

**Migraine and Obesity:
Epidemiology, Mechanisms, & Implications**

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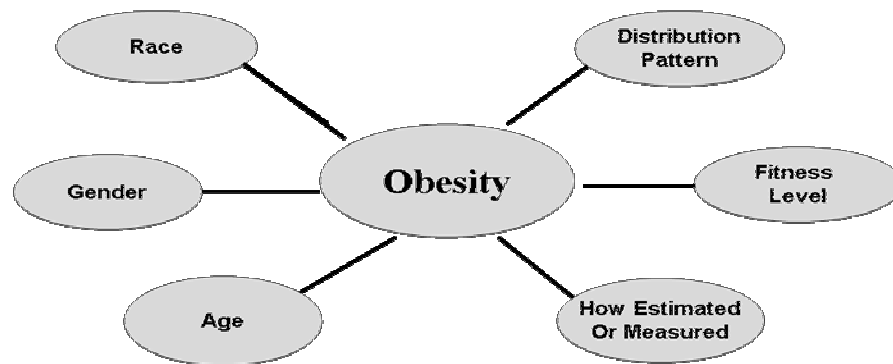
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The health consequences of obesity have been appreciated for centuries—even Benjamin Franklin’s *Poor Richard’s Almanack*¹ advised: “To lengthen thy life, lessen thy meals”—and modern medical scientists have shown that obesity is associated with a wide variety of health conditions, including cardiovascular disease, diabetes, depression, renal disease, liver disease, sleep apnea, and gastroesophageal reflux disease.^{2,3} Adipose tissue, a dynamic neuroendocrine organ involved in multiple physiological and pathological processes, causes obesity when its ratio to lean body mass exceeds normal range.

The best methods for measuring obesity (directly, via computed tomography or magnetic resonance imaging)⁴⁻⁶ are less practical and more expensive than more commonly used indirect measurements, such body mass index (BMI) and waist circumference, which can be limited by gender- and age-related issues, variations in adipose tissue distribution, and reliability in self-reporting (ie, individuals tend to overestimate height and underestimate weight).⁷⁻¹⁰

Practical considerations for evaluating obesity



The effect of obesity on various diseases states is multifactorial.⁷

Clinical and population-based data suggest that migraine and chronic daily headache (CDH) are associated with total body obesity (TBO). In a longitudinal population-based study, Scher et al found that CDH was associated with TBO (OR=1.34) or being overweight (OR=1.26), and subjects with episodic headache and TBO were 5.28 times

more likely to develop CDH than those of normal weight.¹¹ Peres et al compared 74 patients with TBO who presented to an obesity surgery clinic to 70 age-matched controls and found ICHD migraine in 66% of subjects with TBO and 18.5% of non-obese subjects ($P<0.0001$).¹² Horev et al ($n=27$) showed that 48% of subjects with TBO had migraine and 14.8% had episodic tension-type headache.¹³

Among patients of reproductive age, Bigal and colleagues¹⁴ reported that men with TBO were significantly more like to have migraine than those of normal weight (8.8% versus 7.2%, $P<0.01$), although the separation did not remain significant after statistical adjustments. In the same study, participants with TBO were more like to have high-frequency episodic migraine than those of normal weight (13.6% versus 4.4%). In a meta-analysis of patients aged 16 to 94 years, Keith et al compared headache prevalence in subjects who self-reported and measured TBO or a BMI of 20 and found that a BMI of 30 increased the chance of having headache by 35%, and a BMI of 40 increased the risk by 80%.¹⁵ Using measured BMI, Ford et al evaluated subjects aged 20 to 85 years with self-reported migraine or severe headaches and found that those with a BMI above 30 were 1.3 times more likely to have migraine or severe headache than those with a BMI below 30.¹⁶ Several general population studies have evaluated the migraine and obesity relationship in peri- and postmenopausal women and reported no association between TBO and migraine prevalence, attack frequency, or prior history.^{17,18} In other work, Peterlin et al evaluated migraine prevalence among subjects from the NHANES database aged 20 to 55 years and found that TBO increased the likelihood of having migraine or severe headache increased by about 38% in men and women (independent of abdominal obesity), and abdominal obesity increased the risk of having migraine or severe headache by approximately 39% among women (independent of TBO) and 30% among men (not independent of TBO).¹⁹

Central and peripheral mechanisms implicated in migraine have also been shown to contribute to the regulation of feeding, including neurotransmitters (eg, serotonin), peptides (eg, orexin), and adipocytokines (eg, leptin and adiponectin). For example, serum tumor necrosis factor- α and interleukin (IL)-6 are increased ically in episodic migraineurs, and CDH patients have significantly higher total ADP levels than controls ($P<0.024$), mainly due to a significant difference in levels of its high molecular weight multimer.²⁰ Similarly, studies have shown that losing weight can decrease levels of IL-6 and C-Reactive Protein²¹ and significantly reduce the intensity and frequency of migraine attacks ($P<0.001$).²²

A number of medications used for migraine prophylaxis, including antidepressants (eg, amitriptyline), antiepileptic drugs (eg, divalproex sodium), and calcium channel blockers (eg, flunarizine), can cause weight gain.²³ This side effect merits special consideration in obese patients and may be an important factor in the treatment decision.

Migraine is associated with obesity, and the evidence indicates that it is potentially modifiable. Future challenges include further defining the obesity-migraine association using more direct estimates of obesity and identifying adipocytokines and their receptors in pain pathways.

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