Chapter 17

Brain Imaging Studies of Personality: The Slow Revolution

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> . . . a great personality may possibly make a great brain, but no brain can make a great personality (W. Hanna Thomson, *Brain and Personality*, 1911: 234).

> The ground of character [i.e. personality] is to be sought in the nervous organization which governs the inhibitions . . . we should still be on our search for the physical basis and location of the inhibition (A. A. Roback, *The Psychology of Character*, 1928: 541).

> Scarcely anyone has ever thought of questioning the existence of traits as the fundamental dispositions of personality (G. W. Allport, *Personality: A Psychological Interpretation*, 1949: 286). But the information is too meager to warrant at the present time a physiological account of the operation of traits. *Ibid*: 319.

> In psychology, as in other sciences, knowledge has been advanced by new techniques and new instruments, as well as by new modes of thought . . . (Aubrey Lewis, in the Forward to Hans Eysenck's, *The Scientific Study of Personality*, 1952: vii).

> The beauty of a psychobiological approach [to personality] is that progress in understanding biological structure and function is not only possible but is inevitable (M. Zuckerman, *Psychobiology of Personality*, 1991: 427).

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1. Introduction

Once upon a time, not so long ago, many American psychologists believed that personality traits did not exist and that the idea of any neurobiological basis to personality was simply foolish reductionism. Marvin Zuckerman was a lonely exception. I first met Marvin in the late 1970s when, as a true pioneer, he prowled the corridors of the National Institute of Mental Health (NIMH) in Bethesda. He was working with collaborators measuring things like monoamine oxidase (MAO), evoked potentials, and brain chemistry metabolites in cerebral spinal fluid and correlating the various measures to scores on his sensation seeking trait scales (Ballenger *et al*. 1983; Zuckerman *et al*. 1980). Now, there is a resurgence of interest in individual differences in personality (and intelligence) and the revolution in neuroscience has energized the search for a biological basis of personality traits. We know there must be a biological basis simply because genetic studies confirm modest to high heritability for a number of personality traits (Bouchard & Loehlin 2001; Bouchard & McGue 1990; Bouchard *et al*. 1998) and genes work through biology. Modern personality researchers have caught up to Marvin's neurobiological approach (Zuckerman 1979, 1984, 1995) and other early attempts to define neurobiological models of personality (Eysenck 1967; Gray 1970).

Advances in brain imaging technology can be used to help identify the neurobiology and the neuroanatomy of personality traits just as this technology is helping understand learning (Haier 2001; Haier *et al*. 1992), memory (Alkire *et al*. 1996, 1998), intelligence (Haier *et al*. 1988, 2003), and even consciousness (Alkire *et al*. 2000; Alkire & Haier 2001). However, whereas brain imaging methods are now a staple of cognitive research, the transition from personality research based on psychometrics to research using brain imaging methods is still sporadic and at a very early stage. We will review how brain imaging has been used in personality research and highlight some issues that have impeded progress.

2. Review of Imaging Studies

2.1. The First Blood Flow Study of Personality

In a pioneering paper, Mathew *et al*. (1984) used the xenon inhalation technique to correlate regional blood flow with the Eysenck Personality Inventory (Eysenck & Eysenck 1964) scales in 51 normal female volunteers (mean age = 32, SD = 8.3). This technique traced radioactive gas that mixed with air as the subject breathed and the gas entered the blood stream. Detectors were placed over 16 scalp locations (8 in each hemisphere). Blood flow was assessed over a ten-minute period while the subject rested with eyes closed. Significant inverse correlations between blood flow at all 16 detectors and Extraversion were found with the correlations ranging from −0.24 to −0.41. There were no significant correlations with the neuroticism scale. These results were cautiously interpreted as consistent with Eysenck's hypothesis of an inverse association between Extraversion and general cortical arousal. Like EEG measures of the day, the xenon gas technique was limited to surface detections and it was unable to provide detailed spatial resolution. Nonetheless, this study clearly pointed the way for future experiments. Two other subsequent reports used the xenon gas technique to study personality traits in smaller samples (Stenberg *et al*. 1990, 1993). However, the newer brain imaging technology of Positron Emission Tomography (PET) was becoming available with the capability of measuring function throughout the entire brain with much better spatial resolution.

2.2. The First Positron Emission Tomography of Personality

The first attempt at using PET to study personality was reported at the second meeting of the Hans Eysenck and Marvin Zuckerman (among others) inspired International Society for the Study of Individual Differences in 1985. It was subsequently published in a book chapter (Haier *et al*. 1987). PET was first used for clinical research about 1980. I had given personality tests to a number of subjects in PET studies being conducted at the University of California at Irvine 1984–1985. The intention was to see if personality traits correlated with regional brain function. The PET technique is based on injecting a special low-level radioactive sugar tracer, ^{18}F-flurodeoxyglucose (FDG), into a person while they are engaged in a mental task. The harder any part of the brain works to perform the task, the more FDG is taken up by that part of the brain and the more signal would be detected in that location during the scanning. Many early PET studies were done while subjects rested with their eyes closed instead of while engaged in a mental task. Since the choice of task (or no task) determined the regional pattern of brain activity, this was a critical element of PET research design. For studies of personality, no particular task was obviously relevant and even if one was, the expense of PET scans (about $2500 per person in 1985; about $1200 in 2003) precluded an exploratory, non-funded study or even pilot work to develop a proper task. This is a primary problem, which has limited functional brain imaging research in personality to this day.

In 1985, the University of California at Irvine was conducting a PET study of generalized anxiety disorder. I asked the subjects, 18 outpatients with generalized anxiety disorder and 9 normal controls, to complete the Sensation Seeking Scale (Zuckerman 1971) and the Eysenck Personality Questionnaire (EPQ; Eysenck & Eysenck 1975) prior to their PET scans. The design included two baseline, pre-drug PET scans per person. During FDG uptake, one scan used the Continuous Performance Test (CPT) where the subject viewed random digits and pressed a button for each zero, i.e. an attention task condition. For the other scan, a control task of the same CPT stimuli was used but with instructions to view the stimuli passively, i.e. a no-task condition without instructions to press the button for any target. Brain function during each condition was quantified as glucose metabolic rate (GMR) and correlations with personality scores were computed for both quantified GMR and relative GMR, i.e. GMR within an area divided by whole brain GMR to correct for individual differences in whole brain GMR. Brain areas were defined, *a priori*, with a stereotactic brain atlas approach.

By current standards, everything about this design and analysis was rudimentary. The results, based on a small sample and limited accuracy of anatomical localization, were regarded as exploratory and interpreted with caution. Only two-tailed tests were used because there were few clear directional, *a priori*, hypotheses about brain areas and personality traits. Interpretation of increased or decreased GMR in an area was problematic because increased GMR could signify more inhibitory activity as well as more excitatory activity. We found a tentative pattern of positive correlations between GMR in frontal and temporal areas and the EPQ measure of Extraversion. Areas of the caudate and putamen (dopamine areas) were also correlated with Extraversion. Other areas showed negative correlations with EPQ Psychoticism. The cingulate, the thalamus, the hippocampus, and the parahippocampus also showed correlations with various scales, especially in right hemisphere. Correlations with the Zuckerman scales were plentiful throughout the brain, but a clear pattern was not apparent. At the time, it was clear that this data set was not adequate to address personality issues. Despite the many difficulties, this study did demonstrate the potential of brain imaging to identify the functional neuroanatomy of personality traits. We enthusiastically concluded our discussion by saying, "It is now possible to design new experiments to extend the scientific investigation of personality from the realms of behavior and psychometrics to the deep recesses of the brain itself" (Haier *et al*. 1987: 266).

Not much happened. Researchers interested in personality had very limited access to imaging technology, which required collaboration with other specialties not usually interested in personality research and high budgets virtually unknown in psychometric personality studies. Scanning large samples with tasks appropriate to personality issues would be required along with image analysis techniques that could address multiple problems of anatomical localization and statistical inference.

Four years later, an abstract of a PET study (Semple *et al*. 1991) reported a significant correlation between the EPQ Neuroticism Scale and GMR in areas of the frontal lobe in 27 normals, males and females combined (mean age = 29), but this was not replicated in another sample of 44 volunteers scanned with different parameters. Details were limited and a full report was never published so no conclusions can be reached about these findings.

2.3. The First Single Photon Emission Tomography Study of Personality

In 1994, Ebmeier *et al*. used a variation of the PET method, single photon emission tomography (SPECT), to measure regional blood flow in 51 normal, mostly elderly volunteers, who were selected as controls for other studies. The age and sex of the participants was not reported. The scans were obtained while most subjects rested, but subgroups performed various tasks. All subjects completed the EPQ separately from the imaging. Anatomical localization was based on a stereotactic atlas approach to define 15 regions of interest in each hemisphere using only two brain slices. Blood flow within regions of interest was determined and a principal components analysis was used to extract brain factors after controlling for age. Four brain factors were identified, fronto-temporal, cingulate, sub-cortical, fronto-parietal.

The three EPQ scales, Extraversion, Neuroticism, and Psychoticism, were correlated with each factor. Of the 12 possible correlations, only Extraversion and the cingulate factor were correlated ($r = 0.46$). Despite numerous difficulties in this study which were mostly derived from using subjects and task conditions that were selected for other projects, the statistical approach was a good attempt at addressing a fundamental problem in brain imaging, that of having many intercorrelated variables and small sample sizes. As computing technology improved and voxel-by-voxel analysis became possible, however, this problem grew even more complex and required a different statistical approach. The modern studies discussed below now use standard image analysis programs like Statistical Parametric Mapping (Friston *et al*. 1995).

2.4. The NEO Personality Inventory Scales in Imaging Studies

Fischer *et al*. (1997) used PET to measure regional blow flow by scanning the distribution of mildly radioactive water injected into the blood stream. This PET technique is an alternative to measuring glucose metabolic rate with FDG. Both techniques use the same hardware and regional blood flow and GMR are highly correlated. Thirty female volunteers (mean age 32, SD = 6.1) were scanned while viewing an emotionally neutral video for about four minutes as a control condition for an anxiety study. A Swedish version of the NEO Personality Inventory-Revised (NEO PI-R; Costa & McCrae 1992) was used to form groups by a median split on the Extraversion and Neuroticism scales. A number of specific regions-of-interest were defined *a priori* by a brain atlas approach. For extraverts, higher blood flow was observed in caudate and putamen (dopamine areas); no cortical areas differed in blood flow between extraverts and introverts. No differences were found between high and low Neuroticism groups. In a separate analysis, Type A subjects showed higher blood flow than Type B subjects in areas of the hypothalamus and the hippocampus (Fredrikson *et al*. 1999). Overall, this work had a number of methodological strengths and some of the same weaknesses of earlier studies. The strongest results highlighted the potential importance of a relation between dopamine and Extraversion, as had been only suggested in earlier work (Haier *et al*. 1987).

The next PET blood flow study used more sophisticated image analysis procedures that allowed better anatomical localization of findings (Johnson *et al*. 1999). This group scanned 18 normal volunteers, ten males and eight females with a mean age of 30 years (SD = 8.5). Blood flow in every image voxel throughout the entire brain was correlated to scores on only one NEO scale — Extraversion. Using a criterion of $r > 0.60$ ($p < 0.005$, one-tailed), 17 areas had significant correlations, uncorrected for multiple comparisons, with Extraversion. Most of these areas were identified in the earlier less sophisticated imaging studies, although some earlier studies were not cited. It is not clear why one-tailed tests were used instead of more conservative two-tailed tests, since there was no hypothesized *a priori* directional relation between most brain areas and personality. Moreover, none of the correlations were corrected for age, which ranged from 19 to 48 years. Age is a well-known influence on cerebral blood flow. This was a disappointing study because, although it used the most sophisticated analyses to date, the sample size was still too small to study individual differences and the subjects were scanned at rest, which is essentially an uncontrolled condition. The use of only one personality scale also makes interpretation difficult. For all these reasons, the results really provided no new insights as the 1990s "Decade of the Brain" neared its end.

2.5. The Temperament and Character Inventory Scales in Imaging Studies

In another SPECT study, Sugiura *et al*. (2000) correlated regional blood flow during rest with scores on the three scales of the Temperament and Character Inventory (TCI;

Cloninger 1987), Novelty Seeking, Harm Avoidance, and Reward Dependence for 30 volunteers. There were 13 males and 17 females with an age range of 26 to 61 years. Voxel-by-voxel correlations were computed and some promising positive and negative correlations were reported, $p < 0.005$, one-tailed, uncorrected for multiple comparisons, for cingulate, insula, parahippocampus, pre- and post-central gyrus, and parts of the frontal lobe. However, the effects of age and sex on blood flow were not removed and, given there was no correction for multiple comparisons, these one-tailed tests at $p < 0.005$ must be interpreted with caution. Most of the areas showing significant correlations were also noted in previous studies. Because this study shared the limitations of previous studies, these results added little to our understanding of the issue.

A similar study (Youn *et al.* 2002) used PET and FDG instead of SPECT to find correlates of the same three TCI scales. Subjects were 19 normal volunteers (13 males, six females; mean age = 26, SD = 9.9), scanned during rest. Voxel-by-voxel analysis was done with Statistical Parametric Mapping (99) without removing age or sex effects. For statistical tests a criterion of $p < 0.005$, one-tailed, uncorrected for multiple comparisons, was employed. GMR results include negative correlations with novelty seeking for areas in precentral gyrus, parahippocampus, and middle temporal lobe and a positive correlation in middle frontal gyrus. Only negative correlations were found with harm avoidance in areas of temporal cortex and anterior cingulate. Only positive correlations were found with reward dependency in areas of temporal lobe and the orbital frontal gyrus. According to the authors, these areas were somewhat different than those reported by the similar Sugiura *et al.* (2000) SPECT study of the TCI. Like the earlier attempts with Extraversion and Neuroticism, both studies using the TCI scales failed to use a cognitive task instead of rest; both failed to correct for age and sex effects; and both used liberal statistical analyses uncorrected for multiple comparisons in small samples. It is no surprise to find inconsistent results.

A third SPECT study correlated blood flow with scores on seven TCI scales in 20 normal male subjects, 20–33 years of age (Turner *et al.* 2003). A novel aspect of this study was that the imaging occurred while each subject completed the TCI items. Whether this is a good control of mental state is arguable. Because their initial regression analyses did not show linear relations with personality scores, a quartile method was used that revealed many nonlinear relations (activations and deactivations) between the TCI scales and regional blood flow in a number of areas throughout the brain. So many relations were found that additional study is necessary with a larger sample and a more controllable task before these data can be assessed.

2.6. PET Receptor Studies of Personality

The PET technology can also be used to assess various neurotransmitter receptor systems. Glucose or blood flow PET studies are indexes of general activity, closely tied to neuronal function, and regional glucose and blood flow results are often used to infer the activity of neurotransmitter systems known to be involved with the areas identified. PET receptor studies assess specific neurotransmitter systems more directly. Typically, a radiotracer is attached to a drug that has an affinity to block certain receptors (at least more than it blocks other receptors). For example, Farde *et al.* (1997) assessed dopamine D2 receptor density using PET and the radioligand [^{11}C] raclopride. The data were correlated to 15 scales of the Karolinska Scales of Personality (Schalling *et al*. 1987). There were 24 normal participants, 14 men and ten women, who ranged in age from18 to 38 years. Results, uncorrected for age, showed a significant correlation between D2 receptor density in the putamen and scores on the detachment scale and on the irritability scale.

Subsequent attempts to replicate a relation between dopamine and similar scales with PET were mixed (Kestler *et al*. 2000; Laakso *et al*. 2000; Leyton *et al*. 2002; Suhara *et al*. 2001; Yasuno *et al*. 2001). PET studies examining the relation between serotonin receptor activity and personality are similarly inconsistent (Moresco *et al*. 2002; Rabiner *et al*. 2002). For the most part, the samples of participants in PET receptor studies consisted of both males and females with a wide range in age. The studies also employed a variety of personality scales. Nonetheless, in conjunction with other types of research, receptor-imaging studies have great potential to help identify the brain systems that are important to personality.

2.7. The First Uses of Functional Magnetic Resonance Imaging in Personality Studies

In 2001, Canli *et al*. reported a new, potentially exciting approach to research on personality and the brain using functional magnetic resonance imaging (fMRI). Building on imaging experiments of response to emotional stimuli, they scanned 14 female volunteers, with an age range of 19–42 years, while they passively viewed pictures with either a positive or a negative emotional content. Although this study was designed to compare brain activation patterns between positive and negative emotion, each subject also completed the NEO scales. Voxel-by-voxel correlations between positive and negative stimuli were determined for each scale at $p < 0.001$, uncorrected for multiple comparisons and without removing any age effects. Extraversion correlated positively with increased activation to positive stimuli in areas of the frontal lobes, temporal lobes, and parts of the caudate, putamen, and amygdala. Some of the same areas were correlated to Neuroticism (Extraversion and Neuroticism were correlated, $r = -0.42$, NS). Most of these significant areas were reported in previous studies. Although this study also had a small sample and used liberal statistical criteria, the design included a task during the scanning that was relevant to personality. This was a welcome first. The spatial resolution of fMRI is also better than other functional imaging. At the very least, this study demonstrated the important finding that some personality variables can influence emotional response in the brain and therefore, cognitive studies of emotion should take account of individual differences in personality scores among the subjects just as age and sex must be considered. Canli *et al*. (2002) made this point dramatically in another fMRI study of 15 volunteers by showing that Extraversion was correlated to the degree of activation in the amygdala during happy stimuli. Only the amygdala data were reported.

Gray & Braver (2002) conducted an fMRI study of working memory in 14 normal subjects, six males and eight females, with an age range of 19 to 27 years. They also collected data on two personality measures that were based on his personality theory (Gray 1970, 1982). Scores on the measures of behavioral approach sensitivity, an impulsivity dimension, and behavioral inhibition sensitivity, an anxiety dimension, were correlated to activity in regions of interest in parts of the anterior cingulate, the only area reported. The complex analyses involved collapsing two emotion-based stimulus conditions and applying multivariate statistical procedures. The analysis was limited by the small sample size and by combining males and females, uncorrected for age. Consequently, there is a need for replication, but this study follows the recent trend of including an experimental manipulation in an imaging study and investigating how personality variables influence results.

2.8. Structural Magnetic Resonance Imaging and Personality

Another approach with potential may be structural brain imaging. Size and volume of various brain structures can be determined from low cost MRI. For example, one important study (Pujol *et al*. 2002) measured the surface area of the anterior and posterior cingulate in 100 subjects, 50 males and 50 females. They found positive correlations between the TCI Harm Avoidance scale and activity in the right anterior cingulate. The left posterior cingulate was positively correlated with Novelty Seeking. The method used to determine size, however, has a number of limitations and cannot be applied to all brain areas.

Structural MRI can also measure gray and white matter concentrations throughout the entire brain using the recently developed voxel-based-morphometry approach (Ashburner & Friston 2000; Good *et al*. 2001). We are applying this approach to NEO PI-R personality data in 25 normal controls. Preliminary analyses, removing age and sex effects, show several significant correlations. For example, scores on the Neuroticism scale are positively correlated with gray matter concentrations in limbic areas including the amygdala, i.e. more gray matter in these areas for those high on the Neuroticism scale. The Extraversion scale is negatively correlated with the putamen, an important dopamine area (low Extraversion goes with greater gray matter). The Openness scale is positively correlated with gray matter in the left middle and inferior temporal lobe. Unlike functional images, structural images are completely independent of cognitive task, so these relationships between gray matter and personality may prove to be more replicable. A complete analysis and report are underway.

3. Conclusions

We are now at the 20th year anniversary of the Mathew *et al*. (1984) paper correlating cortical blood flow assessed with the xenon technique and Extraversion, and it is 18 years since the first PET study correlated GMR throughout the brain with several personality dimensions. What is the subsequent progress? The bad news is readily apparent. Every functional imaging study trying to identify brain areas correlated to personality traits have major limitations and flaws, as described in the preceding review. Functional brain imaging results are dependent on the cognitive state of the subject, so studies “at rest” are essentially uncontrolled, and in my view, not easily interpretable. Small samples, often confounding sex and age effects, have limited statistical power and similarly yield results difficult to interpret. At this point, inconsistencies abound and replications are few so that no strong specific or general findings about personality and regional brain function are apparent from the imaging studies. The most that can be said is tentative — there may a dopamine connection to Extraversion (via the caudate and putamen) and the amygdala may be involved in Extraversion and Neuroticism; frontal and temporal cortex may also be related to several personality dimensions.

The good news is that this field is wide open for discovery. Most of the shortcomings to date derive from adding the collection of personality data to small sample studies designed for other purposes. The mistakes of the past are easily addressed, given proper funding and studies designed specifically to address personality issues. For example, subjects could be selected for high or low scores on at least two personality traits (median splits are used when subjects have not been selected for high or low scores and medians are not the best way to divide people into personality groups). Then the subjects should be scanned at least twice, once engaged in a task to highlight areas thought to be involved in one personality measure and once engaged in a task to highlight the other personality measure. Although PET remains expensive, fMRI is considerably less so and, as demonstrated in recent studies, has great potential for personality research. Compared to the complexities and expense of obtaining brain imaging, testing subjects on multiple measures of personality is relatively easy and should be considered so that studies using the same measures can be compared.

Imaging studies shine light into the "black box" (as Behaviorists referred to the brain) and they are helping identify the brain areas and systems that underlie some important aspects of personality. Ultimately, this information, combined with other kinds of psychopharmacology and neurotransmitter studies and molecular genetics, will lead to a detailed understanding of the neurobiological basis of personality. Such an understanding is likely to rival the wildest expectations of earlier, modern personality researchers who studied psychophysiology (Gale 1973; Strelau 1983), perception (Witkin *et al*. 1954), and even brain lesions (Powell 1981). This has long been the vision of Marvin Zuckerman and other pioneers of personality research. As more and more psychologists use revolutionary brain imaging and neuroscience techniques, the realization of this vision may be near.

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