

THE CHINESE RESTAURANT SYNDROME: AN ANECDOTE REVISITED

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Abstract—The Chinese Restaurant Syndrome arose from an anecdote of discomfort experienced after eating Chinese cuisine. Monosodium glutamate has been implicated as the causative agent. Work over the past 17 years has consistently failed to reveal any objective sign accompanying the transient sensations that some individuals experience after the experimental ingestion of monosodium glutamate and it is questionable whether the term 'Chinese Restaurant Syndrome' has any validity. When some common food materials are used in the same experimental setting, similar symptoms can be produced in a limited number of people. Double-blind testing of individuals who identify themselves as suffering the 'syndrome' has failed to confirm the role of monosodium glutamate as the provocative agent.

In 1968, Dr Robert Ho Man Kwok recounted in a letter to the *New England Journal of Medicine* his experience of a strange syndrome whenever he ate in a Chinese restaurant (Kwok, 1968). He reported his experience as one of numbness beginning at the back of the neck, radiating to the arms and back and accompanied by weakness and palpitations. He suggested that the cause might be some component of the cooking wine, the high salt content of the northern Chinese food or the monosodium glutamate (MSG) that was used. This letter triggered a deluge of similar anecdotes (*New Engl. J. Med.* 1968) and focused attention on MSG as the causative agent (Schaumburg, 1968).

Direct experiments involving MSG administration (Schaumburg, Byck, Gerstl & Mashman, 1969) more clearly defined a set of symptoms that came to be called the Chinese Restaurant Syndrome (CRS). This was described as a complex consisting of burning or warmth, pressure or tightness, and numbness or tingling confined to the face, neck, upper chest, shoulders and upper arms. Sometimes these sensations were accompanied by chest pain. Typically, the sensations appeared 15–20 min after MSG ingestion and had disappeared within 2 hr. The point was made that the triad of symptoms was extremely rare but individual component symptoms occurred more frequently.

At the time of this intense interest in CRS, evidence appeared of MSG toxicity in the nervous system of the rodent. Glutamate administered in large amounts by non-dietary routes to the immature rodent produced a specific lesion in the hypothalamus which caused functional alteration in terms of reproductive capability and body weight regulation (Olney, 1969). However, this lesion cannot be produced in mature rats (Adamo & Ratner, 1970) nor in the immature animal when glutamate is incorporated in the diet (Takasaki, 1978; Takasaki, Matsuzawa, Iwata *et al.* 1978). Chronic feeding studies (Heywood & Worden, 1978) in a variety of species including dog, rabbit and

monkey at dietary levels ranging from 0.1% to more than 40% by weight have been consistent in showing no neurological lesions even though daily intakes as high as 42 g/kg body weight were achieved. Neurological lesions in the sub-human primate have been reported from only one laboratory (Olney, Sharpe & Geigin, 1972). All other studies indicate that the sub-human primate is totally insensitive to this toxic action (Abraham, Dougherty, Goldberg & Coulston, 1971; Reynolds, Lemkey-Johnston, Filer & Pitkin, 1971; Reynolds, Lemkey-Johnston & Stegink, 1978). These animal toxicity studies thus appear to be irrelevant to the issue of CRS and its relation to MSG. Furthermore, there is evidence from studies in man (Bazzano, D'Elia & Olson, 1970) which shows that dietary administration of glutamate in quantities of up to 120 g/day over extended periods produces only minor side effects (a fall in blood glucose concentration and a small fall in blood pressure) and no evidence of a neurological effect.

The experience of some adverse reactions after food is common. Studies of the frequency of such reactions have been made using the questionnaire technique (Kerr, Wu-Lee, El-lozy *et al.* 1979; Reif-Lehrer, 1977). Some earlier studies were inadequate in design and involved an element of demand bias by directing attention specifically to the reported symptoms of CRS (Kerr, Wu-Lee, El-lozy *et al.* 1978). Large well-controlled studies have been undertaken in the USA (Kerr *et al.* 1979) and in the UK (Bender & Matthew, 1981). The USA study indicated that 43% of the sample population experienced some unpleasant aftermath of eating. When the post-prandial symptoms were compared with those that form the CRS as described earlier, with those that are anecdotally related to Chinese cuisine and with those that are entirely non-specific, it was found that only 1.8% of the individuals who had some discomfort after meals experienced one or more of the CRS symptoms and less than 0.02% of the subjects had the experience after Chinese cuisine.

When the study population was screened to identify those who claimed to have heard of CRS and believed that they knew what it was, it was found that these subjects had a rate of reporting CRS-type symptoms that was ten times greater than the general population and an equally greater rate of reporting non-specific symptoms. It is presumably from this group of dyspeptic individuals that the majority of CRS anecdotes arise.

The general outcome of these epidemiological studies is that the three symptoms that came to be called CRS occur so rarely in association with one another that there is no reason to consider them a syndrome. They do not relate exclusively to Chinese cuisine or to the restaurant location. Therefore the term Chinese Restaurant Syndrome is, at best, misleading.

The second aspect of CRS is the role of MSG in the causation of the symptoms. Over the past 17 yr, a number of laboratory studies have been undertaken on volunteer subjects with the objective of provoking symptoms by administrations of MSG. Double-blind studies have been reported from the USA, (Kenney, 1978; Kenney & Tidball, 1972; Rosenblum, Bradley & Coulston, 1971), Italy (Morselli & Garattini, 1970; Zanda, Franciosi, Tognoni *et al.* 1973) and the UK (Gore & Salmon, 1980). In these studies, MSG was generally administered at concentrations of up to 3.5% in a suitable vehicle (broth, tomato juice or a specifically formulated soft drink). The placebos were similar vehicles—MSG-free, organoleptically matched and of a similar sodium concentration. In the studies reported from the UK and Italy, no difference could be demonstrated between the sensations experienced after MSG or placebo. The studies in the USA, on the other hand, identified individuals who experienced symptoms specific to MSG on a more or less regular basis but only when the MSG was given in amounts or concentrations far in excess of the amount appropriate to the use of MSG as a flavor-enhancer. In the study using the specially formulated vehicle (Kenney, 1978), the sensations of warmth, burning, tingling, numbness, tightness or pressure were reported only after ingestion of the MSG-containing material while non-specific sensations such as headaches, nausea, gastric distress, salivation and weakness occurred with equal frequency in response to both placebo and MSG solutions.

The outcome of the laboratory-based studies may be summarized as follows:

- (1) Symptoms characteristic of CRS can be provoked in a limited number of individuals by high concentrations of MSG, reaching a frequency of about 30% at concentrations greater than 3%;
- (2) Symptom experience is irregular when tested from day to day;
- (3) The experience of symptoms does not correlate with the plasma level of glutamate, suggesting a peripheral rather than a central origin of the sensations;
- (4) The sensations of warmth or burning are not accompanied by any change in skin temperature, and sensations of tightness or pressure are not accompanied by recordable activity of the underlying muscles;

- (5) No difference in blood chemistry or in the activity of transaminase enzymes has been shown between reactors and non-reactors.

This battery of evidence has led to the postulate that the symptoms arise by action on the nerve-endings of a sensitive upper oesophagus and are, in fact, a form of referred pain (Kenney, 1978 & 1980). This position is supported by the observation that when some common dietary items, such as reconstituted frozen orange juice, spiced tomato juice or cold black coffee are given in an experimental setting which reproduces that of the MSG studies, symptoms otherwise regarded as typical reactions to MSG are elicited more frequently by orange juice or tomato juice than by a 2% solution of MSG (Kenney, 1980). The juices have been shown to produce similar sensations when used to superfuse the oesophagus in patients suffering from reflux oesophagitis (Castell, 1978).

Since the symptoms of CRS are entirely without objective correlation, evaluation of the role of MSG in the phenomenon and of its safety as an additive in the human diet rests entirely upon anecdote. In view of the wide publicity that has been accorded CRS in this country, very few of the anecdotes that have appeared in the 17 yr since Dr Kwok's original report can be regarded as spontaneous; the majority have been elicited by questionnaire, solicited by the media or provoked in laboratory studies. Over the course of time, these anecdotes have attributed an ever widening spectrum of adverse post-prandial reactions to MSG, so that even a partial list now includes headache (Sauber 1980), gastric discomfort (Smith, Markadu, Roteller *et al.* 1983), asthma (Allen & Baker, 1981), psychiatric reactions (Colman, 1978), behavioural changes (Cochran & Cochran, 1984), peripheral neuropathy (Freed & Carter, 1982) and cardiac arrhythmias (Gann, 1977).

The only attitude that can be taken with regard to these anecdotes is one of naive realism, which assumes that they are veridical and must be taken at face value until proven otherwise. Such an attitude sets aside considerations such as variation among individuals in the perception, interpretation and reporting of bodily symptoms (Costa & McCrae, 1985). The significance of this individual variation is illustrated by the fact that in the questionnaire study of Kerr *et al.* (1979), individuals who believed themselves to suffer CRS had a higher general rate of reported discomfort after meals than others, and by the fact that in provocative laboratory experiments, those reporting symptoms also reported more frequent post-prandial discomfort. Clearly one could be dealing with individuals who differ in the extent of their concern for bodily symptoms or who are distinguished in a physical sense in terms of the irritability of their alimentary tract.

For the past several years, our laboratory has tried to contact individuals who spontaneously report themselves as reacting adversely to MSG and to test them in a double-blind fashion. Of more than 30 individuals with whom contact has been made, 6 have accepted the invitation to be tested. In our studies, the subjects report to the laboratory fasting on each of 4 days and are given 200 ml of a soft-drink solution

Table 1. Presenting symptoms and double-blind test responses of six subjects that spontaneously reported themselves as reacting adversely to monosodium glutamate (MSG)

Subject and sex	Age	Presenting symptoms	Dietary item implicated	Response to MSG	Response to placebo
HK (F)	42	Headache, warmth in chest and head; palpitation, flutter of diaphragm	Meatloaf, seafood with MSG, dressing containing MSG	Tingling of hands, warmth behind ears	Tingling of hands, warmth behind ears
KB (F)	54	Tightness of face, headache	Meals in Chinese restaurants, pre-mixed dressing, soups	Tightness of face	Tightness of face
FH (M)	55	Disabling headache	Cheese, sausage, bacon, pickles	None	None
GB (F)	50	Headache and nausea	Canned soup, mixed seasonings, heat-in-the-pouch type meals	None	None
RM (M)	57	Swelling of tongue leading to difficulty in breathing	Seafood with dressing, several cocktail food items	None	None
AS (F)	47	Uncontrollable coughing	Salads with dressing, bubble gum, pork sausage, orange-coloured food	None	None

which on 2 of the days contains 6 g MSG. The drink has a unique flavour which effectively conceals the presence of MSG. The placebo solution is MSG-free but is equimolar with respect to sodium. Blood samples are taken for routine chemical analysis and for analysis of transaminase enzymes. Where the presenting symptoms include reports of warmth, pressure, tingling or palpitations, skin temperature, EMG and ECG are recorded.

Two of the subjects so far tested presented symptoms that are a part of the classical CRS (warmth, tingling, tightness) while the remaining four subjects presented symptoms drawn from the extended list of reactions. Table 1 displays the age and sex of the subjects, the presenting symptoms, the dietary associations and the response to testing.

The outcome of the testing divides the subjects into two groups: (i) the two subjects with anecdotal experience of CRS, both of whom experienced a reaction, albeit slight, to both the MSG solution and the placebo, and (ii) the subjects with symptoms other than CRS, who reacted to neither solution. It is tempting to postulate that the subjects HK and KB are of the 'irritable oesophagus' type who suffer a rather general dyspepsia, including a non-specific reaction to MSG, while the remaining four experience specific post-prandial symptoms but have misidentified the causative agent. This is not surprising, since only 20% of individuals adequately tested for purported specific food 'allergy' are confirmed in the diagnosis (Check, 1983).

The subjects tested in this small series were a special population in that they had developed such a level of personal concern that they were prepared to undertake the necessary days of testing. Furthermore, three of the subjects (HK, FH, KB) had been 'diagnosed' as MSG reactors by trusted figures, one a physician, one a brother and one a 'fellow sufferer'. In only one case (RM), did it appear that a putative association between the presenting symptoms and MSG intake was arrived at independently. The point has recently been made that reported adverse effects

of MSG (as well as a host of other food materials) present a diagnostic problem (Ratner, Shoshani & Eshel, 1984). The evidence is strong that the typical MSG reaction that can be provoked with high doses in the laboratory, while uncomfortable, is transient and benign. On the other hand, symptoms of serious disease may be interpreted as an MSG reaction and perhaps be ignored. Furthermore, with a material as ubiquitous as glutamate, inadequate study and inappropriate identification of glutamate as the causative factor of symptoms may lead to the development of a rigorous elimination diet and shift the experience from one of occasional discomfort to one of frank malnutrition. It is clearly important to test those who appear to be sufferers in a tightly controlled double-blind fashion so that the phenomenon may be more fully understood and potentially harmful dietary restriction avoided.

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