Brain Imaging and Eating Disorders

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I. INTRODUCTION

The development and application of new technologies in brain imaging have made possible unique avenues for investigating the roles of neuroanatomy and brain metabolism in the etiology of eating disorders. In the search to identify the pathophysiology of anorexia nervosa and bulimia nervosa, and to better understand the relationship between the two illnesses, we are learning about parts of the brain that may be involved in regulation of appetite, mood, and body image.

Most early theories regarding the etiology of bulimia nervosa and anorexia nervosa involved psychosocial factors and family pathology. However, research over the past decade has begun to identify biological factors that, independent of or interacting with psychosocial environment
and family relationships, may contribute significantly to development of these disorders. The search for pathophysiologic processes involved in eating disorders is supported by neuroendocrine (Levy, 1989) and neurotransmitter studies (Fava et al., 1989), family history research (Hudson et al., 1987; Kassett et al., 1989), and psychopharmacology data (Pope et al., 1983). Family history studies suggest that a genetic background significant for major depression and/or alcoholism may predispose an individual toward development of an eating disorder (Hudson et al., 1987; Kassett et al., 1989). Neurotransmitter studies have found that patients with eating disorders have lower levels of cerebrospinal fluid (CSF) norepinephrine (Kaye et al., 1984a; Kaye et al., 1990), and serotonin has been strongly implicated as significant in eating disorder pathology (Kaye et al., 1984b; Fava et al., 1989).

Brain imaging techniques have been utilized in the past 20 years to search for a physical process that might be involved in eating disorders. Computerized tomography (CT) studies have been performed on both anorectic and bulimic patients. CT provides a view of brain structure by assigning a numeric value determined by the degree of X-ray attenuation of brain tissue. These studies have identified ventricular enlargement and sulcal atrophy in both disorders. Repeated studies when patients with anorexia nervosa regain their body weight, show at least partial and sometimes complete reversal of the conditions. The role of prolonged starvation in the case of anorexia and of intermittent starvation-like states in bulimia may contribute to the structural changes.

There are three studies of magnetic resonance imaging (MRI) in the current literature on eating disorders, two on bulimia (Hoffman et al., 1989a; Hoffman et al., 1990) and one on anorexia nervosa (Hoffman et al., 1989b). MRI provides a higher resolution image of brain structure and has superior sensitivity to CT in detecting brain lesions (Kucharczyk et al., 1985). MRI produces images by applying electromagnetic forces to the brain, causing hydrogen atoms to move. When the force is turned off, the hydrogen atoms return to their original position, producing an electromagnetic signal. Different parts of the brain emit unique signals (referred to as relaxation times T-1, T-2), which, when transformed by computer, provide a high resolution image of brain structure. MRI, like CT, is limited to generating images of brain structure, and cannot provide images of brain function.

Positron emission tomography (PET) provides a method for examining functional brain metabolism. PET uses the mathematics of CT scanning to produce cross-sectional images of tissue in which a radioisotope-tagged chemical has been deposited. In the case of published studies on eating disorder subjects, a positron-emitting atom, fluorine-18, is incorporated into a glucose analog, 2-deoxyglucose, and is injected into the subject. Up-
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into the subject. Up-
take of the fluorine-18-labeled 2-deoxyglucose (tracer) by the brain can
then be monitored. The tracer is injected during a 30-min period prior to
scanning while the subject rests or performs a task. The fluorine-18-labeled
2-deoxyglucose will be only partially metabolized once it is taken
up by brain cells during task performance, and will continue to emit a
positron signal that will be detected by the PET scanner. PET thus pro-
vides an image of mental activity during the period of tracer uptake.
These signals are fed into a computer, which then generates an image of
metabolic brain function during the period of tracer injection prior to PET
scanning. Results are generally reported for absolute units of μmol glu-
cose/100 g brain/min and also as ratios to whole slice glucose metabolic
rate (relative analysis).

In comparing PET data, it is important to note the conditions under
which the study was performed, including tracer used, activity of subject
during tracer uptake (task), and method of analysis of results. PET looks
at brain function, and results are therefore partially dependent on what
the subject is doing at the time of tracer injection and uptake. PET scan
data seek to identify specific brain regions where abnormal function of
the brain could result in the aberrant eating behavior, thought patterns,
and mood disturbances found in eating disorder subjects.

There have been three published studies of anorexia nervosa using PET
(Emrich et al., 1984; Krieg et al., 1986; Herholz et al., 1987) and two studies
of bulimia (Hagman et al., 1990; Wu et al., 1990). No studies using PET
have compared anorexics and bulimics.

II. COMPUTERIZED TOMOGRAPHY STUDIES OF EATING DISORDERS

A. Overview

A number of studies have been published on CT in anorexia nervosa
(Enzmann and Lane, 1977; Heinz et al., 1977; Nussbaum et al., 1980; Sein et
al., 1981; Kohlmeyer et al., 1983; Artmann et al., 1985; Datlof et al., 1986;
Dolan et al., 1988; Krieg et al., 1988). The most common finding among
these studies is cerebral atrophy and ventricular dilatation. The cerebral
atrophy found in anorectics is often called "pseudoatrophy," because it
sometimes resolves when the anorectic subject returns to a normal body
weight (Heinz et al., 1977; Artmann et al., 1985).

Three published studies have compared anorectic, bulimic, and normal
controls using CT (Lankenau et al., 1985; Krieg et al., 1989a; Lauer et al.,
1990). Krieg et al. (1989a) compared CT scans in 50 bulimic subjects (20
with a past history of anorexia) with 50 age-matched anorectics and 50
controls. There were two male subjects in each of the anorectic and control
groups. Control subjects had diagnosed personality or adjustment disorders. All the eating disorder subjects were inpatients, and it was unclear from the paper whether control subjects were also inpatients. Bulimic subjects in the study had a significantly longer duration of illness than anorectics. Enlargement of external CSF spaces was rated as none, slight, or marked. Thirty percent of the bulimics showed slight enlargement and 6% showed marked enlargement, compared with 50% of the anorectic group showing slight and 36% showing marked enlargement. Only 16% of the controls showed slightly enlarged external CSF spaces, and none were rated as marked. Although bulimic subjects had enlarged external CSF spaces significantly more often than controls, this occurred significantly less than in the anorectic group. Similar findings occurred in measurements of ventricular enlargement, with the mean value for bulimics significantly higher than that for controls, but significantly lower than that for anorectics. There was a significant correlation between enlarged external CSF spaces and ventricular enlargement. Bulimic subjects with a past history of anorexia nervosa were more likely to exhibit sulcal widening. Biochemical measures of starvation (cortisol, triiodothyronine [T3], and beta-hydroxybutyric acid [BHBA]) were measured in only the bulimic group. There was a significant negative correlation between ventricle:brain ratio (VBR) and T3 level, with larger ventricles being associated with low T3; however, no significant correlations between plasma levels of BHBA, cortisol, or electrolytes were found. Similar findings have been reported for anorectics (Krieg et al., 1988). The authors hypothesized that "the metabolic and endocrine reactions to starvation are responsible for the morphological brain alterations regardless of whether the periods of starvation lead to emaciation or not (p. 45)."

Lauer et al. (1990) reported on a comparison of 10 subjects with bulimia nervosa (5 with a history of anorexia nervosa) and 9 with anorexia nervosa (2 with a history of bulimic behavior, 2 currently binging and vomiting). Fifty percent of the bulimic sample and 56% of the anorectics had ventricular enlargement, a nonsignificant difference between the groups. The study found no relationship between binging and vomiting behavior and structural brain alterations. Their discussion suggests that because the bulimic sample was of normal weight, emaciation could not be the only cause of the enlargement; rather, there must be a pathogenetic process common to both illnesses. The authors suggested exploring further the association between CT alterations and neuroendocrine abnormalities.

Lankenau et al. (1985) reported enlargement of CSF spaces in 8 of 14 anorectic patients and cortical sulcal atrophy in 4, but did not find any significant ventricular enlargement in 5 bulimic subjects. Subjects in the control group were also studied.
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Subjects with bulimia 19 with anorexia ner-dly binging and vomiting of the anorectics had ed vomiting behavior suggests that because could not be the st be a pathogenetic suggested exploring and neuroendocrine CSF spaces in 8 of 14 it did not find any sig-tts. Subjects in the con-

trol group, which consisted of 14 psychiatric inpatients who were age- and sex-matched to the anorectic sample, had diagnoses of adjustment disorder, personality disorder, and nonpsychotic major depression. CT abnormalities were significantly correlated with rate and degree of weight loss.

A recent study (Krieg et al., 1989b) compared CT and regional cerebral blood flow (rCBF) using xenon-133 and dynamic single photon emission computerized tomography (dSPECT) in 12 anorectics before and after weight gain. Regional CBF, measured by dSPECT, was not diminished in the anorectic state. A decrease in ventricular size, measured by CT, after weight gain was associated with a significant increase in CBF in this area. The authors noted that their PET study (Krieg et al., 1986) also did not find decreased absolute glucose metabolism in the anorectic state, although the subjects had cortical atrophy by CT. Partial volume effects caused by ventricular enlargement could have caused the findings.

B. Summary

Computed tomography, which provides measurements of brain anatomy, shows cerebral atrophy and ventricular dilatation in both anorectic and bulimic patients, with anorectic subjects having more dramatic changes in brain structure. In anorectics, these changes sometimes appear to be at least partially reversible. No studies have been done on bulimics who have recovered from their illness. Future studies using CT should attempt to correlate clinical variables, biochemical parameters, and brain function with changes in brain structure.

III. MRI STUDIES OF EATING DISORDERS

A. Overview

A pilot study (Hoffman et al., 1989b) using MRI found nonsignificant ventricular enlargement when comparing 10 anorectic subjects with a control sample of 10 age-matched outpatients who had been scanned previously for a diagnosis of headache. Significant ventricular enlargement was found when a subset of five anorectics who reported vomiting were compared with controls. The authors hypothesized that more severe malnutrition, dehydration, or abnormal vasopressin release caused by vomiting may have led to more pronounced cerebral atrophy.

The same research group (Hoffman et al., 1989a) also studied eight bulimic women and eight age-matched control women using MRI. None of
the bulimic subjects had a prior history of anorexia nervosa, or a current diagnosis of major affective disorder or alcoholism. Two of the bulimic subjects used laxatives; none reported diuretic use. The controls were women who had previously had MRI scans performed for diagnosis of headache. Measurements of sagittal cerebral : cranial ratios (SCCR) were obtained to assess cerebral atrophy. VBR was measured to assess ventricular enlargement. VBR is most affected by changes in gray matter (basal ganglia) or white matter (corpus callosum) that surrounds the ventricles, whereas SCCR is most affected by changes in the cortical gray volume. The study found that the bulimic group had significant cortical atrophy compared with the normal group. No evidence of ventricular enlargement was found in either group. In the bulimic group, there was a significant positive correlation between VBR and binge frequency. The authors noted that the positive correlation between VBR and binge frequency could be due to chance, but they also suggested that atrophy measures might be expected to increase proportionately with binge frequency (severity of illness). The authors discussed several possible factors that might contribute to the development of cerebral atrophy in normal weight bulimia, including starvation states; hypercortisolism (Heinz et al., 1977); decreased intravascular colloid pressure due to loss of serum protein, with subsequent movement of water into the CSF space (Heinz et al., 1977; Artmann et al., 1985); and loss of brain tissue water due to changes in vascular permeability (Krieg et al., 1987), possibly associated with diminished vasopressin release (Gold et al., 1983; Nishita et al., 1988).

Hoffman et al. (1990) published another study on the same group of bulimic women, measuring proton longitudinal relaxation time (T-1) as measured by MRI; however, a different group of seven control subjects from the community was used. The study examined T-1 values in the cingulate, superior, middle, and inferior gyri of the frontal lobe, the caudate, and the white matter at the level of the corona radiata bilaterally. In general, the bulimic group had lower mean T-1 values in all regions measured, although the difference was only significant in the inferior frontal gray matter. The authors suggested that the lower T-1 values in the bulimic group might represent decreased brain water content, and therefore be related to cerebral atrophy as discussed in their prior publication on the same group of subjects. However, this speculation was not supported by statistical correlation between T-1 for inferior frontal gray matter and the SCCR. Other factors the authors suggested may be involved in decreased T-1 values were reduced levels of potassium, sodium, glycogen, or protein content (Bottlemley et al., 1987). All these values are commonly altered by bulimic behaviors of binging, purging, starving, overexercising, and diuretic or laxative abuse.
b. Summary

Three published reports of MRI findings in patients with eating disorders have yielded significant, yet unexplained abnormal findings. Ventricular enlargement was associated with vomiting in subjects with anorexia nervosa. Decreased T-1 values in the inferior frontal gray matter and cerebral atrophy, without ventricular enlargement, were found in bulimic subjects. If ventricular enlargement in anorexia is due to the presence of vomiting, the bulimics studied should have shown ventricular enlargement as well. It is probable that alterations in appetite regulation, food selection, and consummatory behavior of the subjects contributed to the abnormal findings, as variables such as age, sex, and comorbidity were controlled in the study. Future studies should include attempts to explain underlying mechanisms causing the abnormalities, and should also include scans when patients are recovered or in remission from the illness.

IV. POSITRON EMISSION TOMOGRAPHY STUDIES IN EATING DISORDERS

a. Overview

Two research groups have begun publishing studies using PET to study eating disorders. Herholz et al. (1987), Krieg et al. (1986), and Emrich et al. (1984) of the Max Planck Institute for neurology and psychiatry in Munich, Germany, have published several papers on a sample of seven anorectic females. Wu et al. (1990) and Hagman et al. (1990) of the University of California at Irvine have published a report on a series of eight bulimics, compared with normal controls (Wu et al., 1990), and a more extensive analysis (Hagman et al., 1990) that compared the same groups and added a group of eight women with major affective disorder. No PET studies have been published in which bulimic and anorectic subjects have been studied under the same conditions.

Emrich et al. (1984) reported a pilot study of six anorectic females using 18-fluoro-2-deoxyglucose (FDG) PET. Five of the six subjects also binged and purged. The control group consisted of seven normal males who were on average 10 years older than the anorectic subjects. The anorectic subjects also had CT scans and electroencephalograms (EEGs). Although five of six subjects showed evidence of cortical atrophy on CT, hypometabolism was not found on PET scanning. In contrast, the authors reported high frontal activity, and a tendency toward hypermetabolism in
the cerebellar cortex. No statistical analyses were reported in the paper.

Krieg et al. (1986) compared CT and PET in seven anorectic subjects, all of whom showed evidence of cortical pseudoatrophy on CT. There were no significant differences in the absolute glucose metabolic rates for cerebral cortex between normal controls and patients, or between patients in anorectic and remitted states. Measurement of relative metabolic rates found significantly lower metabolism for anorectics in the cortex and cerebellum and higher rates in the white matter and caudate nuclei. Five of the anorectic subjects received PET scans after weight gain. There were no significant differences within this group; however, when compared with controls, significant differences emerged.

These findings were investigated further by Herholz et al. (1987), who reported PET findings in the five anorectic females scanned during the anorectic state and after weight gain. Four of the subjects were previously reported in the Emrich pilot study, and three of the five also had symptoms of bulimia. Information about bulimic episodes was unavailable for one subject. The control group consisted of 15 normal males who were significantly older than the patient group. Each anorectic subject also had a CT scan, EEG, and plasma measurement of BHBA. During FDG uptake, subjects were in a resting state in a dim room, with eyes closed, and low ambient noise from the fans of the four-ring tomograph. Using a semiautomatic interactive mapping procedure (Herholz et al., 1985), 300 regions of interest were determined and were subsequently organized into 15 clusters for each side, defined with respect to major anatomical structures of the brain. Only absolute values of glucose metabolism were reported. When brain metabolism was compared during the anorectic state and after weight gain, the study found significantly higher metabolism in the caudate nucleus and temporal cortex on both sides, and in the left lentiform nucleus in the anorectic state. A comparison of brain metabolism in subjects during the anorectic state and in the normal control group, found that the caudate nucleus remained significantly elevated bilaterally, and that the right thalamus and left brainstem were similarly elevated. After weight gain, there were no significant differences between patients and controls. The authors speculated that caudate hypermetabolism “could correlate with the clinical observation of increased vigilance and performance (p. 49)” observed in patients with anorexia nervosa. EEG studies (Buchwald et al., 1961) have shown that stimulation of the caudate nucleus influences alertness and response to external stimuli. Herholz et al. also noted a study by Rolls et al. (1983), which found that in monkeys, 25.8% of the neurons in the head of the caudate responded in conditioned tasks to the appearance of food, whereas after unconditioned stimuli, only up to 9.6% of the neurons responded. Herholz et al. (1987) concluded that the caudate nucleus “may actually play an im-

portant role in the functional cerebral metabolic regulation of psychomotor activity.”

Wu et al. (1990) found no prior history or with PET using FDG (Nuechterlein et al., 1986) uptake. This study outlined using FDG PET divided into normal, females were generated (1978) and a PET image. Restricted relative (radial) surface for the metabolic rate of normal activity was in the temporal lobe, the metabolic rate abnormal subjects. In bulimia nervosa, some brain regions were abnormal, while the patients re-ported in a previous study, the caudate, as well as the left temporal cortex, showed a higher metabolism, size, and laterality.
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portant role in integrating environmental influences” and that “increased functional activity in this structure, as indicated by increased glucose metabolism, could represent a neurobiological correlate of altered neuropsychological processes (p. 49).”

Wu et al. (1990) compared eight normal weight bulimic women having no prior history of anorexia nervosa with eight normal control women using FDG PET. The subjects performed the Continuous Performance Test (Nuechterline et al., 1983), which is a visual vigilance task, during FDG uptake. Three PET slices were chosen for analysis. Cortical regions were outlined using a boundary finding technique developed for CT scans, and divided into four anteroposterior sectors. Subcortical regions of interest were generated by digitizing an image from an atlas (Matsui and Hirano, 1978) and automatically transferring the proportional locations to the PET image. Results were reported for both absolute glucose metabolism and relative (ratio to whole slice) glucose metabolic rate. Analysis of cortical surface found that normal women had significantly higher relative metabolic rates in the right hemisphere, whereas bulimic subjects lost this normal asymmetry. The largest difference between patients and normals was in the right posterior sector, which included the right parietal and temporal lobes. Bulimic patients had higher absolute and relative metabolic rates on the left in contrast to higher rates on the right in normal subjects. In subcortical and medial frontal structures, patients with bulimia showed less right lateralization than control subjects. Bulimics had higher absolute and relative metabolic rates in the left hemisphere basal ganglia and thalamus. The loss of right greater than left asymmetry in some brain regions in this sample of bulimic patients suggests that hemispheric lateralization may play a role in development of bulimia. The study did not find hypermetabolism in the caudate or thalamus, as reported in anorectics by Herholz et al. (1987), or hypometabolism in the caudate, as reported in PET studies of depression (Baxter et al., 1985; Buchsbaum et al., 1986). Limitations of the study include the small sample size, and lack of a comparison group of anorectics or depressed subjects.

Our most recent study of bulimic women (Hagman et al., 1990) included a group of eight women with major depression in a more detailed analysis of the sample of eight bulimic women and eight normal control women previously reported by Wu et al. (1990). Brain metabolism in the three groups of subjects was compared using PET and FDG. We included a group of depressed subjects to investigate the relationship between depression and bulimia. Women with bulimia often present with symptoms of depression in addition to binging and purging behavior (Hudson et al., 1983; Pope et al., 1989). Reflecting the controversy over depressive symptoms in bulimia, the American Psychiatric Association (1987), in the revised third edition of the Diagnostic and Statistical Manual of Mental
Disorders (DSM-III-R), deleted depressed mood as a symptom necessary for the diagnosis of bulimia nervosa. A recent review of the published studies (Levy et al., 1989), including studies of clinical data, family history, pharmacotherapy, and neurobiology, concluded that "while many bulimic patients are depressed, a preponderance of evidence suggests that bulimia is not a variant of depression" (p. 167).

All subjects met DSM-III-R criteria for bulimia nervosa, or for major depression in the patient group, as assessed by nonstructured psychiatric interview. None of the bulimic subjects had a prior history of anorexia nervosa. None of the depressed women had a prior history of bulimia nervosa or anorexia nervosa. Normal controls had no history of psychiatric illness. A psychiatrist rated severity of depression in depressed and bulimic subjects with the Hamilton Depression Inventory (HDI), and a 7-point global clinical scale of depression (7 = most severe). Bulimic subjects also completed the 40-item Eating Attitudes Test (EAT) (Garner and Garfinkel, 1979) and a count of the number of episodes per week of binging and purging. There were no significant differences between age, height, or weight among the three groups. Bulimic subjects binged and purged an average of 14 times per week, and had an EAT score of 37.8 ± 10.3. There was a significant difference in the HDI score, with the depressed subjects scoring significantly higher (31.8 ± 5.1) than the bulimic group (20.8 ± 6.9, p < .05), but there was no significant difference in global clinical rating of depression. Six of the bulimic women were contacted after the initial PET study to assess lifetime diagnoses of depression. Four met criteria for dysthymic disorder, and two met criteria for major depressive disorder during the period in which the PET scan was performed. The two bulimic subjects who were not reached for interview had scores of 12 and 17 on the HDI, and global clinical ratings of depression severity of 3 and 4, respectively, suggesting mild depressive symptoms. Subjects were off all psychoactive medications for a minimum of 30 days. None of the subjects had ketone bodies in their urinalysis. During FDG uptake, subjects performed the Continuous Performance Test (CPT) (Nuechterlein et al., 1983).

For analysis of cortical data, the outer brain contour of each slice was outlined with a boundary-finding technique developed for skull CT scans (Buchsbaum et al., 1984; Buchsbaum et al., 1987). For subcortical and medial frontal regions, images from an atlas (Matsui and Hirano, 1978) were photographed, digitized, and stored for reference, and applied to the slices (Buchsbaum et al., 1987). Analysis was carried out both on absolute values of glucose in µmol/100 g tissue/min and on relative glucose expressed as regions of interest divided by mean glucose metabolic rate in whole slices.

Four brain regions (and three structures within each region) were chosen for subcortical analysis: medial frontal structures (paracentral, medial...
frontal, superior frontal), thalamus (anterior, medial, lateral), basal ganglia (caudate, putamen, globus pallidus), and limbic (hippocampus, amygdala, uncus). The three groups had significantly different patterns of cortical brain metabolism. As we found in an earlier analysis of the same bulimic subjects and normal controls, but without a depressed group (Wu et al., 1990), and using data from only three PET slices, subjects with bulimia had significantly greater loss of the normal right hemisphere metabolic rate compared with the left. The cortical surface analysis of both absolute and relative brain metabolism showed bulimic subjects lost normal right hemisphere lateralization in the temporal lobe. The most significant difference between bulimics and controls was in the middle and inferior temporal gyri. Bulimics showed greater left than right hemisphere rates, but normals and depressives were greater on the right. Depressed subjects exhibited normal temporal lobe activity. No differences in whole brain cortical metabolic rate were found. Both the bulimic and the depressed groups had increased right hemisphere lateralization in the occipital lobe as a result of decreases in left occipital activity. Depressed subjects had significantly lower left hemisphere occipital activity and a significantly greater difference between right and left hemisphere occipital metabolism than bulimics and controls.

In subcortical and medial frontal structures, there was a pattern of diminished medial frontal metabolism in both bulimic and depressed subjects, especially in the right hemisphere, associated with reversal of the normal right greater than left hemisphere metabolism pattern. Depressed women had lower metabolic rates than normals and bulimics in the basal ganglia and thalamus, especially in the left hemisphere. Limbic structures were most similar across the three groups.

We did not find decreased relative metabolism in the left frontal lobe in either the bulimic or the depressed group, as would have been expected based on the findings of Baxter et al. (1989), who reported decreased left middle frontal gyrus metabolism in psychiatric disorders accompanied by depressive symptoms. However, one area of similarity between bulimic and depressed subjects involved shifts in lateralization in medial frontal structures.

Both bulimic and depressed subjects had abnormalities in basal ganglia metabolism. Basal ganglia metabolism was lower in our depressed group, as has been reported in other studies of depressed subjects (Baxter et al., 1985; Buchsbaum et al., 1986). Bulimics showed a pattern of decreased relative right hemisphere lateralization in the basal ganglia. The basal ganglia provide significant input into the thalamic relay to the cortex, and are thus involved in processing sensory, and perhaps emotional tone, inputs.

Our PET scan results suggest that although there are a few regions of metabolic similarity, the syndrome of bulimia nervosa and the accompany-
ing symptoms of depression are associated with a pattern of overall brain metabolism that differs from the patterns found in women with major affective disorder (unipolar type) and in normal women (Color Plate 1). Bulimic subjects differed most from controls and depressed subjects in loss of right hemisphere lateralization, and the few similarities between bulimic and depressed subjects involved shifts in right hemisphere lateralization. Hemispheric lateralization has been recognized as an important factor in affect regulation (Flor-Henry, 1984).

The finding of significantly different patterns of brain metabolism between women with bulimia and women with depression, despite the presence of dysphoric mood in many bulimic patients, suggests that there may be various sequences of events (biological or environmental) that can lead to the development of depressive symptoms, with subsequently unique alterations in functional brain metabolism. Johnson-Sabine et al. (1984) suggested that the dysphoric mood in bulimic persons is not due to major affective disorder, but rather to the presence of abnormal eating behavior and its subsequent impact on brain chemistry. Bulimic patients often fast between binges, inducing a state of semistarvation. Keyes et al. (1950) found that normal subjects deprived of food developed depressive symptoms when they lost weight. However, this does not explain the presence of depression prior to the onset of an eating disorder (Piran et al., 1985; Walsh et al., 1985). It is possible that variations in the severity of affective disorder in patients with bulimia are associated with measurable differences in brain metabolism and neurochemistry. These results suggest that although women with bulimia frequently present with symptoms of depression, often are co-diagnosed with affective disorder, and typically respond to pharmacologic treatment with antidepressant medications, the pathophysiologic basis of bulimia differs from that of major affective disorder. Further studies of brain metabolism in bulimic patients with and without depressive symptoms will clarify the role of depressive symptoms in the illness.

B. Summary

The results of PET studies of anorexia nervosa and bulimia nervosa suggest that both disorders are associated with altered brain metabolism patterns. The etiology and underlying significance of the changes observed in brain metabolism remain unclear. Due to the small sample size in the published studies, results must be interpreted with caution; however, the significance of the findings, despite small sample sizes, strongly supports the value of pursuing further research on brain function with PET. Although anorexia nervosa and bulimia nervosa share some common clinical features, it would appear on the basis of these metabolic
pattern of overall brain women with major af- nen (Color Plate 1). Bu- nesses in loss of urities between bulimic nsphere lateralization. an important factor in

brain metabolism be- depression, despite the ns, suggests that there nvironmental) that can ans, with subsequently h Johnson-Sabine et al. ic persons is not due to of abnormal eating be-istry. Bulimic patients starvation. Keyes et al. developed depressive does not explain the g disorder (Piran et al., is in the severity of af- ated with measurable ry. These results sug- y present with symp- effective disorder, and antidepressant medi- ers from that of major sm in bulimic patients fy the role of depres-

and bulimia nervosa red brain metabolism e of the changes ob- the small sample size d with caution; how- sample sizes, strongly n brain function with osa share some com- is of these metabolic

Fig. 1. Typical positron emission tomography scans in patients with bulimia nervosa, major affective disorder, and a normal control. Note that the control has greater right than left hemisphere metabolic rates, unlike the bulimic, who is symmetrical. The patient diagnosed with major depression shows reduction of metabolism in the basal ganglia.
studies that the two illnesses may be associated with different alterations in brain metabolism. This question can be best addressed by a PET study that directly compares anorexics and bulimics using the same PET method and analysis of data.

V. CONCLUSIONS

Anorexia nervosa and bulimia nervosa are illnesses that strike primarily young women, causing severe and usually chronic dysfunction, associated with often serious medical complications. There is evidence to suggest that abnormalities in brain structure and function are at least partially responsible for the development and maintenance of the conditions. Whether these changes are primary or secondary to development of the eating disorder remains unclear. To develop a more complete understanding of anorexia nervosa and bulimia nervosa, and therefore to devise more effective treatment methods, we must continue to explore the complicated relationship between mood, behavior, cognition, and brain structure, function, and neurochemistry. Future research must combine neurochemical probes with studies of brain structure and function, while remaining sensitive to sociocultural variables in the patient population. As brain imaging technology advances, future PET studies should include neurotransmitters (serotonin, norepinephrine and dopamine) and psychopharmacologic probes (fluoxetine, desipramine, cyproheptadine, fenfluramine, cholecystokinin) as tracers, and attempt to apply tasks during isotope uptake that might enhance metabolism in brain areas involved in eating disorders. Possible tasks might involve ingestive behavior, measurement of perceived body size, and visual tasks involving food-related subjects. Combined MRI–PET studies will provide the most complete information about the relationship between brain structure, function, and subsequent effect on behavior and mood.

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