A Curious Consensus: "Brain Scans Prove Disease" ?

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Abstract: Presumably in recognition of the fact that there is no chemical test which can be used to diagnose any of the alleged mental illnesses, journalists and medical opinion leaders have proclaimed that brain scans – particularly, *functional* imaging studies -- can be used to confirm the presence of psychiatric disease. Although the scientific record contradicts these assertions, the news media have ignored a critical evaluation of what, exactly, the new technologies purport to explain. The article which follows presents a critical analysis of the theoretical, practical, and philosophical limitations of the *functional* neuroimaging modalities (fMRI, PET, SPECT), and why these methods are *not* used outside of the research setting in the clinical practice of psychiatry today.

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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." (Doss, 2005)
>
> 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." (Doss, 2005)
>
> 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 (Dougherty, Rauch, and Rosenbaum, 2004; U.S. Department of Health and Human Services, 1999; Hales, Yudofsky, and Talbott, 1999).

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., brain regions which are active or silent during the processes of remembering, learning, perceiving, emoting, intending).

Referring to the images on a functional brain scan in the course of a recent television 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]." (Doss, 2005)

> **Note: Multiple messages were sent by this writer to CNN, in an effort to identify the source of the brain scans which were featured in this telecast. The network did not respond to these inquiries.*

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 single photon emission computed tomography or SPECT) 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 in the field of psychiatry 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 Theoretical & Practical Limitations of Functional Imaging Technologies
(Aine, 1995; Heeger & Ress, 2002; Honey, Fletcher, and Bullmore, 2002; Hoshi, Onoe, Watanabe, et. al., 1994; Manoach, Halpern, Kramer, et al., 2001; Poldrack, 2000)

- **the theory of neurovascular coupling**

The clinical utility of most functional neuroimaging technologies 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 brain's 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. Human studies have demonstrated analogous discontinuities. Among survivors of stroke or traumatic brain injury, for example, the presence of cerebral hypoxia (low oxygen) and/or hypoglycemia (low glucose) has not been reliably associated with surges in blood flow. Similarly, in a study of thirty-three healthy subjects subjected to a mathematical performance test, researchers found that almost one-third of the participants exhibited significant decreases in regional blood flow during the execution of the assigned tasks (Hoshi, Onoe, Watanabe, et. al.).

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 brain (e.g., visual cortex, cerebellum) can experience a process of neurovascular *decoupling* under certain conditions (Heeger and Ress, 2002). What this means is that changes in blood flow may reflect changes in neuronal input or intracellular processing (EPSPs, for example) without a consequential output (no action potential is fired). 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 *immediately* 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.

- **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 television 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 (Gofman, 1996; Gofman, 1999), and the potential risks (of cancers, birth defects, heart disease) are cumulative, not fleeting.

The Philosophical Problems of the Functional Neuroimaging Technologies

Remarkably, the neuropsychiatric literature seldom addresses the broader philosophical concerns which attend the very notion of a *functional* test for mental illness. While some may argue that it is possible to define functional equivalents of *organic*, neurological disease (e.g., frontal and temporal lobe processes related to the cognitive features of dementia), it is far more difficult to define the functional equivalents of psychological distress (i.e., brain processes *specifically* related to temperament, misconduct, or inattention). Given the inherent sociocultural and historical subjectivity of the classification of psychiatric conditions (normal functioning, meaning: appropriate thoughts, perceptions, and behavior), the functional imaging technologies have introduced a very dangerous tautology which few professionals have addressed: if two brains can be scanned and they look different, one of them must be diseased.

Even if abnormal mentation *could* be objectively defined and reliably determined, it remains unclear how any functional imaging technology could differentiate the brain processes which reflect the *cause*, rather than the *consequence*, of an allegedly impairing trait or state. Such a distinction is crucial because of the clinical and prognostic significance which some observers have come to attach to the new technologies. For example, it would not be prudent for a physician to administer medications which obliterate the suspect features on a brain scan, if those features represent adaptive responses of the central nervous system, rather than the source of a person's symptoms.

Conclusion

It is notable that the official website of the American Psychiatric Association has featured a position paper (drafted in 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…
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> "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…" (Flaherty, Arroyo, Chatoor, Edwards, Ferguson, et al., 2005)

Contrary to the reports which have been emphasized by the major news outlets, there is no evidence at this time to justify the claim that brain scans discern the presence of psychiatric disease, based upon anatomic or physiological abnormalities in the brain. For a variety of theoretical and practical limitations, the functional imaging technologies addressed in this paper cannot reliably predict the presence of psychopathology. For philosophical reasons, it is highly doubtful that they ever will.

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