behavioral changes observed within a few hours of exposure to ionizing radiation are quite different from those that occur months later. These early and late effects have been described as different syndromes with different causes. Early behavioral alterations may be primarily due to changes in the nervous system, while later dysfunctions are based more on hemopoietic disruptions [D. J. Kimeldorf and E. L. Hunt, *Ionizing Radiation: Neural Function and Behavior* (Academic Press, New York, 1965) pp. 3–6]. Therefore, endorphins may or may not be involved in long-term behavioral effects of radiation.

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13 January 1983; revised 11 March 1983

Urinary Phenyl Acetate: A Diagnostic Test for Depression?

Abstract. *The compound 2-phenylethylamine is an "endogenous amphetamine" which may modulate central adrenergic functions. 2-Phenylethylamine is mainly metabolized by monoamine oxidase to form phenyl acetate (PAA). The 24-hour urinary excretion of PAA was measured in normal healthy volunteers and depressed patients. Patients were diagnosed according to the* Diagnostic and Statistical Manual of Mental Disorders, *edition 3. In 70 percent of healthy volunteers of both sexes, the excretion of PAA ranged between 70 and 175 milligrams per 24 hours (mean = 141.1 ± 10.2). Inpatients with major depressive disorder (unipolar type) (N = 31) excreted less PAA (68.7 ± 7.0 milligrams per 24 hours) and 55 percent of them excreted less than 70 milligrams per 24 hours; there were no significant differences in the PAA excretion between untreated patients (N = 13) and those treated with antidepressants that were not effective (N = 18). The PAA excretion was reduced to a lesser extent in 35 less severely depressed unipolar outpatients (drug-free for 1 week) (86.3 ± 11.8 milligrams per 24 hours). These results suggest that low PAA urinary excretion may be a reliable state marker for the diagnosis of some forms of unipolar major depressive disorders.*

The phenylethylamine hypothesis of affective behavior states that 2-phenylethylamine (PEA) is a neuromodulator responsible for triggering or sustaining wakefulness, alertness, and excitement, possibly by the modulation of brain catecholamine synapses (*1*). A decrease in the brain concentrations or turnover of endogenous PEA may therefore play a major physiopathological role in certain forms of endogenous depression, whereas an increase in the concentrations of PEA in the brain or the activation of specific PEA receptors in brain neurons may be responsible in part for the actions of antidepressant and stimulant drugs (*2*).

Structurally, PEA is closely related to amphetamine and to catecholamines; PEA induces behavioral and electrophysiological effects similar to those of amphetamine. These effects are markedly enhanced by monoamine oxidase (MAO) inhibitors because PEA is rapidly metabolized by MAO type B (*3*), forming phenyl acetate (PAA). Pharmacological studies in animals have shown a fairly consistent relation between the affective changes induced by drugs in man and their effects on PEA in the brain (*2*). Behavioral studies suggest that amphetamine mimics and haloperidol blocks the receptors for PEA in brain neurons (*2*). The concentrations of PEA in the brain are increased by all types of antidepressant treatments, including not only classical MAO inhibitors but also tricyclic antidepressants of the imipramine type and electroshock (*2*). This action is remarkably selective in the case of tricyclic antidepressants, which do not modify the brain concentrations of catecholamines or serotonin. On the other hand, MAO inhibitors and electroshock also increase the brain concentrations of other amines. Among antipsychotic drugs, chlorpromazine does not alter concentrations of PEA in the brain, whereas reserpine (which can cause depression in humans) reduces the concentration of PEA in the brain (*2*). The euphoriant agent marihuana (tetrahydrocannabinol) increases brain PEA concentrations and reduces the disposition of PEA in the brain (*2*) with only minor changes in other neuroamines.

Because the amounts of PEA excreted in the urine are very low and highly variable in both control and depressed subjects, clinical studies in which investigators attempted to apply the above concepts have not been successful. We have now studied the 24-hour urinary excretion of its metabolite PAA. After acid hydrolysis of phenylacetylglutamine, the total amount of PAA as its trimethylsilyl derivative was measured by gas-liquid chromatography with flame ionization detection (*4*).

We studied the 24-hour excretion of PAA in three populations of adults of both sexes: (i) 48 healthy adult volunteers, mainly hospital staff members and their relatives, students and their relatives, who were drug-free; (ii) 31 inpatients at admission (of whom 13 had not had antidepressants for two or more days before urine collection); and (iii) 35 outpatients, drug-free for at least 1 week. In each case, the completeness of the collection was stressed, volumes were checked, and several samples were obtained and averaged in many cases. Inpatients were diagnosed according to the *Diagnostic and Statistical Manual of Mental Disorders,* edition 3 (DSM-III), and the severity of their symptoms was evaluated by means of the Beck depression scale, the Zung depression and anxi-

Table 1. Urinary excretion of phenyl acetate (mean ± standard error).

Subjects			Phenyl acetate excreted (mg/24 hours)	Percentage of group excreting		
Group	*N*	Age		< 70 mg/24 hours	70–175 mg/24 hours	> 175 mg/24 hours
Adult controls	48	16–59	141.1 ± 10.2	15	70	15
Depressed (unipolar) inpatients	18	18–76	68.6 ± 8.8*	50	50	0
Depressed (unipolar) inpatients, untreated	13	22–48	68.8 ± 7.0*	62	38	0
Depressed (unipolar) outpatients, untreated	35	26–59	86.3 ± 11.8*	54	37	9

*$P < .001$ (t-test).

ety scales, and the Global Assessment Scale (*5*). Outpatients were diagnosed according to DSM-III, after a Schedule for Affective Disorders and Schizophrenia (SADS) interview (*5*). Both patient groups included only major depressive disorders of the unipolar type (MDD). In healthy volunteers 16 years or older, the PAA excretion averaged 141.1 ± 10.2 mg per 24 hours, with 70 percent of the subjects excreting between 70 and 175 mg per 24 hours (Table 1). Low values for PAA excretion were found at admission in patients (N = 31) with unipolar depression: average = 68.7 ± 7.0 mg per 24 hours. Fifty-five percent of these depressed subjects excreted less than 70 mg per 24 hours, whereas only 15 percent of the controls excreted as little. There were no cases of high PAA excretion in this group (15 percent of the controls excreted more than 175 mg per 24 hours). The PAA excretion was equally low in untreated unipolar depressed inpatients and in patients who had received antidepressant medication prior to admission without clinical improvement. Ongoing longitudinal studies during treatment (*6*) showed that effective antidepressant treatment increases PAA excretion. Outpatients with less severe forms of MDD who still meet DSM-III criteria as shown by scores in SADS interviews excreted PAA in a range intermediate between that of more severely depressed inpatients and that of controls.

These results suggest that measurement of PAA urinary excretion may be a valuable diagnostic test in affective disorders, particularly because PAA is excreted in very high amounts (milligram range) in comparison to other amine metabolites. Since PAA is the major metabolite of PEA, the observed differences between control and depressed subjects supports the PEA theory of affective behavior. However, there may be other sources for the PAA found in urine, such as dietary and bacterial transformation of phenylalanine by the gut flora. Several lines of evidence support the view that urinary PAA reflects mainly PEA metabolism in the body rather than in the gastrointestinal tract. Stein *et al.* (*7*) reported no difference between the amounts of PAA excreted by normal individuals while fasting and those on a normal diet; they concluded that diet has no effect on PAA excretion. Seakins (*8*) reported that an oral phenylalanine load did not increase PAA excretion. It has also been observed that after the ingestion of neomycin, which kills gut flora, the PAA urine excretion is not altered (*9*). Moreover, PAA excretion has been reported low in some chronic cases of schizophrenia (*10*), and high PAA concentrations in plasma were observed in aggressive psychopaths (*11*).

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27 January 1983; revised 7 March 1983

Serological Visualization of Interleukin 2

Abstract. *Interleukin 2, a lymphokine that acts as a second signal of cellular immune response by way of its action as a T-cell growth factor, was morphologically identified by immunoperoxidase staining. With the use of a monoclonal antibody to interleukin 2 and several complex-forming antisera, the lymphokine was readily distinguished in cytocentrifuge preparations of peripheral blood leukocytes stimulated with a T-cell mitogen. When preparations of cloned interleukin 2 producer and responder cells were stained by the same procedures, discrete patterns of both responder and producer cell phenotypes were revealed. Interleukin 2 producer T cells exhibited a characteristic intense, ringlike cytoplasmic staining, whereas the responder cells (as exemplified by interleukin 2–dependent cell lines) exhibited a less intensive, spotlike membrane staining. In addition, intense membrane localization of interleukin 2, reminiscent of potential capping phenomena, could be observed in stained preparations of cloned responder cells.*

The lymphokine interleukin 2 (IL-2), also referred to as T-cell growth factor, is an obligatory soluble factor that promotes mitogen- and antigen-induced T-cell proliferation (*1*). Interleukin 2 acts to promote the differentiation of cytolytic effector cells both in vitro and in vivo (*2*). Investigators at our laboratory recently described the generation of B-cell hybridomas whose antibody products neutralized IL-2 in several discrete experiments, including inhibition of T-cell mitogenesis and generation of alloreactive cytolytic T cells (*3*). On the basis of recent studies documenting the existence of IL-2 surface receptors on lymphokine responsive cell lines (*4, 5*), we questioned whether a monoclonal immunoglobulin G (IgG) antibody to IL-2 could also be used for the morphological demonstration of IL-2. By means of such a monoclonal antibody and an immunoperoxidase staining procedure we were able to visualize IL-2 deposits both in the cytoplasm and on the surface of producer and responder subpopulations of human T cells. In this report we summarize our findings and describe the differential staining patterns associated with IL-2 producer and responder cell phenotypes.

The monoclonal IgG antibody to IL-2, of the γ_2b subclass, was produced and purified as described (*6*). One hybridoma clone (4E12B2F7) produced particularly high titers of the antibody in the supernatant and ascites; these were therefore used as the starting materials for the