Muscle-Strengthening Activity and Its Association With Insulin Sensitivity

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OBJECTIVE — Muscle-strengthening activities (MSAs) may increase insulin sensitivity, thereby reducing the risk of diabetes. The purpose of this study was to assess the relationship between MSAs and insulin sensitivity among American adults.

RESEARCH DESIGN AND METHODS — We analyzed data on 4,504 adults without diabetes, aged 20–79 years, who participated in the National Health and Nutrition Examination Survey 1999–2004 and had information on MSAs. Self-reported frequency (times/week) of MSAs was grouped as low (<1), moderate (1–2.9), or high (≥3). Insulin sensitivity was measured by the fasting quantitative insulin sensitivity check index × 100 (QUICKI).

RESULTS — After adjustment for age, race/ethnicity, physical activity other than MSAs, BMI, smoking, alcohol consumption, and daily total caloric intake, the mean values for QUICKI by low, moderate, and high MSA were 33.6, 33.9, and 34.2, respectively (*P* for linear trend = 0.008) for men and 34.2, 34.6, 34.6, respectively (*P* for linear trend = 0.009) for women. Mean fasting insulin (picomols per liter) concentrations were 75.0, 68.9, and 65.9, respectively (*P* for linear trend = 0.017) for men and 66.9, 63.3, 61.2, respectively (*P* for linear trend = 0.007) for women. There were no significant differences across MSA groups for fasting glucose among men or women.

CONCLUSIONS — MSA is independently associated with higher insulin sensitivity among U.S. adults. Efforts to increase MSA may be a realistic, feasible, and effective method of reducing insulin resistance among the U.S. population.

Diabetes Care **30:2264–2270, 2007**

Studies (1,2) have demonstrated the association of muscle-strengthening activities (MSAs) with improved insulin sensitivity and enhanced glycemic control among people with type 2 diabetes. These observations, along with the recognized benefits of MSA in terms of maintaining functional status and reducing the odds for other risk factors for chronic disease, have led several organizations to recommend MSAs at the level of two or three times per week (3,4).

Despite this general agreement about the value of strength training, experimental interventions have largely lasted only 3–6 months (3). Such interventions may not reflect the patterns of MSAs typically performed in the real world, and they may not reveal its natural impact on risk of diabetes or long-term outcomes, as would be available from a population-based, cross-sectional study in which participants report on their customary use of MSAs.

In these analyses, we examine whether MSAs and other lifestyle factors are independently associated with insulin sensitivity among U.S. adults by using the U.S. National Health and Nutrition Examination Survey (NHANES) 1999–2004.

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Received for publication 22 February 2007 and accepted in revised form 14 June 2007.

Published ahead of print at http://care.diabetesjournals.org on 22 June 2007. DOI: 10.2337/dc07-0372.

Abbreviations: MSA, muscle-strengthening activity; NHANES, National Health and Nutrition Examination Survey; QUICKI, quantitative insulin sensitivity check index × 100.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

RESEARCH DESIGN AND METHODS

Study population and data sources

The NHANES, which is conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention, is an ongoing representative survey designed to measure the health and nutrition status of the civilian noninstitutionalized U.S. population. NHANES 1999–2004 used a complex, multistage probability sample. Data were collected by household interviews and through standardized physical examinations conducted in mobile examination centers in different locations around the U.S. (5). Half of the participants were randomly assigned to the morning session of the mobile examination center and asked to fast from 8 to <24 h. In the 1999–2004 survey, the overall response rate was 82% for those in the interviewed survey and 77% for those in mobile examination center examination. Informed consent was obtained for all participants.

There were 5,554 participants, aged 20–79 years, who attended the morning examination and who had fasted at least 8 h. We excluded women who were pregnant (n = 318), participants who had been diagnosed with diabetes (n = 430), participants with fasting glucose ≥7.0 mmol/l (n = 180), participants who had missing insulin or glucose measurement (n = 77), and those who were missing a weight or height measurement (n = 45). The remaining 4,504 participants were included in the analyses. Among this final sample, median values of cotinine (men: 0.24 ng/ml, women: 0.06 ng/ml, n = 41), total kilocalories (kcal) of energy intake (men: 2,502 kcal/day, women: 1,754 kcal/day, n = 45), and alcohol consumption (0 drinks/week, n = 136) were used to impute missing values for these variables, all of which were used in the analysis.

Measures of insulin sensitivity

Fasting plasma glucose and insulin concentrations were measured on participants who fasted from 8 to <24 h before the examination. All insulin and glucose assays were performed at the Diabetes Diagnostic Laboratory at the University of Missouri, Columbia, Missouri. Fasting

plasma glucose was measured enzymatically by the hexokinase method. Serum insulin was measured by radioimmunoassay with the double-antibody batch method. Details about these laboratory procedures and quality control have been previously published (6).

We measured insulin sensitivity using the quantitative insulin sensitivity check index (QUICKI) percent (100/[log fasting insulin {uU/ml} + log glucose {mg/dl}]) or (100/[0.48 + log fasting insulin {pmol/l} + log glucose {mmol/l}]) (7), which largely reflects hepatic insulin sensitivity and basal hepatic glucose production (8). The higher the QUICKI value the higher the predicted insulin sensitivity.

Physical activity

History of physical activity was obtained by a questionnaire administered during the home interview. The MSA level was evaluated by asking, "Over the past 30 days, how often did you do any physical activities designed to strengthen your muscles such as lifting weights, push-ups, or sit-ups? Include all such activities even if you have mentioned them before."

The American Heart Association (3) has recommended that resistance exercise be done at least twice per week, and Sigal et al. (4) recommend that resistance training be performed three times a week. Accordingly, we divided self-reported MSA (times/week) into three groups: low (<1), moderate (1–2.9), and high (≥3), whose associated medians were 0, 2, and 5 times/week, respectively.

Participants were also asked to report the frequency and duration of moderate and vigorous physical activity during the past month, allowing for 51 anticipated activities and other reported activities that were not anticipated (9). MSAs such as push-ups, sit-ups, weight lifting, and wrestling were excluded from the list for calculating physical activities other than MSAs (non-MSAs) levels. Non-MSAs estimated metabolic cost in metabolic equivalents (METs) were assigned according to a standardized coding system developed by Ainsworth et al. (10) and was defined as the ratio of work metabolic rate to standard resting metabolic rate. We assigned MET codes of 4.5 and 7.0 for moderate and vigorous activity, respectively. One MET is equivalent to the oxygen consumed during seated rest (~3.5 ml of oxygen · kg^{-1} · min^{-1}. Individuals who did not report any activity lasting at least 10 min were classified as sedentary. In those who reported any physical activity lasting at least 10 min, physical activity was categorized into two groups based on the median of the MET distribution: moderate (<14.4 MET × h/week) and high (≥14.4 MET × h/week).

Other variables

Exposure to tobacco smoke increases the concentration of nicotine in the blood, and nicotine is highly specific for such exposure. Cotinine is a major metabolite of nicotine. Using their serum cotinine concentrations (in ng/ml), we classified participants in four groups: nonsmoker (<14), light smoker (14–99), moderate smoker (100–199), and heavy smoker (≥200) (11).

The data on daily intake obtained by interview were used to estimate total intake of energy, nutrients, and nonnutrient food and beverages that were consumed during the 24 h before the interview on any day of a week. Drinking levels were categorized by weekly drinks (nondrinker, <1; moderate drinker, 1–7; and heavy drinker, ≥8). A drink was defined as 12 ounces of beer, 4 ounces of wine, or 1.5 ounces of 80-proof distilled spirits (12). Daily intake of calories was divided into rounded tertiles with cut points of 2,000 and 3,000 for men and 1,500 and 2,000 for women.

Weight with minimal clothing (on a digital electronic scale) was measured. Standing height is measured with a fixed stadiometer with a vertical backboard and a moveable headboard. BMI was calculated as weight in kilograms divided by the square of height in meters and was used to measure obesity (three groups). Waist circumference was measured just above the uppermost lateral border of the ilium to provide sex-specific tertiles (cut points for men: 92.1 and 103.3 cm; for women: 83.8 and 96.8 cm). Because BMI is more widely used as an index for measurement of obesity and may affect subjects' MSA behavior more than waist circumference does, BMI was used in most of our multivariate analyses. Age (in years) was categorized as 20–39, 40–59, or 60–79 in multivariate analyses. Race/ethnicity was divided into three groups: non-Hispanic white, non-Hispanic black, and others.

Statistical analysis

SAS (version 9.1; SAS Institute, Cary, NC) was used for data management. Statistical analyses were performed with SAS-Callable SUDAAN software (version 9.0.1; Research Triangle Institute, Research Triangle Park, NC) to obtain point estimates and SEs applicable to the U.S. population. We applied fasting sample weights to the data that indicated the inverse of the probability of being sampled. Linear regression models were used as primary analyses. Adjustment was made for age, sex, race/ethnicity, non-MSA, smoking and alcohol consumption, and BMI groups in the multivariate regression model. There were no significant interactions between MSAs and the other covariates included in the multivariate analysis (all P values >0.05) except between MSAs and sex on QUICKI, fasting insulin, and fasting plasma glucose (all P values for interaction terms <0.001). In light of the interaction between MSAs and sex on dependent variables, as well as the major biological and lifestyle differences between men and women, most analyses were stratified by sex.

RESULTS — Of 4,504 study participants, aged 20–79 years, 84.7% performed MSAs less than three times per week, and 76.9% performed MSAs less than once a week. The latter prevalence (less than once a week) increased to 83.0% among subjects aged ≥60 years. The average age of subjects included in this analysis was 44 years, and 48.9% were men. Descriptive and other characteristics for the study sample are shown in Table 1 by MSA category. Participants who performed MSAs less than one time per week were older, more likely to be people without physical activities other than MSAs, and to be heavy smokers. Women who performed MSAs less than one time per week tended to have a higher BMI than other groups. Higher MSA was related to higher insulin sensitivity, lower fasting insulin, and lower fasting glucose.

After adjustment for age and race/ethnicity, MSA was positively related to higher insulin sensitivity (Table 2). Mean levels of QUICKI among subjects with lower, moderate, and high MSA were 33.5, 34.1, and 34.4, respectively (P for linear trend <0.001) and 34.0, 35.0, and 35.3, respectively, for women (P for linear trend <0.001). The association between higher MSA and lower QUICKI was influenced more by lower insulin levels than glucose levels. As expected, higher BMI was strongly related to lower insulin sensitivity and higher fasting insulin and fasting glucose concentrations. Moderate and heavy smokers tended to have higher insulin sensitivity than nonsmokers (P < 0.05). Being a moderate drinker was as-

Table 1—*Description of variables for sample population* (n = *4,504) aged 20–79 years by sex and level of MSAs*

	Men					Women				
Variable	*n* (%)	<1*	1–2.9	≥3	*P*	*n* (%)	<1	1–2.9	≥3	*P*
Total	2,275 (100)	1,739 (74.9)	170 (8.5)	366 (16.7)	—	2,229 (100)	1,816 (78.9)	136 (7.2)	277 (13.9)	—
Age (years)	2,275 (100)	44.0 ± 0.5	38.5 ± 1.2	39.0 ± 0.9	<0.001	2,229 (100)	45.3 ± 0.5	41.0 ± 1.4	42.2 ± 1.0	<0.001
Age-group (years)										
20–39	919 (46.5)	43.1 (1.6)	58.5 (4.8)	55.8 (3.1)	<0.001	802 (40.9)	38.7 (1.6)	53.3 (5.6)	46.9 (3.4)	0.024
40–59	745 (38.4)	40.1 (1.5)	34.7 (4.6)	32.5 (2.7)		804 (40.4)	41.6 (1.4)	34.3 (5.8)	36.8 (3.2)	
60–79	611 (15.1)	16.8 (0.9)	6.7 (1.4)	11.7 (1.7)		623 (18.8)	19.8 (1.0)	12.5 (3.1)	16.3 (2.4)	
Race/ethnicity										
Non-Hispanic white	1,154 (72.5)	72.7 (2.1)	75.5 (3.6)	70.0 (3.0)	<0.001	1,140 (73.5)	71.7 (2.1)	78.6 (3.1)	81.4 (2.4)	0.025
Non-Hispanic black	409 (9.9)	8.5 (1.0)	12.6 (2.0)	15.2 (2.1)		428 (11.0)	11.2 (1.2)	12.8 (2.4)	9.2 (1.9)	
Others	712 (17.6)	18.8 (2.0)	11.9 (2.9)	14.8 (2.2)		661 (15.4)	17.1 (2.1)	8.6 (2.5)	9.5 (1.7)	
Non-MSA (MET × h/week)										
Sedentary	942 (34.5)	41.7 (1.9)	11.6 (2.9)	13.6 (2.0)	<0.001	953 (36.4)	42.5 (1.5)	13.9 (3.6)	13.8 (1.8)	<0.001
Moderate (0.1–14.3)	615 (30.1)	30.3 (1.5)	36.6 (4.0)	26.1 (2.9)		700 (34.4)	35.8 (1.7)	35.4 (3.3)	25.4 (2.4)	
High (≥14.4)	718 (35.4)	28.0 (1.5)	51.8 (4.2)	60.4 (3.3)		576 (29.2)	21.7 (1.8)	50.8 (4.6)	60.8 (3.0)	
Body composition										
Weight (kg)	2,275 (100)	87.3 ± 0.6	84.6 ± 1.6	85.5 ± 1.1	0.107	2,229 (100)	75.1 ± 0.6	72.1 ± 1.8	68.2 ± 1.3	<0.001
Height (cm)	2,275 (100)	176.5 ± 0.2	178.0 ± 0.6	177.3 ± 0.5	0.056	2,229 (100)	162.6 ± 0.2	165.2 ± 0.4	163.4 ± 0.4	<0.001
BMI (kg/m^2)	2,275 (100)	27.9 ± 0.2	26.7 ± 0.4	27.2 ± 0.3	0.007	2,229 (100)	28.4 ± 0.2	26.3 ± 0.6	25.5 ± 0.4	<0.001
BMI group (kg/m^2)										
Normal (<25)	721 (32.0)	30.5 (1.3)	36.2 (4.2)	36.8 (2.7)	0.153	780 (41.2)	36.7 (1.7)	53.9 (4.7)	60.2 (3.3)	<0.001
Overweight (25–29.9)	954 (41.7)	41.8 (1.7)	44.7 (3.8)	39.7 (2.9)		687 (28.5)	29.8 (1.6)	24.9 (5.5)	23.1 (2.8)	
Obese (≥30)	600 (26.2)	27.7 (1.3)	19.1 (4.1)	23.5 (2.8)		762 (30.3)	33.5 (1.3)	21.2 (4.1)	16.8 (2.6)	
Smoking status (cotinine, ng/ml)										
None (<14)	1,534 (65.3)	62.5 (1.9)	74.9 (3.3)	73.0 (2.7)	<0.001	1,778 (77.2)	74.5 (1.4)	84.8 (2.9)	88.5 (2.3)	<0.001
Light (14–99)	178 (7.0)	7.1 (0.7)	8.5 (2.4)	6.0 (1.4)		86 (4.1)	4.5 (0.5)	3.2 (1.5)	2.6 (1.3)	
Moderate (100–199)	185 (9.1)	9.7 (0.9)	5.8 (2.0)	7.9 (1.6)		155 (8.4)	9.2 (0.8)	7.7 (1.6)	4.6 (1.5)	
Heavy (≥200)	378 (18.6)	20.7 (1.5)	10.8 (2.7)	13.1 (2.4)		210 (10.2)	11.8 (1.1)	4.4 (2.1)	4.2 (1.1)	
Alcohol consumption (drinks/week)										
None (<1)	1,533 (65.3)	68.1 (1.6)	57.9 (4.1)	56.7 (3.3)	<0.001	1,891 (82.0)	83.5 (1.2)	77.6 (4.3)	75.9 (2.5)	0.035
Moderate (1–7)	385 (17.6)	15.2 (1.4)	26.1 (3.9)	23.7 (2.8)		243 (12.7)	11.3 (0.9)	15.4 (3.0)	19.2 (2.2)	
Heavy (≥8)	357 (17.1)	16.7 (1.0)	16.0 (3.2)	19.6 (2.7)		95 (5.3)	5.2 (0.9)	7.1 (2.5)	5.0 (1.5)	
Daily total caloric intake (kcal)	2,275 (100)	2,689 ± 35	2,752 ± 100	2,678 ± 55	0.803	2,229 (100)	1,870 ± 17	1,979 ± 70	1,930 ± 57	0.125
QUICKI	2,275 (100)	33.5 ± 0.1	34.2 ± 0.2	34.5 ± 0.2	<0.001	2,229 (100)	34.0 ± 0.1	35.1 ± 0.2	35.4 ± 0.2	<0.001
Fasting insulin (pmol/l)	2,275 (100)	76.4 ± 2.5	64.4 ± 6.3	62.1 ± 3.1	<0.001	2,229 (100)	69.0 ± 1.4	57.6 ± 2.6	52.3 ± 2.1	<0.001
Fasting glucose (mmol/l)	2,275 (100)	5.32 ± 0.02	5.22 ± 0.03	5.20 ± 0.02	<0.001	2,229 (100)	5.21 ± 0.02	5.07 ± 0.04	5.08 ± 0.03	<0.001

Data are means ± SE, % (SE), or *n* (%). *Times/week

Table 2—*Age-race/ethnicity adjusted means (95% CI) of the QUICKI, fasting insulin, and fasting glucose, by sex*

Variable	QUICKI	*P*	Fasting insulin (pmol/l)	*P*	Fasting glucose (mmol/l)	*P*
Men						
MSA (times/week)						
Low (<1)	33.5 (33.3–33.7)	Ref.	76.4 (71.3–81.6)	Ref.	5.41 (5.37–5.46)	Ref.
Moderate (1–2.9)	34.1 (33.7–34.6)	0.007	64.2 (52.0–76.4)	0.010	5.39 (5.32–5.47)	0.608
High (≥3)	34.4 (33.9–34.8)	0.001	62.1 (55.8–68.4)	0.001	5.33 (5.27–5.40)	0.022
Non-MSA (MET × h/week)						
Sedentary	33.6 (33.4–33.8)	Ref.	75.4 (66.7–84.1)	Ref.	5.45 (5.40–5.50)	Ref.
Moderate (0.1–14.3)	33.5 (33.2–33.8)	0.613	75.7 (69.5–82.0)	0.935	5.41 (5.36–5.47)	0.270
High (≥14.4)	34.0 (33.6–34.3)	0.124	68.3 (62.3–74.4)	0.169	5.34 (5.29–5.39)	0.003
BMI (kg/m^2)						
Normal (<25)	35.6 (35.4–35.9)	Ref.	44.8 (43.2–46.3)	Ref.	5.28 (5.23–5.33)	Ref.
Overweight (25–29.9)	33.7 (33.5–33.9)	<0.001	66.3 (62.7–70.0)	<0.001	5.41 (5.37–5.45)	<0.001
Obese (≥30)	31.3 (31.0–31.6)	<0.001	118.1 (103.1–133.1)	<0.001	5.53 (5.47–5.58)	<0.001
Smoking status (cotinine, ng/ml)						
None (<14)	33.5 (33.2–33.7)	Ref.	75.2 (70.5–80.0)	Ref.	5.41 (5.37–5.46)	Ref.
Light (14–99)	33.4 (32.9–33.9)	0.777	83.6 (67.0–100.1)	0.304	5.43 (5.33–5.52)	0.785
Moderate (100–199)	34.1 (33.7–34.6)	0.012	63.7 (57.5–69.8)	0.005	5.33 (5.25–5.40)	0.028
Heavy (≥200)	34.4 (34.0–34.8)	<0.001	65.8 (54.4–77.2)	0.038	5.37 (5.30–5.44)	0.242
Alcohol consumption (drinks/week)						
None (<1)	33.4 (33.2–33.7)	Ref.	78.5 (71.2–85.7)	Ref.	5.40 (5.36–5.45)	Ref.
Moderate (1–7)	34.2 (33.9–34.6)	0.001	63.1 (59.1–67.0)	0.001	5.36 (5.29–5.42)	0.220
Heavy (≥8)	34.2 (33.8–34.6)	0.002	62.7 (57.3–68.1)	0.001	5.42 (5.36–5.48)	0.617
Daily total caloric intake (kcal)						
Low tertile (<2,000)	33.9 (33.6–34.3)	Ref.	69.2 (60.4–77.9)	Ref.	5.40 (5.33–5.45)	Ref.
Middle tertile (2,000–2,999)	33.7 (33.3–34.0)	0.249	73.7 (66.1–81.3)	0.173	5.40 (5.34–5.45)	0.913
High tertile (≥3,000)	33.5 (33.3–33.8)	0.065	75.3 (69.1–81.4)	0.294	5.40 (5.35–5.46)	0.836
Women						
MSA (times/week)						
Low (<1)	34.0 (33.8–34.2)	Ref.	68.9 (65.9–71.8)	Ref.	5.21 (5.17–5.25)	Ref.
Moderate (1–2.9)	35.0 (34.6–35.5)	<0.001	57.9 (52.9–62.8)	<0.001	5.12 (5.04–5.20)	0.048
High (≥3)	35.3 (34.8–35.7)	<0.001	53.1 (48.9–57.3)	<0.001	5.10 (5.03–5.16)	0.002
Non-MSA (MET × h/week)						
Sedentary	33.9 (33.6–34.2)	Ref.	70.5 (66.8–74.3)	Ref.	5.23 (5.17–5.28)	Ref.
Moderate (0.1–14.3)	34.2 (33.9–34.6)	0.126	66.4 (61.5–71.4)	0.176	5.18 (5.12–5.24)	0.102
High (≥14.4)	34.7 (34.4–35.0)	<0.001	59.5 (56.4–62.6)	<0.001	5.14 (5.10–5.19)	0.013
BMI (kg/m^2)						
Normal (<25)	36.1 (35.9–36.4)	Ref.	44.1 (42.0–46.1)	Ref.	5.03 (4.99–5.07)	Ref.
Overweight (25–29.9)	34.0 (33.8–34.2)	<0.001	64.3 (61.3–67.4)	<0.001	5.21 (5.16–5.27)	<0.001
Obese (≥30)	32.0 (31.8–32.2)	<0.001	97.0 (92.7–101.4)	<0.001	5.36 (5.32–5.41)	<0.001
Smoking status (cotinine, ng/ml)						
None (<14)	34.2 (34.0–34.5)	Ref.	65.8 (62.9–68.7)	Ref.	5.19 (5.15–5.22)	Ref.
Light (14–99)	33.6 (32.9–34.4)	0.126	74.8 (64.0–85.6)	0.126	5.19 (5.06–5.32)	0.945
Moderate (100–199)	34.1 (33.5–34.8)	0.705	69.9 (59.7–80.0)	0.422	5.20 (5.10–5.30)	0.697
Heavy (≥200)	34.8 (34.3–35.3)	0.039	59.7 (54.7–64.7)	0.053	5.16 (5.07–5.26)	0.653
Alcohol consumption (drinks/week)						
None (<1)	34.1 (33.8–34.3)	Ref.	68.3 (65.4–71.2)	Ref.	5.19 (5.15–5.23)	Ref.
Moderate (1–7)	35.3 (34.7–35.9)	<0.001	54.3 (49.3–59.4)	<0.001	5.13 (5.08–5.19)	0.072
Heavy (≥8)	34.9 (34.3–35.6)	0.015	55.7 (51.2–60.1)	<0.001	5.20 (5.08–5.33)	0.854
Daily total caloric intake (kcal)						
Low tertile (<1,500)	34.3 (34.0–34.6)	Ref.	64.7 (60.5–69.0)	Ref.	5.20 (5.15–5.26)	Ref.
Middle tertile (1,500–1,999)	34.3 (34.0–34.6)	0.954	65.2 (62.3–68.2)	0.845	5.17 (5.11–5.23)	0.351
High tertile (≥2,000)	34.2 (33.9–34.5)	0.712	67.3 (63.6–71.1)	0.317	5.18 (5.13–5.24)	0.519

Ref., reference group.

sociated with higher insulin sensitivity. After adjustment for MSA, age, and race/ethnicity, the means for QUICKI according to non-MSA levels of activity (sedentary, moderate, or high) were 33.7, 33.5, and 33.8, respectively, for men (*P* for linear trend = 0.236) and 34.06, 34.27, and 34.49, respectively, for women (*P* for linear trend = 0.091).

Table 3—*Multivariate adjusted means (95% CI) for QUICKI, fasting insulin, and fasting glucose, by sex

Variable	QUICKI	*P*	Fasting insulin (pmol/l)	*P*	Fasting glucose (mmol/l)	*P*
Men						
MSA (times/week)						
Low (<1)	33.6 (33.3–33.8)	Ref.	75.0 (70.4–79.7)	Ref.	5.41 (5.36–5.45)	Ref.
Moderate (1–2.9)	33.9 (33.5–34.4)	0.091	68.9 (54.5–83.3)	0.294	5.42 (5.34–5.49)	0.789
High (≥3)	34.2 (33.8–34.6)	0.003	65.9 (59.9–71.9)	0.007	5.36 (5.31–5.42)	0.163
Women						
MSA (times/week)						
Low (<1)	34.2 (34.0–34.4)	Ref.	66.9 (64.3–69.6)	Ref.	5.19 (5.15–5.23)	Ref.
Moderate (1–2.9)	34.6 (34.2–35.1)	0.025	63.3 (58.2–68.5)	0.103	5.16 (5.08–5.24)	0.386
High (≥3)	34.6 (34.3–35.0)	0.021	61.2 (57.5–65.0)	0.007	5.15 (5.08–5.23)	0.366

*Logistic regression adjusted for non-MSA, age-group, race/ethnicity, BMI group, smoking status, alcohol consumption, and daily total caloric intake. Ref., reference group.

To more fully evaluate the relationship of MSA with insulin sensitivity, fasting insulin, and fasting glucose, we calculated multivariate-adjusted means (Table 3). After adjustment for age, leisure-time non-MSAs, race/ethnicity, BMI, smoking status, alcohol consumption, and daily total caloric intake, MSA levels were positively associated with insulin sensitivity in both men and women. Higher MSA was also associated with lower fasting insulin. The statistically significant contrasts were mainly found between the highest and lowest MSA groups but not between referent and mid-categories. The *P* values of the linear trend test of QUICKI and fasting insulin by MSA were 0.008 and 0.017, respectively, among men and 0.009 and 0.007, respectively, among women. There was no evidence of a significant association between MSA and fasting glucose. BMI was strongly and negatively associated with QUICKI and positively associated with fasting insulin and fasting glucose. In men, age and daily total caloric intake were significantly and negatively associated with insulin sensitivity. The association of smoking with insulin sensitivity was still present in men in this multivariate model.

In additional multivariate analyses, we adjusted for waist circumference expressed as sex-specific tertiles along with non-MSA, age-group, race/ethnicity, smoking status, alcohol consumption, and daily total caloric intake. The resulting adjusted means of QUICKI for low, moderate, and high MSA groups were 33.6 (referent), 33.8 (*P* value = 0.317), and 34.0 (*P* value = 0.059) (*P* for linear trend = 0.128), respectively, among men and 34.2 (referent), 34.7 (*P* value = 0.004), and 34.7 (*P* value = 0.013) (*P* for linear trend = 0.002), respectively, among women.

CONCLUSIONS — MSAs have important implications for health. Resistance training, which is the most effective method for developing musculoskeletal strength (13), is correlated with an individual's physical function (14) and is particularly appropriate among older adults with low cardiorespiratory function (15,16). Given the safety and acceptability of MSAs, it is disappointing that we have confirmed a low prevalence of MSA with our nationally representative sample of nondiabetic U.S. adults aged 20–79 years (17). We found that MSAs were associated with higher insulin sensitivity as evaluated by QUICKI and lower fasting insulin among U.S. adults in the age range we analyzed. Moreover, this association was independent of non-MSAs and actually stronger in magnitude than the association between non-MSAs and insulin sensitivity.

Most of the previously reported studies of MSAs and insulin sensitivity were performed among selected subpopulations evaluated after a few months of structured training (18,19). In these studies, the benefits of MSA plateau during subsequent months, particularly if the exercise training program did not contain adequate variation (20). In contrast, our population-based study provides a perspective on the role of habitual resistance exercise in natural settings.

There have been reports that suggest potential physiologic mechanisms by which MSAs are related to high insulin sensitivity (3). In an early report, Miller et al. (18) showed that the increased muscle mass resulting from strength training was responsible for the attenuated insulin response to a standard 100-g oral glucose challenge in men. Others, however, have suggested that the effect of training is not caused solely by an increase in muscle mass and is likely also influenced by effects on peak aerobic and maximal working capacity (e.g., $V_{O_{2max}}$) (21). In a population of older men, 9 weeks of high-intensity resistance training of the legs followed by 9 weeks of aerobic training on a cycle ergometer resulted in changes in both the $V_{O_{2max}}$ and the size of the capillary-fiber interface that were similar to those obtained from 18 weeks of aerobic training on the ergometer. In another study, the number of capillaries per length of fiber perimeter was increased after both resistance and aerobic training in men aged 65–74 years, paralleling the changes in $V_{O_{2max}}$, and there was a significant positive correlation between the change in capillary supply and $V_{O_{2max}}$ (22). In brief, the mechanisms behind the effect of strength training seem similar to those seen with aerobic training, even though MSAs mainly recruit type II muscle (fast-twitch fibers), especially type IIb fibers, that are less sensitive to insulin than type I muscle (slow-twitch fibers) (23).

Other studies, however, have demonstrated that without altering $V_{O_{2max}}$, resistance training improves insulin sensitivity in patients with diabetes (24) and can reduce risk factors for cardiovascular disease (25). After 6 weeks of one-legged resistance training performed three times per week, 10 men with diabetes and 7 men without diabetes had produced (independent of increased muscle mass) increased protein content of GLUT4, insulin receptor, protein kinase B-α/β, glycogen synthase, and glycogen synthase total activity (26).

In our study, the relation of MSAs and QUICKI among men was attenuated after adjusting for tertiles of waist circumference but did not change significantly after adjustment for BMI. This finding supports previous research (27) that waist circumference may account for >40% of the variance in insulin action. Hence, we propose that MSAs may be a potentially beneficial health behavior for which the relationship with insulin sensitivity may be reflected through reductions in waist circumference. We also propose that identifying the precise mechanism of MSA's influence on insulin sensitivity is worthy of further exploration.

Structured aerobic training has been related to the treatment and prevention of insulin resistance (28). We found initially that non-MSA was associated with higher insulin sensitivity and with lower concentrations of fasting insulin and fasting glucose, especially among women (Table 2). For both sexes, however, these statistical associations disappeared following adjustment for MSA levels. In this study, non-MSA is not equal to aerobic physical activity. The lack of an association may also be related to the use of absolute MET values for categorizing activity into moderate or vigorous activity.

Findings on the relationship between smoking and insulin sensitivity and diabetes are controversial (29,30). Our results showed that the relation of smoking to insulin sensitivity tends to be J shaped (Table 2). However, it is possible that smoking may damage not only pulmonary cells but also pancreatic cells (31), which will give the incorrect estimation of insulin sensitivity by using QUICKI.

Overweight and obesity, as measured by BMI, were negatively related to insulin sensitivity, a relationship that has been well defined by many studies (32). Weight loss reduces the lipid content of skeletal muscle in morbidly obese individuals, which may contribute to the improvement of insulin action (33). Our study supports the notion that physical activity and body weight are independently related to insulin sensitivity (34). Regarding consumption of alcohol, as did a study among women aged 64 years (35), we found that moderate drinking was related to higher insulin sensitivity and lower concentrations of insulin. In addition, our cross-sectional study found a statistically significant association in men between lower intake of energy and higher insulin sensitivity (after adjusting for other variables, $P = 0.024$); this association was attenuated among women. These findings were consistent with those of Weiss et al. (36), who found that caloric restriction improved glucose tolerance and insulin action among nonobese, healthy men and women aged 50–60 years in a 12-month randomized trial. In contrast, Joseph et al. (37) found that 4 weeks of energy restriction did not improve insulin sensitivity among women aged ~63 years.

This is the first large study to examine how insulin sensitivity is associated with levels of MSAs as they are performed among the U.S. public. While our study had good data quality, was well designed, and was intensively controlled and evaluated, it still had a few limitations. With the data available, we were able to perform only a cross-sectional analysis of the population, which limits our understanding of the cause-and-effect relationship between the variables we evaluated. In addition, we lacked direct measurements of peripheral insulin sensitivity. We thus relied on QUICKI, which is derived from fasting glucose and insulin concentrations and reflects primarily hepatic insulin sensitivity and basal hepatic glucose production (7,8). Hepatic insulin resistance, however, correlates strongly with peripheral (muscle) insulin resistance (38). Although the NHANES computerized interview used the multipass method, the reliability and validity of self-reported physical activity and daily total caloric intake in NHANES have not been reported. The physical activity questionnaire covered the previous month, and the nutrition questionnaire only covered the previous 24 h. The information provided by these questionnaires, therefore, might not represent the participants' routine lifestyle over a longer time interval. We lacked information on the intensity and duration of MSAs. The intensity with which the general population exercises may be lower than that prescribed in trials of muscular training, and therefore our analysis might underestimate the relationship between MSAs and insulin sensitivity. The use of medications such as insulin, metformin, or thiazolidinediones might modify the associations between MSAs and body composition or insulin sensitivity, but our analytical sample is unlikely to include participants using these drugs because we excluded people with diabetes. In an extra analysis, adjusting for estrogen and progestin use among nonpregnant, nonbreastfeeding women, the average QUICKI values were 34.1, 34.5, and 34.6 (P for linear trend = 0.007), the average fasting insulin (in pmol/l) were 67.2, 63.5, and 61.6 (P for linear trend = 0.008), and the average fasting glucose (in mmol/l) were 5.20, 5.17, and 5.16 (P for linear trend = 0.521) among women with low, moderate, and high MSA, respectively. Regardless, most studies of MSAs and insulin sensitivity have been based on small clinical trials and involved small samples of people with diabetes. We have not found any such studies on general populations without diabetes.

In summary, this cross-sectional study found that MSAs are related to higher insulin sensitivity among U.S. adults in a manner that is independent of age, race/ethnicity, non-MSA, BMI, smoking, alcohol consumption, and total energy intake. MSAs may be a realistic and effective way to prevent diabetes and cardiovascular disease.

Acknowledgments— Centers for Disease Control and Prevention disclaimer: The findings and conclusions in this presentation have not been formally disseminated by the Centers for Disease Control and Prevention and should not be construed to represent any agency determination or policy.

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