DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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Mental Health Administration
National Institute of Mental Health
Intramural Research Program
Bethesda MD 20892

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Professor Richard Frackowiak
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Dear Richard:

This letter is in regard to your recent inquiry about my opinions on the future of PET in functional imaging of cognitive functions in the human brain, particularly in regard to its possible replacement by functional MRI imaging of the same processes. I can assure you that PET continues to have a bright future despite the sometimes extravagant claims of the MRI enthusiasts. The PET activation studies make use of established methods that measure quantitatively functions that are known to be related to true functional activity in the brain. These functions are blood flow and energy metabolism, both of which increase with increased functional activity and decrease with decreased functional activity. Changes in blood flow and/or energy metabolism that PET measures are used to localize the sites of altered functional activity in the nervous system.

Recently, MRI has been used to detect and image changes in MRI signals in specific regions of the brain that are known to be associated with specific functions when the functional activity is these regions is altered. The physiological mechanisms that are responsible for these changes in the MRI signals are being misrepresented. The MRI enthusiasts prematurely attribute the changes in MRI signals to changes in blood flow, but I believe that they are wrong. There is a strong physiological basis for the belief that the changes that they see are due to changes in the hematocrit in the regions of interest and are not specifically and directly related to changes in blood flow. As you know, the hematocrit in the brain is considerably less than that in the peripheral blood, and anything that would dilate the arterial resistence vessels would bring in more oxygenated blood. Because the brain is contained within a rigid container, blood in the low pressure vessels, i.e., the venules and veins would be expressed from the region of interest and from the cranial cavity. The net effect would be a fall in the amount of reduced hemoglobin in the field of interest and, therefore, an enhancement of the proton MRI signal. These changes in hematocrit may correlate with blood flow changes, but not always necessarily so. Local hematocrit can change with other factors. The uncertainties in the mechanisms underlying the changes in the MRI signals serves to limit the usefulness of MRI for studies of physiological mechanisms.

I do not mean to imply that MRI imaging of functional activity in the nervous system has no future. I think that there is potentially a very great future for it, but it will take years to understand what they are looking at and why the changes occur. With PET we already know the physiological basis for the changes.

When the relationship of MRI signals to physiological mechanisms in the nervous system are better understood, then MRI imaging may achieve a status equal to or maybe even greater than that of PET in activation studies.

You can feel secure that there is a future for PET for the next 5, 10 or more years in studies of cognitive functions, and I would recommend that you continue those elegant studies which you have already been carrying out with PET.

I am enclosing a couple of photocopies that I believe are very relevant to the current excitement about MRI. The cartoon applies particularly to the current propaganda in the MRI field. So also does the copy of the article from the Washington Post.

With best regards,

Yours sincerely,

Louis Sokoloff, M.D.
Chief, Laboratory of Cerebral Metabolism, National Institute of Mental Health

Enclosures