A Curious Consensus: "Brain Scans Prove Disease" ?

By Grace E. Jackson, MD
July 10, 2005

Introduction

Recently, a series of physicians have appeared on national news programs, reassuring the public that psychiatric disorders have been confirmed as "real" diseases of the brain. Perhaps the context of these announcements – a heated exchange between two Hollywood celebrities who have clashed over the medicalization and treatment of postpartum depression – has prevented the media from noticing serious inaccuracies in the recorded testimony of their selected discussants:

> "When you don't have enough neurotransmitters firing, making the connections, your brain doesn't act like it should. And you can see what a normal brain should look like. That is an objective measure."[1]
>
> Dr. Sanjay Gupta
> neurosurgeon / CNN Sr. medical correspondent

> "…we can see differences between brain images of someone who is depressed and someone who is not depressed. And if we give medications, the brain of the depressed person goes back to looking like a person not depressed."[2]
>
> Dr. Nada Stotland
> psychiatrist / Secretary, American Psychiatric Association

As none of the featured authorities has clarified the essential distinction between *anatomic* and *functional* studies of the human brain, a corrective analysis is necessary and overdue.

The Difference Between Anatomic and Physiological Studies of the Brain

Anatomic studies depend upon technologies such as computed tomography (CT) and magnetic resonance imaging (MRI) to capture static images of the brain. Because these techniques have been well replicated and validated, they are routinely used by physicians to identify somatic abnormalities, such as tumors, abscesses, or vascular malformations. Despite attempts to the contrary, however, more than fifty years of research have failed to confirm radiographic evidence linking any psychiatric condition to a *structural defect* within the brain.[3-5]

Functional studies, on the other hand, depend upon technologies such as functional MRI (fMRI) and positron emission tomography (PET). These methodologies employ strong magnetic fields or radioactive isotopes, respectively, for the purpose of evaluating brain processes when a person is at rest or engaged in specific activity. Intra- and inter-individual investigations of this kind seek to identify the underlying substrates of the nervous system which are presumed to be uniquely involved in certain mental and psychological phenomena (e.g., during the processes of remembering, learning, perceiving, emoting, intending).

Referring to the images on a functional brain scan in the course of a recent news broadcast, Dr. Sanjay Gupta repeatedly avowed that the new technologies display a visual record of brain activity:

> "An ADHD brain is on the left side there. You can see, it's mainly on the right side of the brain that things are activating. They should be activating all over and on the left side as well. You see a non-ADHD brain, again, it's different than the ADHD brain. These are measurements that people take. This is the science that people have been talking about and this is what a lot of treatment is predicated on [sic]."[6]

However well intended, Dr. Gupta's remarks were nevertheless misleading. First, there was no mention of the fact that fMRI, PET, and other functional imaging modalities (such as magnetic resonance spectroscopy and single photon emission computed tomography) are incapable of measuring brain *activity*. Rather, what these technologies actually reflect are transient changes in *blood flow*. Second, there was no reference to the numerous confounds which undermine the validity of most (if not all) comparison studies, as researchers commonly fail to control for the influence of age, gender, body size (weight and height), drugs (licit or illicit), medical conditions, physical activity, education, and diet. Third, there was no acknowledgement of the fact that the use of these technologies remains controversial. Due to theoretical and practical limitations, their application is restricted to research settings at this time. Why this is true is the untold story which the news media and its chosen experts have ignored.

The Limitations of Functional Imaging Technologies [7-11]

- **the theory of neurovascular coupling**

The clinical utility of functional neuroimaging depends upon the premise that changes in regional blood flow correspond directly to neural activity. This theory of *neurovascular coupling* suggests that cellular activity (primarily within neurons) creates changes in the consumption of oxygen and sugar. These cellular processes are believed to recruit a regenerative surge in blood flow. Interestingly, refutations of this theory have been provided by animal research documenting shifts in regional blood flow in the absence of oxidative metabolism or glycolysis. Similarly, the presence of cerebral hypoxia and/or hypoglycemia in survivors of stroke or traumatic brain injury has not been reliably associated with surges in blood flow. As perplexing as these contradictions may seem, one can easily imagine the existence of an alternative scenario, in which the homeostatic mechanisms of the brain might shift blood into areas of *underactivity* in an effort to revive cells which are sluggish or dormant. Until neurophysiologists understand the cause and timing of changes in cerebral blood flow, the implications of functional imaging technologies will remain ambiguous.

- **the time lag associated with blood flow**

Electrical brain events happen in a span of hundreds of milliseconds. In contrast, the movement of fresh blood into an active tissue is delayed by 1 to 3 seconds. This time lag limits the temporal resolution of functional imaging technologies, because the scanner and the brain are never in temporal synchrony (in the language of still photography: the brain activity is like a flash of lightning for which the scanner lacks an appropriate shutter speed). This results in the unfortunate reality that functional imaging technologies may be able to provide information about certain *locations* associated with mental phenomena, but not about the onset or duration of the inciting events.

- **the localization of neuronal activity**

Since vascular and electrical processes cannot be co-determined *inside* the brains of humans, researchers have experimented upon a variety of non-human species.
A significant body of work has revealed the fact that sections of the neocortex can experience changes in blood flow and metabolism without firing an action potential of their own (no spiking). These findings have tremendous scientific import, for they suggest that the intensities which appear on functional brain scans might *not* reflect the electrical activity of the underlying regions. Rather, the bright spots might reflect the activity of remote (invisible) cell populations whose action potentials have propagated a certain distance but not moved on (inhibitory post-synaptic potentials > excitatory post-synaptic potentials).

- **the statistical averaging of images**

Because the contrast resolution of the functional neuroimaging technologies is so poor (the "activated vs. baseline" differences which they capture are extraordinarily small – on the order of a mere 2-5%), multiple scans must be obtained for the purpose of achieving statistical significance (i.e., to rule out the possibility that the observed changes have occurred simply by chance). Consequently, when reports about "between group" differences are based upon functional technologies, it means that the brain scans of several individuals have been integrated by computer software in order to produce a composite or average result.

When physicians like Dr. Gupta display the picture of an ADHD brain, they are not referring to any *specific* child or adult. Rather, they refer to an image which reflects a subset of the population whose brain features have been averaged together. The final graphic may or may not resemble any *real* person. High rates of intra- and inter-individual variability reduce the sensitivity and specificity of these procedures, so that they cannot be used dependably in the clinical setting.

- **the subtraction method of analysis (paired image subtraction)**

The subtraction method of analysis infers neural activity by subtracting baseline from activated scans, or by subtracting the images of controls from "abnormals." For example, if an experimental task activates zones 1, 2, and 3 in a healthy subject, and zones 1, 2, 3, and 4 in the brain of a patient, zone 4 would be interpreted as the substrate responsible for aberrant behavior. The problem with this approach lies in the assumption that the difference between two tasks (active vs. resting) or two conditions (healthy vs. ill) can be divided into separable and mutually exclusive cortical or subcortical components, and that changes in regional blood flow will correspond neatly to these specialized units of the brain.

- **the premature assumptions of safety**

Functional neuroimaging technologies pose dangers which remain largely unexplored. The magnetic fields used in MRI have been found to disrupt the blood brain barrier in several animal studies. If similar perturbations occur in humans, it is possible that even transient changes arising from the exposure to these increasingly powerful devices (up to 7 Tesla) might permit toxins and other plasma components to enter the brain parenchyma, where they could initiate inflammatory or autoimmune responses. Furthermore, the long term health effects of ionizing radiation (i.e., the gamma rays produced by the annihilation photons of PET) are equally unclear. It is important to appreciate the fact that the potential mutagenicity of radioisotopes is greater when a given dose is administered over minutes to hours (as occurs in psychiatric research protocols) as compared to gradual exposures over months to years. No dose of ionizing radiation is hazard free,[12-13] and the potential risks (of cancers, birth defects, heart disease) are cumulative, not fleeting.

Conclusion

It is notable that the official website of the American Psychiatric Association features a position paper (January 2005) regarding the use of functional imaging technologies in children and teens:

> "Imaging research cannot yet be used to diagnose psychiatric illness and may not be useful in clinical practice for a number of years… Specifically, no published investigation in the field has determined that any structural or functional abnormality is specific to a single psychiatric disorder. Additionally, imaging studies examine groups of patients and groups of healthy controls; therefore, findings may not apply to all individuals with a given disorder. Even when significant differences are identified between groups, there is a substantial overlap among individuals in both groups…
>
> "We conclude that, at the present time, the available evidence does not support the use of brain imaging for clinical diagnosis or treatment of psychiatric disorders…"[14]

Contrary to the reports which have been emphasized by the major news outlets, there is no evidence to justify the claim that psychiatric disorders arise from anatomic or physiological abnormalities in the brain. Based upon a variety of theoretical and practical limitations, the functional imaging technologies cannot identify the origin of mental phenomena. Philosophical observers might suggest a host of reasons (epistemological and ontological) why they never will.

The media have the power to shape popular and professional perceptions by disseminating the facts of science, or by perpetuating science fictions. Responsible journalism accepts the challenge of embracing the former, while avoiding the latter.

==========

Notes

1 "Scientologist Explains Tom Cruise's Recent Anti-Psychiatry comments," *Anderson Cooper 360 Degrees*. CNN, New York. 30 JUN 2005. Transcript.

2 Ibid.

3 Darin D. Dougherty, Scott L. Rauch, and Jerrold F. Rosenbaum, Ed., *Essentials of Neuroimaging for Clinical Practice*, (Washington, DC: American Psychiatric Publishing, Inc., 2004), pp. 13-14, 49-51.

4 U.S. Department of Health and Human Services, *Mental Health: A Report of the Surgeon General*, (Rockville, MD: U.S. Department of Health and Human Services, 1999), p. 15.

5 Robert E. Hales, Stuart C. Yudofsky, and John A. Talbott, Ed., *The American Psychiatric Press Textbook of Psychiatry*, 3rd Edition, (Washington, DC: American Psychiatric Press, Inc., 1999), pp. 300-304.

6 "Scientologist Explains Tom Cruise's Recent Anti-Psychiatry comments," *Anderson Cooper 360 Degrees*. CNN, New York. 30 JUN 2005. Transcript.

7 Cheryl J. Aine, "A Conceptual Overview and Critique of Functional Neuroimaging Techniques in Humans: I. MRI/fMRI and PET," *Critical Reviews in Neurobiology* 9 (1995), pp. 229-209.

8 David J. Heeger and David Ress, "What Does fMRI Telll Us About Neuronal Activity?" *Nature Reviews* 3 (2002): 142-151.

9 Russell A. Poldrack, "Imaging Brain Plasticity: Conceptual and Methodological Issues – A Theoretical Review," *NeuroImage* 12 (2000): 1-13.

10 Dara S. Manoach, Elkan F. Halpern, Todd S. Kramer, Yuchiao Chang, Donald C. Goff, et. al., "Test-Retest Reliability of a Functional MRI Working Memory Paradigm in Normal and Schizophrenic Subjects," *American Journal of Psychiatry* 158 (2001): 955-958.

11 G.D. Honey, P.C. Fletcher, and E.T. Bullmore, "Functional brain mapping of psychopathology," *Journal of Neurology, Neurosurgery, and Psychiatry* 72 (2002): 432-439.

12 John W. Gofman, *Preventing Breast Cancer: The Story of a Major, Proven, Preventable Cause of This Disease*, 2nd Ed., (San Francisco: C.N.R. Book Division, 1996).

13 John W. Gofman, *Radiation from Medical Procedures in the Pathogenesis of Cancer and Ischemic Heart Disease: Dose-Response Studies with Physicians per 100,000 Population*, (San Francisco: C.N.R. Book Division, 1999).

14 Loris Talbott Flaherty, William Arroyo, Irene Chatoor, Roxanne Dryden Edwards, Yvonne B. Ferguson, et. al., "Brain Imaging and Child and Adolescent Psychiatry With Special Emphasis on SPECT," (January 2005), retrieved on 09 JUL 05 at: <www.psych.org/psych_pract/clin_issues/ populations/**child**ren/SPECT.pdf>.