Schizophrenia: A Biological Marker of Good Prognosis?" is of great interest considering their model of cholinergic/dopaminergic interactions in schizophrenia. I would like to make a short comment.

We presented an abnormal second messenger mechanism in platelet signal transduction in schizophrenic patients. As Drs. Tandon and Greden considered, the abnormality may be caused by a malfunction of neurotransmitters corresponding to the second messenger system (i.e., acetylcholine). Another possibility is that the abnormality may exist in the second messenger metabolism itself. We are of the latter opinion and presented a platelet phospholipid model for the pathogenesis of schizophrenia (Kaiya 1990). In this hypothesis, the pathogenesis is thought to be a systemic metabolic disorder related to a disturbance in essential fatty acid, excess in prostaglandin E_2, deficiency in prostaglandin E_1, decrease in cAMP formation, increase in diacylglycerol, increase in phospholipase A_2, and increase in free arachidonic acid, all of which were demonstrated in schizophrenic platelets or plasma.

Hisanobu Kaiya

Dept. of Neurology and Psychiatry
Gifu University School of Medicine
Gifu 500, Japan

Reference

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Basal Ganglia Mineralization in Schizophrenia

To the Editor:

I read with great interest the two recent reports by Casanova et al (1990a, b) on basal ganglia mineralization in schizophrenic and control subjects. Based on state-of-the-art image analysis techniques applied to both computed tomography (CT) scans and to postmortem brain sections, they found no difference in the prevalence of palladial mineralization between schizophrenics and controls. They further suggest that this mineralization is probably iron, an identification made likely by the use of selective staining in their postmortem article.

These are interesting findings, but I have some difficulty with the concept that these data are quantitative. Although the authors are clear about their methodology, they refer to iron "concentrations" in both reports. In fact, what has been determined is the area over which they can detect mineralization. By setting a window with the computer and counting pixels, they have identified regions that have the same approximate density as the mineral deposition in an index case. Though image analysis with the Loats system cannot be expected to do much more than this, especially with the CT scans, to suggest that the results are quantitative beyond the measurement of area involved seems premature. For example, is there a correlation between the area mineralized and the absolute concentration of iron (or other mineral) in that particular region? Given the method that has been chosen to measure this area (the use of a boundary function), it seems possible that 2 subjects might have different concentrations of deposited iron, but nevertheless involving the same area. It is possible that although the prevalence of mineralization and the total areas involved may be similar between controls and schizophrenics, the actual amounts of deposited iron may be different between those subjects that have demonstratable mineralization.

This distinction may have relevance to schizophrenic pathophysiology. It may be that in those subjects with mineralization, schizophrenics could have higher concentrations of iron deposited within the same area as controls, which would not be detected by the methodology of these two studies. This higher concentration then may be more likely to be of regulatory significance vis-à-vis catecholamine synthesis and/or dopamine receptor function in those occasional patients with basal ganglia mineralization.

These are two interesting and important studies, demonstrating the utility of image analysis techniques in psychiatry. Although the specific techniques used cannot answer the question of whether these areas of mineralization also have similar absolute mineral concentrations, tools do exist to address this issue. Hopefully, these will be used to answer this question in future studies.

James H. Meador-Woodruff

Department of Psychiatry
University of Michigan Medical Center
Mental Health Research Institute
205 Washtenaw Place
Ann Arbor, MI 48109-0720

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Response

To the Editor:

The letter by Dr. Meador-Woodruff is both interesting and flattering, but I believe it reflects a biased interpretation of the data presented. In essence, Dr. Meador-Woodruff indicates that (1) in both of our recent articles we misuse the term "iron concentration"; (2) the measurements analyzed represent area rather than absolute concentrations of minerals; (3) the probable relation between basal ganglia mineralization and psychiatric manifestation still awaits elucidation with other quantitative techniques.

Although it is true that we used the term "iron concentration" once in our first article (Biol Psychiatry 27:145, 1990), this represented a lapse that was not repeated. The mistake should have been understood as a variant, but more acceptable terms were used when discussing our results. The idea of our postmortem article was to perform a relative quantitation of the amount of minerals in the globus pallidus of schizophrenic patients. As the evidence supporting the rationale of our study was based on the subjective impression of neuropathologists (Josephy 1930; Stevens 1982; Hopf 1952) judging the area covered by minerals in stained tissue sections, we decided to use a similar approach that enjoyed the advantages of quantitation afforded by a computerized image analysis system. That the measurements represented area rather than absolute concentrations is not the conclusion of Dr. Meador-Woodruff but that of the authors. Thus, in page 147 of our first article we state that "the computer image analysis method when coupled with the Perl's stain portrays, with a high degree of accuracy, the topography and area occupied by iron rather than its density or absolute consent." Furthermore nowhere in our articles was there a statement indicating that either study provided a definitive answer to the probable role of minerals in schizophrenia. We were cautious in our abstract when we stated that the negative findings could have been the result of the large variation present in our measurements, and the small number of patients. Similarly, in the discussion we suggest that other quantitative techniques capable of analyzing a larger patient population should provide more definite results than those reported in our study. Since our initial publications we have pursued our research and reported some preliminary findings at the recent Biological Psychiatry Annual Convention. Our results suggest an overabundance of iron in the caudates (not the globus pallidus) of schizophrenic patients which we believe is a side effect of neuroleptic treatment. At present, we are trying to corroborate this finding with combustion analysis.

Contrary to what is stated, we did not quantitate the area occupied by minerals by using a boundary function. This software technique was used only once when selecting the threshold optical density for pixel counting.

Manuel F. Casanova

Neurosciences Center
NIMH Saint Elizabeths Hospital
Washington, DC 20032