Research Article

A CROSS-NATIONAL RELATIONSHIP BETWEEN SUGAR CONSUMPTION AND MAJOR DEPRESSION?

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We have preliminarily investigated the hypothesis that sugar consumption may impact the prevalence of major depression by correlating per capita consumption of sugar with the prevalence of major depression. *Major depression prevalence data (annual rate/100) was obtained from the Cross-National Epidemiology of Major Depression and Bipolar Disorder study [Weissman et al., 1996]. Sugar consumption data from 1991 was obtained from the Food and Agricultural Organization of the United Nations. For the primary analysis, sugar consumption rates (cal/cap/day) were correlated with the annual rate of major depression, using the Pearson correlation coefficient.* ***For the six countries with available data for the primary analysis, there was a highly significant correlation between sugar consumption and the annual rate of depression*** *(Pearson correlation 0.948,* **P=0.004***). Naturally,* ***a correlation does not necessarily imply etiology.*** *Caveats such as the limited number of countries with available data must be considered. Although speculative,* ***there are some mechanistic reasons to consider that sugar consumption may directly impact the prevalence of major depression. Possible relationships between sugar consumption, β-endorphins, and oxidative stress are discussed.*** *Depression and Anxiety 16:118–120, 2002.* © *2002 Wiley-Liss, Inc.*

Key words: *sucrose; endorphins; cytokines; sweetening agents; taste; diet; oxidative stress; depression*

INTRODUCTION

Old World simians developed the sweetness receptor 35 million years ago. The sense of taste, and specifically sweetness, evolved to direct consumption toward nontoxic substances, to recognize chemical compounds (D-forms of some amino acids) [Solms et al., 1965], and to increase pleasure. Naturally occurring sweeteners exist in 30 different classes of plants. Evidence exists of the date palm in southern Mesopotamia to 50,000 B.C., whereas sugar cane was first recorded in Asia in 8000 B.C. Sugar did not become generally known of in Central Europe until the 16th century [Glaser, 1999]. Sugar now enjoys an unprecedented proportion of the human diet. We have preliminarily investigated the hypothesis that sugar consumption may impact the prevalence of major depression by correlating the per capita consumption of sugar with the prevalence of major depression.

METHODS

Major depression prevalence data (annual rate/100) was obtained from the Cross-National Epidemiology of Major Depression and Bipolar Disorder study [Weissman et al., 1996]. Sugar consumption data from 1991 was obtained from the Food and Agricultural Organization (FAO) of the United Nations (data on file, FAO). Sugar consumption data from 1991 were selected, a priori, because the depression data were collected between 1990 and 1992. The sugar consumption data reflect the total amount of refined sugar produced, added to the amount imported, minus nonfood use and losses, adjusted per capita.

All data points for which both depression and sugar consumption data were available were included in the analysis. Of note, sugar consumption data was not

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available for Taiwan and Puerto Rico. For the primary analysis, sugar consumption rates (cal/cap/day) were correlated with the annual rate of major depression (as described above), using the Pearson correlation coefficient. Cognizant of the fact that other dietary factors may be driving the correlation between sugar and depression, we correlated fish consumption with sugar consumption, based on recent theories of omega-3 fatty acids and depression, as well as the prior work of Hibbeln [Hibbeln, 1998]. FAO fish consumption data were obtained from World Health Organization [1996].

RESULTS

For the six countries with available data for the primary analysis, there was a highly significant correlation between sugar consumption (cal/cap/day) and the annual rate of depression (Pearson correlation 0.948, P=0.004).

Fish consumption and sugar consumption were not significantly correlated (Spearman correlation −0.210, P=0.375) for the countries examined, even after removal of Iceland, which was a statistical outlier (Spearman correlation −0.384, P=0.105).

DISCUSSION

We report a correlation between sugar consumption and the prevalence of major depression. Naturally, a correlation may be due to a variety of factors, such as the action of a third, unobserved variable, and does not necessarily imply etiology. Individual-level correlations cannot be assumed to correlate with aggregate-level correlations. It is also possible that the methodology employed may lead to spurious findings, and caveats must be considered. For example, the limited number of countries with available data for both depression epidemiology and sugar consumption warrants a cautious interpretation of the data. In addition, although the Weissman et al. study is perhaps the most rigorous examination of the cross-national prevalence of major depression, results from other studies have varied widely. A recent study has suggested that the Chinese underreport depressive symptoms, which may help to explain the cross-national differences in the prevalence of depression, especially in the Far East [Parker et al., 2001]. In addition, other factors that vary across cultures may be related to both the incidence of depression and sugar consumption. Hibbeln and other have postulated a relationship between omega-3 fatty acids and depression [Hibbeln, 1998]. Investigation of the relationship between fish intake, as used by Hibbeln and others to assess omega-3 intake in a population, and sugar consumption, did not reveal a significant correlation.

Although speculative, there are some mechanistic reasons to consider that sugar consumption may directly impact the prevalence of major depression.

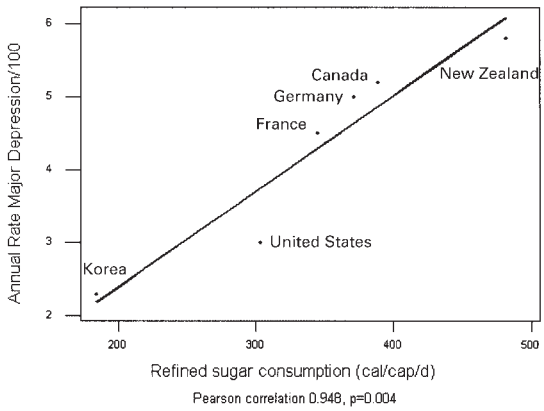

Figure 1. Refixed sugar consumption and prevalence of major depression.

Yamamoto et al. have found that sucrose taste stimulation significantly increases levels of β-endorphins in rats [Yamamoto et al., 2000]. In addition, the administration of opioids has been found to increase sugar intake [Zhang and Kelley, 1997], whereas opioid antagonists cause marked reduction in sugar intake [Ostrowski et al., 1980]. Hence, it appears that sugar ingestion and opioid production may exist in a reinforcing cycle. The possibility that abnormalities in endorphins may contribute to depression has been investigated for many years. Cytokine theories of depression have also been proposed [Maes et al., 1993; Leonard, 2001]. A number of studies show that opioids have effects on cytokines [Apte et al., 1989; Apte et al., 1990; Chao et al., 1994; McCarthy et al., 2001].

Also of interest is a growing body of work that links major depression with oxidative stress in humans [Bilici et al., 2001]. Although the link between increased sugar consumption, increased oxidative stress, and major depression is entirely speculative, one study has reported persistent hyperglycemia in rats fed a sucrose-rich diet long-term [Lombardo et al., 1996]. Hyperglycemia, in turn, has been associated with increased generation of reactive oxygen species [Giugliano et al., 1996] and inhibition of glucose-6-phosphate dehydrogenase (G6PD) [Zhang et al., 2000]. G6PD from rabbit brain has been reported to be markedly sensitive to inactivation by oxidants and free radicals [Ninfali et al., 2001].

Also of note, a neuroimaging study in humans has shown pleasant and aversive tastes to activate the orbitofrontal cortex, anterior insula, and amygdala [O'Doherty et al., 2001]. These same regions demonstrate neurophysiologic abnormalities in major depression [Drevets, 2001].

In summary, a correlation between increasing sugar consumption and increased prevalence of major depression may exist. Future research plans include a study of the cross-city relationship between consumer-level sugar consumption and level of

prescribed antidepressant medications within in the United States. While recognizing that prescription levels may not correlate with the prevalence of depression such a study might examine the relationship between sugar consumption and major depression without cross-national biases. Theories relating sugar consumption to depression also have clear implications for studying the relationship between diabetes mellitus and major depression. We are also interested in the possible implications for oxidative stress as a contributing factor in the development of mood disorders.

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