IGF-1 For Control Group ($n=23$) and High Resistance Exercise Group ($n=20$)

Variable		Before		After		ES_g	ES_t
		M	*SD*	*M*	*SD*		
Visual Analogue Mood Scale							
Anxiety	Control	62.18	2.34	61.08	2.29		
	Exercise	62.91	1.30	56.13^{ad}	3.81	1.24	1.86
Physical Sedation	Control	56.73	1.21	55.76	1.65		
	Exercise	56.85	0.95	52.42^{bd}	3.37	1.08	1.38
Mental Sedation	Control	55.68	0.97	54.95	1.62		
	Exercise	55.43	1.04	53.13^{bd}	2.16	1.00	1.00
Other Feelings and Attitudes	Control	54.80	0.45	54.23	1.69		
	Exercise	54.70	0.78	52.89^{bd}	1.87	0.60	0.76
Trait Anxiety	Control	37.22	4.70	35.91	7.94		
	Exercise	38.45	4.15	31.00^{ad}	6.03	0.92	1.20
State Anxiety	Control	36.00	7.69	35.17	7.27		
	Exercise	35.85	3.80	28.95^{ad}	4.74	0.91	1.35
IGF-1 (ng/mL)	Control	242.13	95.40	216.73	102.88		
	Exercise	232.56	92.20	313.29^{ac}	75.15	0.68	0.81

Note.—Effect Sizes are ES_g, the between-groups effect size, and ES_t, the within-groups effect size between measurements (before and after treatment), from ANOVA for repeated measurements with Duncan's *post hoc* tests. Superscripts on means indicate statistically significant differences between: groups, $^a p<.05$ and $^b p<.001$; measurement times, $^c p<.05$ and $^d p<.001$.

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 the high resistance Exercise group on all exercises compared with the Control group.

A number of other improvements are currently being attributed to resistance training for the elderly. Tsutsumi, Don, Zaichkowsky, Takenaka, Oka, and 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 wk. 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 daily life activities. Researchers reported both exercise groups showed improved mood and anxiety in relation to controls after intervention. In a recent study, McLafferty, *et al.* (2004) tested 28 sedentary elderly participants after resistance training three times a week for 24 wk. and evaluated their mood profiles. One group trained at 80% of 1RM intensity and the other group trained at a varying percentage (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. Both the above-cited studies have some important limitations, the most serious being the activity of the control groups, which may have had less social interaction.

In the present study, the protocol used with the Control group diminished the potential bias of additional socialization in the Exercise group. After 24 wk. of intervention, the high resistance Exercise group showed improvement in mood as seen in lower mean scores on all four VAS measures (Anxiety, Physical sedation, Mental sedation, and Other feelings and attitudes) compared with the pretraining means. In addition to this reported overall improved mood, the high resistance Exercise group also had lower State and Trait Anxiety than the Control group after the 24 wk. of training. The results support those from the studies conducted by Tsutsumi, *et al.* (1998) and McLafferty, *et al.* (2004). Therefore, the improvements are not attributable to the socialization occurring during exercise.

In elderly patients with clinical depression, Singh, *et al.* (2005) conducted an elegant randomized study submitting subjects to high resistance (80% of 1RM) or low resistance (20% of 1RM) weight training for 8 wk. After this period, 61% of patients in the high resistance training group had improved depression scores, compared to only 29% of patients in the low resistance training group. These results for elderly patients with depression match findings for the elderly persons in the present study who were free of mood disorders. High resistance weight training has positive effects on mood and anxiety of elderly persons with or without clinical depression.

The mechanisms through which these changes in mood take place are as yet unknown. Effects from socialization and attention paid to participants in different groups were eliminated in this study. There are likely biological factors associated with antidepressant effects through which resistance training improves mood and decreases anxiety. The present study showed that IGF-1 was increased in the high resistance Exercise group; the increase from baseline was statistically significant as was the difference between mean IGF-1 levels in the two groups. Considering the similarity to observations of a negative relation between depression and IGF-1 concentration in the brain (Khawaja, *et al.*, 2004; Hoshaw, *et al.*, 2005), it is possible that increases in IGF-1 serum concentration have the same relation with mood. High resistance weight training for elderly participants free of mood disorders raised IGF-1 concentration peripherally and perhaps in the central nervous system (CNS); serum IGF-1 is transported to the brain through the blood-brain barrier and cephalic fluid (Trejo, Carro, & Torres-Aleman, 2001).

Involvement of serotonin and noradrenergic systems in addition to central IGF-1 may be modulated by various molecules such as brain-derived neurotrofic factor and boost neurogenesis (Trejo, *et al.*, 2001; Cotman & Berchtold, 2002; Kramer & Willis, 2002), thereby improving symptoms of depression and anxiety or mood disorders. 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 antidepressants (selective serotonin re-uptake inhibitors) and antipsychotics, in which activation of IGF-1 and brain-derived neurotrofic factor pathways seem to drive the therapeutic effects. But, in addition to IGF-1 involvement in the neurobiology of depression, there are other possible biological pathways, such as hormonal involvement, neurotransmitter levels, and the balance between sympathetic and parasympathetic central activity.

Present results indicate a need for research on mechanisms underlying the effect of exercise on depression and other disorders with similar mechanisms. Socialization and attention do not appear to be major factors in the observed improvements in mood and anxiety through resistance exercise. In addition to improving mood and anxiety, high resistance weight 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 pharmacological treatment and should be taken into consideration, especially for elderly persons presenting not only clinical depression but also physical weakness or sarcopenia.

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