Dietary-Free Glutamate: *Implications for Research on Fear-Overconsolidation and PTSD*

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The focus on glutamate neurotransmission presented in the October 2005 *CNS Spectrums*[1,2] was a turning point in the conceptualization of overconsolidational fear disorders, such as posttraumatic stress disorder (PTSD). We would like to draw attention to a potential confounding factor that can be controlled in future studies. Dietary free glutamate (DFG) is not only a common flavor enhancer (most often as monosodium glutamate [MSG]) in several American fast-food chains and as an unlabeled ingredient in many condiments and prepared foods, but also occurs naturally in common foods, such as hard cheeses and mushrooms, and in other foods as hydrolyzed protein or as a result of fermentation.[3,4] DFG additives originated in Japan following the discovery that the fermented "1,000 year-old egg" and some other highly prized Asian condiments (utilized for enhancing the taste of low protein foods) contained very high levels of free glutamate.

Free glutamate molecules are released by animal protein and receptors for detecting the taste of glutamate were evolutionarily highly conserved during rodent, primate, and pre-paleolithic human evolution[5,6] since dietary animal protein was scarce among these omnivore species. Studies of knockout mice and of macaques have demonstrated the existence of glutamate receptors (originally known as "umami" receptors) on the lingual surface of non-human primates and rodents.[5]

Unlike food additives, such as sodium and sugar, the Food and Drug Administration has not established a maximum recommended daily allowance, nor required mandatory labeling for DFG. The consensus in the nutrition research literature is that DFG food additives are safe for the "majority" of individuals when consumed at "normal levels."[3] However, what is meant by "normal levels" of DFG intake and the percentage of individuals who experience DFG-triggered symptoms has never been specified. DFG challenge studies conducted to date (all food industry-funded) only include volunteers who are young, self-selected, and otherwise healthy.[4]

We are unaware of any published DFG challenge studies of individuals with disorders, such as PTSD (or even bipolar depression). It is unknown whether DFG consumption triggers a relapse of psychiatric disorders which respond to Glutamate release inhibitors (GRIs) (or which are comorbid with MSG-triggered migraine or MSG-triggered medically unexplained muscle pain).[7] Additionally, removal of perisynaptic glutamate is an active process. It is unknown whether DFG consumption triggers a relapse in psychiatric disorders in which mitochondrial neuroenergetics[8] or glial dysfunction may be present.

A functional magnetic resonance imaging study of healthy humans has demonstrated the activation of the insular/opercular cortex, the caudolateral orbitofrontal cortex, and a part of the rostral anterior cingulate cortex in response to DFG.[6] Similar functional imaging studies in mood disorders and overconsolidational disorders, especially warzone-related PTSD, are warranted.

Diet has been a common confounding factor in psychiatric research. Future clinical and functional imaging studies involving central nervous system glutamate may be strengthened by using a comprehensive diet checklist (H.S. Bracha, MD, The Dietary Free Glutamate Exposure Checklist, unpublished research instrument, 2005). to control for recent DFG consumption of all research participants. Dietary consumption of supraphysiological levels of glutamate in the United

States has dramatically increased over the last 60 years.

After World War II flavoring of United States military combat rations with DFG additives began. Only recently has DFG flavoring been removed from the military Unitized Group Rations and the Meals Ready to Eat used by US combat troops.[10] The prevailing explanations proposed for the increase in the prevalence of PTSD in Vietnam veterans as compared with World War II veterans are mostly psychosocial. However, we speculate that an additional factor contributing to this increase may be the several-fold rise in DFG concentration in the diet of American active-duty military personnel that began in 1946. On a more clinical note, research can examine the predictions that the history of "MSG sensitivity" may predict a favorable GRI response and also that, a low-glutamate diet may offer a benign GRI augmentation option, or a GRI alternative for psychiatric patients for whom GRIs may pose a problem.

Sincerely,
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