Food allergy and infantile autism

S. LUCARELLI, T. FREDIANI, A. M. ZINGONI, F. FERRUZZI, O. GIARDINI, F. QUINTIERI*, M. BARBATO, P. D’EUFEMIA, and E. CARDI

The etiopathogenesis of infantile autism is still unknown. Recently some authors have suggested that food peptides might be able to determine toxic effects at the level of the central nervous system by interacting with neurotransmitters. In fact a worsening of neurological symptoms has been reported in autistic patients after the consumption of milk and wheat. The aim of the present study has been to verify the efficacy of a cow’s milk free diet (or other foods which gave a positive result after a skin test) in 36 autistic patients. We also looked for immunological signs of food allergy in autistic patients on a free choice diet. We noticed a marked improvement in the behavioural symptoms of patients after a period of 8 weeks on an elimination diet and we found high levels of IgA antigen specific antibodies for casein, lactalbumin and β-lactoglobulin and IgG and IgM for casein. The levels of these antibodies were significantly higher than those of a control group which consisted of 20 healthy children. Our results lead us to hypothesise a relationship between food allergy and infantile autism as has already been suggested for other disturbances of the central nervous system.

KEY WORDS: Food allergy - Autism.

The etiopathogenesis of infantile autism is still unknown. Most authors believe that an organic or functional defect of the Central Nervous System (CNS) is at the base of this condition although the precise nature of such a defect is an enigma. Recently Reichelt hypothesised that some peptides might be able to cause noxious effects on the CNS by interacting with neurotransmitters. He also observed that a slight improvement in behavioural symptoms was achieved in autistic children after a cow’s milk elimination diet. Furthermore, he noticed that some patients had high levels of IgA antibodies which were specific for the incriminated foods. This was interpreted as a consequence of the increased absorption of protein fragments by the intestinal mucosa due to a peptidase defect.

The aim of our study was to verify the effectiveness of a cow’s milk elimination diet (or any other food which was positive in a cutaneous food allergy test) in patients who were diagnosed as having infantile autism. We also studied autistic patients on a free choice diet to see if they had immunological signs of food allergy.

Materials and methods

We studied 36 patients, 30 males and 6 females aged between 8 and 13 years of age (median age 11)
TABLE I.—Autistic behavior evaluation scale (BSE)* grouped into symptoms.

I. Autistic isolation
   1) is eager for aloneness
   2) ignores people
   3) poor social interaction
   4) abnormal eye contact

II. Verbal communication disturbances
   5) does not make an effort to communicate using voice and/or words
   6) lack of appropriate facial expression and gestures
   7) stereotyped vocal and voice utterances, echolalia

III. Particular reactions to the environment
   8) lack of initiative, poor activity
   9) inappropriate relating to inanimate objects or to dolls
   10) resistance to change and to frustration

IV. Motor disturbances
   11) stereotyped sensorimotor activity
   12) agitation, restlessness
   13) bizarre posture and gait

V. Inappropriate emotional responses
   14) auto aggressiveness
   15) hetero aggressiveness
   16) soft anxiety signs
   17) mood difficulties

VI. Primary instinc disturbances
   18) disturbances in feeding behavior

VII. Disturbances in concentration; perception and intellectual functions
   19) unstable attention, easily distracted
   20) bizarre responses to auditory stimuli

*) Adapted from Jacobson and Ackerman.

who had been diagnosed as autistic following the criteria of the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R).

At the beginning of our study the autistic behaviour of each patient was evaluated using the Behavior Summarized Evaluation (BSE) scale which consists of 20 items. Each of these is scored on a scale from 0 to 4 according to its frequency: 0, if the disorder is never observed; 1, if sometimes; 2, if often; 3, if very often; 4, if it is always observed.

The 20 items were then grouped together with others for the calculation of a mean (Table I).

Skin tests were carried out on all patients using prick tests with glycerinated food antigen extracts with readings after 15 minutes. The extract concentration was constant at 10,000 AU/ml.

Our autistic patients followed a cow milk protein elimination diet for 8 weeks. Other foods were eliminated in those cases where a positive skin test to allergens was verified. At the end of the diet period we recorded any symptomatic or behavioural modifications by comparing them with the BSE scale results obtained at the start of our study. In those cases where we observed an improvement in symptoms in any of the scale categories a double blind placebo controlled challenge with the food allergen or allergens was carried out. The patients received the opaque white capsules with lyophilised food or placebo (sucrose) in randomized order with a “washout” period of one week. We kept the patients under close observation for 4-6 hours after the administration of the oral challenge as is normal practice in all allergic cases. In patients who did not have immediate reactions the behavioural clinical pattern was re-examined after a period of not more than two weeks.

We measured the total IgE levels by applying the RIA method (Phadebas PRIST). Using this method (Phadebas RAST) we also searched for the specific IgE antibodies for antigens which were positive in the skin tests.

We also determined serum levels of IgG, IgA and IgM which were specific for cow milk and egg proteins using the Enzyme Linked Immuno Sorbent Assay (ELISA). The following antigen antibodies were evaluated: casein, lactalbumin, β-lactoglobulin and ovalbumin. The control group consisted of 20 healthy subjects aged between 5 and 14 (median 8 years).

The prick test, as well as the total and specific IgE results for both groups were compared using the χ² test with the Yates correction. We also evaluated the differences between the IgG, IgA and IgM specific antibodies and the score variations on the autism behavioural scale using the Student's ‘t’-test.

Results

A significant improvement in behavioural disturbances was achieved in our patients in 5 of the 7 groups on the BSE scale which was applied before and after the elimination diet. The oral challenge led to a worsening of symptoms in only three of the 7 categories after an observation period of at least 15 days (Fig. 1).

The skin prick tests were positive in 13/36 (36%)
of the autistic patients and in 1/20 (5%) of the control group (p<0.05). Specific IgE were present in 3/18 (15%) of patients who had tested positive in the skin prick tests and absent in the healthy children (p=n.s.). Skin tests and specific IgE were more frequently positive for casein, lactalbumin, β-lactoglobulin, egg white, rice and soy. IgE levels were higher than the mean ±2 SD in 12/36 (33%) of the autistic patients and in none of the controls (p<0.01).

We found that the autistic patients compared to controls had significantly higher levels of IgA specific antibodies for casein, lactalbumin, β-lactoglobulin and ovalbumin and high levels of IgM and IgG for casein and IgM for lactalbumin. Table II shows a comparison between the values of single allergens in the autistic group and the healthy control group together with the statistical results.

**Discussion**

Many studies in the last few years have underlined the relationship between various foods and the appearance of disturbances in the CNS such as migraine, epilepsy and hyperkinetic syndrome. Dohan noticed an improvement in the psychiatric symptoms of schizophrenic patients on a gluten free diet, and this study further supports the idea that dietary manipulation may provide a beneficial therapeutic approach for autistic patients.
diet regimen. This idea was confirmed by the anti-gliadin antibodies which were found in 17-20% of his schizophrenic patients. It was then hypothesised that an immunological mechanism could be at the root of psychiatric disturbances. Later research did not seem to confirm these observations. Dohan also hypothesised that schizophrenics might have a genetic defect in the intestinal barrier that allows the passage of neuroactive peptides of food origin which are able to interfere directly with the CNS. This later hypothesis with regard to cow’s milk has been taken up by Reichelt in studies with autistic patients. The author does not give much importance to the presence of higher than normal levels of IgA antibodies specific for gluten, gliadin, β-lactoglobulin and casein found in some of his patients but considers these as simply a reaction to the passage of food peptides into the circulation. Uptake of peptides across the intestinal lining has been established and inhibition of peptides increases this uptake.

Our study on autistic patients brought to light a significant improvement in behavioural disturbances after a period of 8 weeks on an elimination diet while the oral challenge led to a deterioration of only some behavioural symptoms after an observation period of at least 15 days. The failure of other symptoms to appear after the oral challenge could be put down to the brevity of the observation period which is inadequate for any disclosure concerning the involvement of delayed immune mechanisms. This observation has already been made by Egger and by our group in other disturbances of the CNS. The absence of a close temporal connection between the intake of food and the appearance of symptoms suggests the necessity for a longer period of clinical observation.

The results of our immunological studies showed a moderate immediate immuno-allergic response in most of our autistic patients. Only 36% of patients had positive skin tests for food antigens and an even smaller percentage (33% and 15% respectively) had high total IgE and specific IgE positivity. However, a large percentage of patients had higher levels of antigen specific antibodies, not only belonging to the IgA class as noted by Reichelt but also to the IgG and IgM classes for casein. The levels of these antibodies were significantly higher than in the control group. Our data lead us to hypothesise that food allergy can have a certain role in the pathogenesis of infantile autism as in other diseases of the CNS. The IgA antigen specific antibodies seem to be more significant in autistic patients. This in fact has already been verified in studies on atopic patients. The collateral presence of specific IgG and IgM antibodies could in its turn give further confirmation of the involvement of the immunological system. Indeed, if an increase in IgA antigen specific antibodies is considered by some authors as a local response by the intestinal mucosa to the abnormal passage of macromolecules because of their altered digestion, the high levels of IgG and IgM antibodies give weight to the hypothesis of a global and more complex stimulation of the immune system because of the higher levels of antigens. The limited number of patients and the difficulty in evaluating the variations in clinical symptomatology in relation to diet oblige caution in the interpretation of the data. Nevertheless, the hypothesis that food allergy can worsen the clinical pattern in infantile autism appears provocative even though we shall have to wait for confirmation from studies on larger patient populations.

References


