Annals of Internal Medicine | Article

Brief Communication: Pituitary Volume and Function in Competing and Retired Male Boxers

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Background: Pituitary consequences of chronic head trauma in boxing have not been investigated in detail.

Objective: To investigate the pituitary function in retired or active amateur boxers.

Design: Cross-sectional, observational study.

Setting: Turkey.

Participants: 61 actively competing (*n* = 44) or retired (*n* = 17) male boxers of the Turkish National Boxing Team.

Measurements: Body composition variables, pituitary volume (in 38 of 61 boxers), and pituitary function.

Results: 9 of 61 boxers (15%) had growth hormone (GH) deficiency and 5 of 61 boxers (8%) had adrenocorticotropic hormone deficiency. All boxers with GH deficiency except 1 were retired from boxing. Of 17 retired boxers, 8 (47%) had GH deficiency. Retired boxers with GH deficiency had significantly lower pituitary volume than retired boxers with normal GH.

Limitation: Pituitary volume was measured in only 38 of 61 boxers, and the study had no comparison group.

Conclusion: This study suggests that retired boxers have a high rate of pituitary dysfunction. Therefore, investigation of pituitary function in boxers, particularly retired ones, is recommended.

Ann Intern Med. 2008;148:827-831. www.annals.org
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Recent data clearly demonstrated that traumatic brain injury (TBI) is an important public health problem and may result in hypopituitarism (1, 2). After TBI, 25% to 50% of patients have some degree of pituitary dysfunction—growth hormone (GH) deficiency in particular (1–3). Concussion is reported to be the main diagnosis after TBI. This injury is associated with such sports as boxing, kickboxing, and football (4). Recent data suggest that sports injury may cause TBI and pituitary dysfunction (5–7).

Boxing, which is among the most common combative sports, is associated with chronic head trauma that may cause unconsciousness, brain injury, and neurologic abnormalities (8). Although the relationship between boxing and TBI is well documented, pituitary consequences of chronic head trauma in boxing have not been investigated in detail. We investigated pituitary function in 61 retired or active amateur boxers.

Methods

After obtaining permission from the Turkish Boxing Federation, we approached all amateur, elite boxers on the Turkish National Boxing Team. We included all 61 actively competing (*n* = 44) or retired (*n* = 17) male boxers (mean age, 26 years [range, 17 to 53 years]) (**Table 1**). The ethics committee of Erciyes University Medical School, Kayseri, Turkey, approved this study, and we obtained informed consent from each participant. None of the boxers reported any comorbid conditions or previous pituitary disorders, and none was currently taking any medications.

Variables Assessed in the Participants

Age categories and measured variables of the boxers are shown in **Table 1**.

Assessment of Lipid Profile and Body Composition

We measured total serum cholesterol (reference range, 1.8 to 5.7 mmol/L [70 to 220 mg/dL]), high-density lipoprotein cholesterol (0.8 to 1.8 mmol/L [30 to 70 mg/dL]), and triglyceride (0.4 to 2.3 mmol/L [40 to 200 mg/dL]) by using an autoanalyzer (Konelab, Espoo, Finland). We estimated low-density lipoprotein cholesterol (1.5 to 4.4 mmol/L [60 to 170 mg/dL]) levels according to the formula suggested by Friedewald and colleagues (9).

We also measured body mass index (BMI) and waist circumference. We assessed body composition variables, including fat ratio, fat mass, abdominal fat ratio, and abdominal fat mass, by using a bioelectrical impedance analyzer (Tanita Body Composition Analyser BC-418, Tokyo, Japan).

Assessment of Pituitary Volume

We performed pituitary volume measurement with magnetic resonance imaging in 38 of 61 boxers who were randomly selected by a computerized random-number generator. We used coronal- and sagittal-weighted 3-dimen-

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Context

Reports suggest that 25% to 50% of patients with traumatic brain injury have pituitary dysfunction. Boxing carries a high risk for traumatic brain injury, yet there has been little systematic study of pituitary function in boxers.

Contribution

In this cross-sectional study of 61 active and retired boxers from the Turkish National Boxing Team, growth hormone and adrenocorticotropic hormone deficiencies were more frequent than would be expected in a general population. Nearly one half of retired boxers, the study participants with the longest boxing histories, had growth hormone deficiency.

Implication

Physicians should be alert for pituitary dysfunction in patients who have participated in boxing.

—The Editors

sional magnetic resonance imaging volumetry to obtain the pituitary volume as described elsewhere (Philips Gyroscan Intera 1.5 Tesla, Best, the Netherlands) (10). Two radiologists, who were blinded to demographic data of the groups and hormone status of the boxers, measured the volume.

Assessment of Pituitary Function

Basal Hormone Levels

We measured serum-free triiodothyronine (normal range, 1.8 to 5.7 pmol/L), free thyroxine (9.9 to 21.8 pmol/L [7.7 to 17.1 ng/dL), thyroid-stimulating hormone (TSH) (0.2 to 3.7 mU/mL), adrenocorticotropic hormone (ACTH) (3.9 to 23.3 pmol/L), prolactin (0.09 to 0.81 nmol/L), follicle-stimulating hormone (1.4 to 18 U/L), luteinizing hormone (1.5 to 9.3 U/L), total testosterone (4.6 to 21.7 nmol/L [134 to 625 ng/dL]), free testosterone (39.9 to 85.0 pmol/L [11.5 to 24.5 pg/mL]), and insulin-like growth factor I (IGF-I). The IGF-I reference ranges were 25 to 62 nmol/L for 18- to 30-year-olds, 13 to 64 nmol/L for 31- to 40-year-olds, and 13 to 39 nmol/L for 41- to 50-year-olds.

We defined gonadotropin deficiency (follicle-stimulating hormone and luteinizing hormone) as both basal total and free testosterone levels below the normal range in the presence of normal or low gonadotropin values. We defined TSH deficiency as a free thyroxine level below the normal range in the presence of normal or low TSH values (11, 12).

Assessment of Somatotropic and Corticotropic Function

We used GH-releasing hormone (GHRH) plus GH-releasing peptide-6 (GHRP-6) test and glucagon-stimulation test (GST) to assess the GH–IGF-I axis in boxers. We used the GHRH plus GHRP-6 test as described elsewhere (13). We performed the GST to assess ACTH deficiency (14). The details of the tests and the cutoff values for the diagnosis of GH and ACTH deficiencies were recently published (7).

Analytic Hormone Measurement

We measured all other serum hormones by using radioimmunoassay, immunoradiometric assay, or chemiluminescent methods with commercial kits.

Statistical Analysis

We performed statistical analysis by using SPSS software, version 10.0 (SPSS, Chicago, Illinois). All data are presented as means (SDs); $P < 0.050$ was considered statistically significant. We compared the differences between 2 groups by using unpaired *t* tests and among more than 2 groups by using 1-way analysis of variance (post hoc Scheffe analysis). We used Pearson correlation analysis to determine whether statistically significant correlations existed between chosen variables.

Role of the Funding Source

This study was funded by the Scientific and Technical Research Council of Turkey. The funding source had no role in the study design, data collection, data analysis, or data interpretation or in the decision to submit the manuscript for publication.

RESULTS

Sixty-one actively competing (21 young boxers [age range, 17 to 19 years] and 23 adult boxers [age range, 19 to 28 years]) and retired boxers (age range, 32 to 53 years) were included.

Evaluation of Pituitary Hormone Deficiencies

The boxers had no TSH or follicle-stimulating hormone and luteinizing hormone deficiencies. Nine of 61 boxers (15%) had GH deficiency on the GH-stimulation

Table 1. **Age Categories and Measured Variables***

Age categories (*n* = 61)†
Young boxers (*n* = 21): mean age, 18 years (range, 17–19 years)
Adult boxers (*n* = 23): mean age, 22 years (range, 19–28 years)
Retired boxers (*n* = 17)‡: mean age, 42 years (range, 32–53 years)
Measured variables
Lipid profile
Body composition
Pituitary volume
Pituitary function: basal hormone levels and dynamic tests (GST and GHRH + GHRP-6)

* GHRH + GHRP-6 = growth hormone–releasing hormone plus growth hormone–releasing peptide-6; GST = glucagon stimulation test.
† The official age requirement for classification as a young boxer is 17 years to 19 years and 6 months. For the adult group, the requirement is ≥19 years and 6 months. Mean duration of boxing career for all boxers was 8 years (range, 2–20 years).
‡ Retired boxers were official trainers and were not actively boxing. The mean time since retirement was 16 years (range, 8–28 years).

test. All boxers with GH deficiency except 1 were retired. Therefore, 8 of the 17 retired boxers (47%) had GH deficiency. On the basis of GST results, 5 of 61 boxers (3 on the active team and 2 retired) (8%) had peak cortisol levels lower than the cutoff value; we classified them as ACTH-deficient. Of the 61 boxers, 8 (13%) had isolated hormone deficiencies (6 had isolated GH deficiency and 2 had isolated ACTH deficiency) and 3 (5%) had combined GH and ACTH deficiencies. Overall, 11 of 61 boxers (18%) had pituitary dysfunction.

Comparison of Boxers with Normal versus Abnormal Pituitary Function

Table 2 compares boxers who had normal ($n = 50$) versus abnormal ($n = 11$) pituitary function. Age, age at retirement, total number of bouts, body composition variables, and triglyceride levels were statistically significantly higher in boxers with abnormal pituitary function ($P <$ 0.050). Levels of high-density lipoprotein cholesterol, IGF-I, peak cortisol after GST, peak GH after GST, and peak GH after the GHRH plus GHRP-6 test were statistically significantly ($P <$ 0.050) lower in boxers with pituitary dysfunction than in those with normal pituitary function.

Results of Volumetric Pituitary MRI

We measured pituitary volume in 11 young boxers (mean age, 17 years [SD, 0.3]), 17 adult boxers (mean age, 22 years [SD, 2.8]), and 10 retired boxers (mean age, 44 years [SD, 4.7]). Mean pituitary volume was statistically significantly lower in adult (446 mm^3 [SD, 140]) and retired (423 mm^3 [SD, 120]) boxers than in young boxers (681 mm^3 [SD, 141]) ($P = 0.001$).

When we compared the pituitary volumes of 7 GH-deficient boxers (6 retired and 1 active) and 31 GH-normal boxers (4 retired and 27 active), mean pituitary volume was statistically significantly lower in GH-deficient boxers (373 mm^3 [SD, 93]) than GH-normal boxers (538 mm^3 [SD, 173]) ($P = 0.019$). In addition, GH-deficient retired boxers had statistically significantly lower pituitary volume (364 mm^3 [SD, 99]) than GH-normal retired boxers (510 mm^3 [SD, 101]) ($P = 0.040$), and mean ages were similar in both groups (45 years [SD, 3.9] and 43 years [SD, 6.2], respectively).

Correlation Analysis in Boxers

There were statistically significant ($P <$ 0.050) negative correlations between GH peak values after GHRH plus GHRP-6 testing versus all body composition variables (data not shown). We also demonstrated statistically significant negative correlations between length of boxing career and IGF-I level (Pearson $r = -0.46$; $P \leq 0.001$), GH peak value after GHRH plus GHRP-6 testing ($r = -0.28$; $P = 0.026$), and GH peak value after GST ($r = -0.36$; $P = 0.005$).

DISCUSSION

This systematic study of pituitary function and volume in amateur competing and retired male boxers suggests that chronic head trauma due to sports injury in boxers may be associated with pituitary dysfunction and decreased pituitary volume. Growth hormone deficiency was the most frequent hormone deficiency, particularly in retired boxers.

A literature search (English-language studies in MEDLINE to December 2007) identified only 2 studies evaluating the pituitary function in combative sports (5, 7); both were done in Turkey. The first study included 11 amateur boxers, 5 (45%) of whom had isolated GH deficiency (5). The second study included 22 male and female kickboxers, of whom 5 (23%) had GH deficiency and 2 (9%) had ACTH deficiency. A statistically significant negative correlation was found between IGF-I level and length of time the kickboxer had participated in the sport (7). In our study of 61 boxers, 8 retired and 3 competing boxers (18%) had pituitary dysfunction—GH deficiency in particular—and 8 of the 17 retired boxers (47%) had hypopituitarism. In a population-based study, the prevalence of hypopituitarism in men (mean age at diagnosis, 48 years [SD, 17]) was reported as 33 cases per 100 000 persons, suggesting that the pituitary dysfunction rate is substantially higher in our group of retired boxers than in similarly aged men in the general population (15). Furthermore, we found negative correlations between length of boxing career and IGF-I level and between length of boxing career and GH peak values by using dynamic tests. All of these findings suggest that chronic head trauma in boxers has a cumulative effect on the development of pituitary dysfunction. In addition, the statistically significantly higher mean retirement age in GH-deficient trainers implies that retirement age might be another important factor in developing GH deficiency.

Another important point is the semiconscious state of the boxers ("knockdown") during boxing matches after a strong blow, which occurs more frequently than a knockout. Most of the retired boxers and experienced adult boxers in our cohort had had this kind of trauma several times in their boxing careers. Because the boxers lose consciousness for a few seconds, a knockdown may be accepted as a microconcussion. Correlation analysis between hormone levels and length of boxing career in our study may reflect the cumulative effects of these injuries.

The pathogenesis of TBI is poorly understood. A recent study reported that 93% of patients with TBI had normal findings on conventional MRI (16). We found that pituitary volume was significantly lower in adult competitive and retired boxers than in young boxers. Growth hormone–deficient retired boxers also had significantly lower pituitary volumes than GH-normal retired boxers. Lower pituitary volume suggests that boxing may affect both the function and anatomy of the

Table 2. **Body Composition, Hormone Variables, and Lipid Profiles in Boxers with Normal and Abnormal Pituitary Function***

Variable	Normal Pituitary Function (n = 50)	Abnormal Pituitary Function (n = 11)†	*P* Value‡
Age (range), *y*	24 (17–53)	37 (19–50)	0.003
Boxing career (SD), *y*	8 (3.9)	10 (2.9)	0.173
Retirement age (range), *y*§	25 (22–28)	27 (24–30)	0.040
Total number of bouts (SD)‖	860 (485)	1235 (636)	0.032
Waist circumference (SD), *cm*	79 (7.5)	88 (10.6)	0.004
Body mass index (SD), *kg/m²*	23 (2.7)	26 (2.1)	0.005
Fat ratio (SD), %	9 (4.6)	16 (2.5)	<0.001
Fat mass (SD), *kg*	7 (4.5)	12 (3.5)	0.001
Abdominal fat ratio (SD), %	9 (5.7)	17 (3.7)	<0.001
Abdominal fat mass (SD), *kg*	4 (2.9)	7 (1.9)	<0.001
Triglyceride level (SD)			0.001
mmol/L	0.6 (0.32)	1.1 (0.58)	
mg/dL	53 (28)	97 (51)	
Total cholesterol level (SD)			0.36
mmol/L	4.3 (0.94)	4.6 (0.98)	
mg/dL	166 (36)	177 (38)	
HDL cholesterol level (SD)			0.003
mmol/L	1.2 (0.23)	0.9 (0.1)	
mg/dL	46 (9)	35 (4)	
LDL cholesterol level (SD)			0.34
mmol/L	2.8 (0.87)	3.1 (0.86)	
mg/dL	108 (34)	119 (33)	
Free T_3 level (SD)			0.35
pmol/L	3.9 (0.64)	3.7 (0.69)	
ng/L	2.5 (0.4)	2.4 (0.4)	
Free T_4 level (SD)			0.156
pmol/L	14 (1.9)	15 (2.8)	
ng/dL	1 (0.1)	1 (0.2)	
TSH level (SD), *U/L*	1.9 (0.70)	1.9 (0.56)	0.98
Prolactin level (SD), *nmol/L*	0.3 (0.15)	0.2 (0.05)	0.32
FSH level (SD), *U/L*	3.8 (2.58)	3.6 (1.85)	0.82
LH level (SD), *U/L*	3.1 (1.46)	2.3 (0.98)	0.063
ACTH level (SD), *pmol/L*	5.0 (3.17)	4.6 (3.38)	0.69
Total testosterone level (SD)			0.73
nmol/L	17 (6.5)	17 (8.7)	
ng/dL	490 (187)	490 (251)	
Free testosterone level (SD)			0.24
pmol/L	52 (16.9)	45 (17.3)	
ng/L	15 (5)	13 (5)	
IGF-I level (SD), *nmol/L*	52 (14)	41 (12)	0.023
Basal cortisol level (SD), *nmol/L*	306 (88)	251 (71)	0.059
GST peak cortisol level (SD), *nmol/L*	441 (129)	344 (154)	0.039
Basal GH level (SD), *pmol/L*	66 (106)	6 (12)	0.065
GST peak GH level (SD), *pmol/L*	228 (204)	67 (111)	0.014
GHRH + GHRP-6 test peak GH level (SD), *pmol/L*	1906 (632)	916 (795)	<0.001

* All data are means. ACTH = adrenocorticotropic hormone; FSH = follicle-stimulating hormone; GH = growth hormone; GHRH + GHRP-6 = growth hormone–releasing hormone plus growth hormone–releasing peptide-6; GST = glucagon stimulation test; HDL = high-density lipoprotein; IGF-I = insulin-like growth factor I; LDL = low-density lipoprotein; LH = luteinizing hormone; T_3 = triiodothyronine; T_4 = thyroxine; TSH = thyroid-stimulating hormone.
† 8 are retired boxers (2 have GH and ACTH deficiency and 6 have isolated GH deficiency) and 3 are competitive adult boxers (1 has GH and ACTH deficiency and 2 have isolated ACTH deficiency).
‡ *P* value was computed by using an unpaired *t* test; $P < 0.050$ was considered statistically significant.
§ Retirement age was estimated in 9 retired boxers with normal pituitary function and 8 retired boxers with abnormal pituitary function.
‖ Total number of championships and training fights throughout their career.

pituitary gland. It has been demonstrated that acquired or developmental pituitary signals may bring out plastic growth responses, including hypoplasia or hyperplasia (17). Plasticity of the pituitary gland in response to pathogenic insults, such as head trauma, might be another mechanism.

Our study has limitations. First, we measured pituitary volume in only 38 of 61 boxers. In addition, boxers selected for the national team had more boxing experience than nonselected boxers and might have been at higher risk for pituitary dysfunction. Future prospective studies with large numbers of amateur and professional boxers are warranted to understand the natural history of pituitary dysfunction and to establish preventive measures.

In conclusion, our study of amateur boxers suggests that retired boxers are at a high risk for pituitary dysfunction—GH deficiency in particular. Growth hormone deficiency might be responsible for impaired body composition and lipid profile. Therefore, we recommend the investigation of pituitary function in retired boxers. Competing boxers who have a history of concussion may also need screening of pituitary function.

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Acknowledgment: The authors thank Caner Doğaneli (Head of Turkish Boxing Federation and General Secretary of World Boxing Federation), Faruk Hasetçi (Executive Member of Turkish Boxing Federation), and Dr. Mustafa Demirel (Member of Turkish Boxing Federation) for giving permission for the study. They also thank all the national boxers and trainers who participated in the study.

Grant Support: By the Scientific and Technical Research Council of Turkey (TÜBITAK, project no. SBAG-3017).

Potential Financial Conflicts of Interest: *Consultancies:* F.F. Casanueva (Pfizer). *Honoraria:* F.F. Casanueva (Pfizer). *Grants received:* F.F. Casanueva (Pfizer).

Reproducible Research Statement: *Study protocol:* Not available. *Statistical code:* Available by contacting Dr. Tanriverdi (e-mail, fatihtan@erciyes.edu.tr). *Data set:* Not available.

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