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# The toxic mind: the biology of mental illness and violence

**E. Van Winkle**

*Retired Research Scientist, Millhauser Laboratories of the Department of Psychiatry, New York University School of Medicine, New York, USA (Mail to: Murray Hill Station, PO Box 893, New York, NY 10156, USA)*

**Summary** The continual suppression of emotions during fight or flight reactions results in atrophy and endogenous toxicosis in noradrenergic neurons. Diminished synaptic levels of norepinephrine are associated with depression. During periodic detoxification crises excess norepinephrine and other metabolites flood synapses. The norepinephrine overexcites postsynaptic neurons and causes symptoms ranging from mild anxiety to violent behavior. Some of the other metabolites, which may include dopamine, epinephrine, serotonin, gamma-aminobutyric acid, peptides, amino acids, and various metabolic waste products, are bound by noradrenergic receptors and alter neurotransmission. When they prevent norepinephrine from exciting postsynaptic neurons, depression returns. A mechanism is proposed for the binding of norepinephrine and for the effects of the other metabolites, many of which have been thought to be neurotransmitters. The diverse receptor proteins presumed to be specific for false neurotransmitters may instead encode specific memories. The shift in depressive and excitatory behavior is characteristic of nearly all nervous and mental disorders, including addictions, Alzheimer's disease, Parkinson's disease, and psychosomatic disorders. When toxins accumulate in regions of the brain that control specific activities, the symptoms observed will be related to those activities, giving rise to supposedly distinct disorders that represent the same detoxification process. Recovery can be facilitated by therapy and self-help measures that involve the releasing and redirecting of repressed emotions.

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## INTRODUCTION

In 1962 A. J. Friedhoff and I isolated a toxic methylated derivative of dopamine, the precursor of norepinephrine, from urine of schizophrenic patients (1). This substance had a structure similar to the hallucinogen mescaline and had a depressant effect on the central nervous system. Some researchers concluded that this substance was dietary, but whether it was endogenous or a methylated derivative of an exogenous substance, its appearance suggested increased catechol-*O*-methyltransferase (COMT)

activity in these patients. Since methylation inactivates norepinephrine, an increase in COMT activity suggests toxic amounts of norepinephrine and is consistent with the catecholamine hypothesis, which states that, 'in general, behavioral depression may be related to a deficiency of catecholamine (usually norepinephrine) at functionally important central adrenergic receptors, while mania results from excess catecholamine' (2). After an extensive literature search and re-evaluation of this finding, I have determined that endogenous toxicosis is a primary biological etiological factor in nervous and mental disease and violent behavior.

Albert Einstein once said, '[m]ost of the fundamental ideas of science are essentially simple, and may, as a rule, be expressed in a language comprehensible to everyone' (3). The toxic mind theory is based on the simple premise that the ability to restore mental health is inherent in every neuron. In the history of medicine there has been a

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Correspondence to: Elnora Van Winkle, Murray Hill Station, P.O. Box 893, New York, NY 10156, USA (e-mail: [clearpathway@earthlink.net](mailto:clearpathway@earthlink.net), [er26@nyu.edu](mailto:er26@nyu.edu)) Full text on: <http://pages.nyu.edu/~er26/toxicmind.html>

forgetting of the basic difference between living and non-living matter – the power of the living cell to sustain life and to repair itself. Whether a one-celled organism or a highly specialized neuron, the cell is endowed with genetic intelligence directed toward survival. Most toxic cells that die are replaced, but nerve cells must repair portions of injured or toxic cytoplasm. This basic physiological mechanism provides evidence that detoxification events cause excitatory symptoms of nervous and mental disease. As scientists we tend to want new theory to arise from current research findings, forgetting that known physiological processes reflect empirical knowledge gained from years of observation and experimentation, and that this knowledge can provide adequate evidence for developing theory.

### **THEORY**

The following hypotheses are proposed: (a) the continual suppression of emotions during fight or flight reactions results in atrophy and the accumulation of toxic metabolites in noradrenergic neurons; (b) detoxification crises are responsible for excitatory symptoms of nervous and mental disease and violent behavior; (c) dopaminergic, serotonergic, peptidergic, and other neurons presumed to specifically release substances as neurotransmitters are toxic noradrenergic neurons that have accumulated these substances; (d) the diverse postsynaptic receptor proteins thought to be specific for false neurotransmitters may instead provide for the encoding of specific memories; (e) when toxins accumulate in regions of the brain that control specific activities, the symptoms observed will be related to those activities, giving rise to supposedly distinct disorders that represent the same detoxification process; (f) recovery from nervous and mental disease is a detoxification process and can be facilitated by therapy and self-help measures that involve the releasing and redirecting of repressed emotions.

### **TOXICOSIS**

Since the time of Hippocrates it has been understood that symptoms of most diseases, other than degenerative disorders where irreversible organic damage has been sustained, represent the efforts of the body to eliminate toxins (4). Any substance, endogenous or exogenous, that cannot be utilized by the cells is recognized as toxic and eliminated. When elimination is impaired, toxins accumulate. The cells adapt to toxicosis, but when levels of toxin become intolerable the body initiates a detoxification process. Toxicosis is the true disease, and what we call disease is remedial action, a complex of symptoms caused by the vicarious elimination of toxins. Recovery

from disease is not because of remedies but in spite of them. The illusion that remedies cure disease is based on the periodicity that characterizes functional disorders. When levels of toxin are reduced to the toleration point, the sickness passes and health returns. But the true disease is not cured. With continued enervation toxins again accumulate and another crisis occurs. Unless the causes of toxicosis are discovered and removed, crises will recur until functional derangements give way to irreversible organic disease. In 1848 Thomas Sydenham, the English Hippocrates, wrote, '[a] disease, however much its cause may be adverse to the human body, is nothing more than an effort of Nature who strains with might and main to restore the health of the patient by the elimination of the morbid matter' (5).

### **THE ETIOLOGY OF NERVOUS AND MENTAL DISEASE**

Toxicosis is widespread in neurons, and the concept that symptoms of nervous and mental disease represent the body's action to eliminate toxins is not new (4,6). Genetic predisposition may influence which tissues are susceptible to disease, or there may be a specific defect, but the development of symptoms of most nervous and mental disorders depends on environmental factors. The information in DNA is insufficient to specify the vast synaptic pathways that form in the brain. The number of synaptic connections in the brain, possibly as many as  $10^{15}$ , far exceeds the number of genetic possibilities, which only approach  $10^5$  (7).

The most profound and long-lasting influence one individual has on another is in the parent/child relationship. A necessary part of this relationship is the child's right to self-defense, which is expressed in the instinctive fight or flight reaction. This reaction is controlled primarily by the hypothalamus and includes the expression of anger. Except for the incomplete myelination of certain nerve tracts in the central nervous system, the human nervous system is anatomically mature at birth (8). The child's capacity to learn exists even before birth, and training in communication begins with the first angry cry. When parents mistreat or neglect their children, whether physically or emotionally, they nearly always force them to suppress their justifiable anger, and this sets up a pattern of suppressing emotions throughout life. Childhood abuse in itself is enervating, but the primary cause of mental illness is the continual suppression of emotions.

Correlations between childhood abuse, mental illness, and adult violence are found everywhere in society and are well documented. Former psychoanalyst Alice Miller has written extensively about the devastating effects of suppressing emotions.

Since children in this hurtful kind of environment are forbidden to express their anger, however, and since it would be unbearable to experience their pain all alone, they are compelled to suppress their feelings, repress all memory of the trauma, and idealize those guilty of the abuse. Later they will have no memory of what was done to them. Disassociated from the original cause, their feelings of anger, helplessness, despair, longing, anxiety, and pain will find expression in destructive acts against others (criminal behavior, mass murder) or against themselves (drug addiction, alcoholism, prostitution, psychic disorder, suicide) (9).

Psychiatrists have discovered modulators in the parent/infant relationship that regulate neural mechanisms and influence future behavior and predisposition to disease (10). Rat pups traumatized by separation from their mothers exceed normally mothered pups in rates of accumulation of brain norepinephrine and dopamine (11). I intend to show that norepinephrine, dopamine, and other metabolites contribute to toxicosis and will provide evidence that this leads to symptoms of nervous and mental disease.

### THE DEVELOPMENT OF SYMPTOMS

When thoughts and emotions are continually suppressed, nerve impulses through noradrenergic neurons are diminished. Low levels of synaptic norepinephrine are associated with symptoms of depression. Like muscle cells deprived of nerve signals, these neurons atrophy. Metabolism is impaired, and waste products of metabolism accumulate in the cytoplasm. Exogenous toxins may accumulate in the hypothalamus, which is not protected by the blood-brain barrier, but this barrier prevents toxins from reaching most regions of the brain. Thus, many of the toxins are endogenous metabolites and may include excess norepinephrine, dopamine, epinephrine, serotonin,  $\gamma$ -aminobutyric acid (GABA), amino acids, peptides, and various other metabolic waste products. Excess norepinephrine may cause a shift in accumulation toward dopamine or epinephrine. Noradrenergic neurons can accumulate serotonin as well as norepinephrine, and only 1–2% of serotonin is found in the brain (2). Much of the serotonin is found in the pineal body, which is considered by some as vestigial. It is possible serotonin had a function in nervous tissue of our ancestors. GABA is important for glucose metabolism in the brain. Amino acids and peptides would also be found because they are building blocks and breakdown products of proteins.

When intracellular levels of toxin become intolerable, the body initiates a detoxification process consisting of periodic crises during which norepinephrine overexcites postsynaptic neurons. Billions of used-up and toxic cells in the body are destroyed daily by autolysis and replaced

by new cells (8), but since neurons generally do not replace themselves, only a portion of the neuron is broken down and repaired. Lysosomes responsible for the degradation of damaged cytoplasm are active in all atrophied cells (8) and are 'particularly prominent in neurons' (12). Most metabolic breakdown products that accumulate as a result of normal wear and tear are acidic. The membranes of lysosomes break in an acidic or otherwise toxic environment, and hydrolytic enzymes digest the damaged cytoplasm. The hydrolytic enzymes degrade proteins, nucleic acids, mucopolysaccharides, lipids, and glycogen but do not degrade catecholamines, serotonin, GABA, and amino acids. During detoxification crises the latter substances flood the synapses. The excess norepinephrine overexcites postsynaptic neurons causing excitatory symptoms ranging from mild anxiety to violent behavior. These symptoms usually involve sympathetic discharge and often represent exaggerated fight or flight reactions – with anger released as rage.

External factors necessary for life include light, warmth, touch, air, water, and nutrients, but non-vital factors and excess vital factors are stimulants. 'Any stimulant, (physical, chemical, mechanical, electrical, thermal, or mental), applied to a nerve first increases and later decreases the number of nerve impulses going over that nerve' (6). Stimulants are toxic, and toxins are stimulatory. Stimulants increase levels of acidic waste products and other toxins. If cellular levels of toxin are already high, a stimulant may cause lysosomes to break and in this way trigger a detoxification crisis. There is an initial 'high' from stimulants caused by increased synaptic levels of norepinephrine. Stimulants are useful in triggering needed detoxification crises, but in the absence of toxicosis stimulants are not needed or desired.

Fifty to 80% of the norepinephrine is removed by rapid reuptake of the neurotransmitter back into the presynaptic neuron where it is stored in vesicles or in granular pools (8). This is an adaptive response to reduce levels of norepinephrine at synapses. Norepinephrine is inactivated by the enzyme monoamine oxidase and by catechol-*O*-methyltransferase. Dopamine and other substances may compete with norepinephrine for the degrading enzymes. Increased levels of norepinephrine then cause continued excitation of postsynaptic neurons, and symptoms may be intensified.

Until the detoxification process is completed, the detoxification crises are likely to be followed by depression. Detoxification crises are remedial and self-limiting. Physiologists have discovered that cortisol and other glucocorticoids, whose secretion from the adrenal cortex is mediated by the hypothalamus, appear to stabilize the membranes of lysosomes (8). Increased levels of cortisol correlate with depression. Another mechanism for terminating detoxification crises lies in the physiological

action of postsynaptic receptors. Metabolic waste products that have flooded synapses may be bound by noradrenergic receptors. Many of these substances, whose effects are primarily inhibitory, are considered as neurotransmitters. Prior to the 1950s neuroscientists were content with norepinephrine and acetylcholine as the two true neurotransmitters. Neurons are already formed at birth, but when they specialize in the mature nervous system they utilize different chemical neurotransmitters. The immature cells migrate to the appropriate locations where they will function, and originally they all differentiate biochemically into noradrenergic neurons (13). At some point during maturation these noradrenergic neurons are influenced by electrical activity in the spinal cord and probably by chemical factors in the muscle or gland cells. Some of them become cholinergic neurons. Most continue to secrete norepinephrine but are capable of synthesizing a number of other substances. This growth pattern suggests that neurons are either noradrenergic or cholinergic.

During the second half of the 20th century, and because certain drugs appeared to alter catecholamine levels, nearly fifty other substances, including dopamine, epinephrine, serotonin, GABA, amino acids, and a number of peptides, were suggested as neurotransmitters in the brain. The scientific literature is filled with somewhat confusing statements about the existence of multiple neurotransmitters. As stated by a number of authors:

[N]eurochemically homogeneous vesicles from central synapses have never been completely purified ... Although it has generally been conceived that a neuron makes only one transmitter and secretes that same substance everywhere synaptic release occurs, neuropeptide exceptions to this rule have become common ... Neuroactive peptides started showing up in autonomic neurons where there was no need for additional transmitters (2). The existence of two neurotransmitter in the same neuron has been demonstrated in some neurons (13). Many substances that will excite or inhibit neurons have been found, but none of these has been proved with real certainty to be a functional transmitter (8).

The research in the past fifty years supports the concept that norepinephrine is a true neurotransmitter (2) and that its release in appropriate amounts results in normal behavior. Based on this research and on known physiological mechanisms, the evidence supports the conclusion that the so-called dopaminergic, serotonergic, GABAergic, peptidergic, and similarly specified neurons are noradrenergic neurons that, as a result of atrophy and abnormal metabolism, have accumulated these substances. That neurons presumed to specifically release these substances have been suggested as having normal

functions is an indication that toxicosis is a condition that exists, not just in the emotionally ill or violent person, but in a large percentage of the so-called normal population as well. Civilization has inadvertently caused this to happen.

Some of these endogenous substances relieve excitatory symptoms, as do many drugs. It might be accurate to classify them as protective neuromodulators because they can bring about an end to the detoxification crisis and therefore have safeguarding effects. They do not produce these effects themselves; rather, it is the adaptation of neurons to the presence of these substances that brings about the alleviation of symptoms. The receptors bind these substances, which then interfere with neurotransmission. It has been demonstrated that the binding of amine agonists and antagonists to the  $\beta$ -adrenergic receptor involves an interaction between the amine group of the ligand and the carboxylate side chain of Asp113 in the third hydrophobic domain of the receptor (14). The gates that open and close on channels are thought to be positive charges at channel openings (8). The terminal amino groups of the  $\beta$ -adrenergic receptor molecules are extracellular (15). These groups and other R groups, for example on lysine, arginine, and histidine, that can accept protons may constitute the positive electric field that blocks positive ion permeability. Protonated amino groups are found mainly on the surface of globular proteins and affect the electrostatic properties of proteins (16). The 3- and 4-hydroxy carbons and  $\beta$ -hydroxy carbon of norepinephrine may form covalent linkages with these protonated amino groups on the receptor protein. Linkages such as these would diminish the positive field and allow increased permeability to sodium ions. This may be part of the mechanism for opening the gates and triggering an excitatory postsynaptic potential. The synthesis of new superficial receptor protein via activation of the adenylyl cyclase effector system may be secondary to this mechanism. The N-methyl group of the neurohormone epinephrine may account for its affinity for a different receptor, and a methoxy group on the 3-carbon of the ring may interfere with linkage for both norepinephrine and epinephrine. If this has not already been postulated and established, perhaps modern techniques in molecular biology will confirm this.

Covalent linkages that are not genetically controlled are common (16). Proteins can be modified after formation, and prosthetic groups, such as lipoate, are covalently attached to some enzymes (17). Some membrane proteins contain covalently attached sugar residues, which tend to be located at the membrane surface rather than in the hydrocarbon core (17). There is growing evidence that the effects of hyperglycemia on diabetic vascular and renal tissues are mediated by late products of glucose-protein or glucose-lipid interactions (18).



Nonenzymatic glycosylation of proteins by reducing sugars results in the formation of advanced glycosylation end products (AGEs), which affect functionally important lysine groups and amino-terminal amines. Their turnover is regulated in part by specific cellular receptors. AGEs also form in foods during heating. In the brain covalently attached sugar residues in postsynaptic membranes may be a factor in the well established adverse effects of excess and cooked or processed sugar on behavior. In the case of the endogenous protective neuromodulators, some of which lack hydroxyl groups, or have a large ring or long chain that may interfere with linking, there would not be sufficient linking of hydroxyl groups to diminish the positive field and allow excitation. A glance through a pharmacology textbook (19) is enough to see that the structures of numerous agonist and antagonist drugs appear to fit this concept.

Unfortunately, endogenous and exogenous toxins often remain bound. Numbers of receptors in the brain have been found to increase or decrease as an adaptive response (20). A long-term change in the number of receptors is not observed under normal physiological conditions but is commonly noted where drugs have been administered (2). Receptors are found in increased density in postmortem brain tissue of schizophrenic patients (20). Using the lock/key analogy, some of these substances are like keys that don't work but get stuck in the locks. Receptors metastasize, are clogged up, and there is a diminution of noradrenergic and sympathetic activity. After a detoxification crisis excitatory symptoms subside and depression returns. This accounts for the secondary depressant action of stimulants. This shift in depressive and excitatory behavior reflects the periodicity of the detoxification process and is characteristic of nearly all nervous and mental disorders.

This description of the development of symptoms is necessarily oversimplified since nerve transmission involves highly intricate patterns of impulses. A detoxification crisis is the sum of many crises in separate neurons, and depressive and excitatory symptoms may occur simultaneously. Whether symptoms will develop depends upon the extent of toxicosis, and persons who are experiencing symptoms are healthier than those who are not because they are detoxifying their nervous systems.

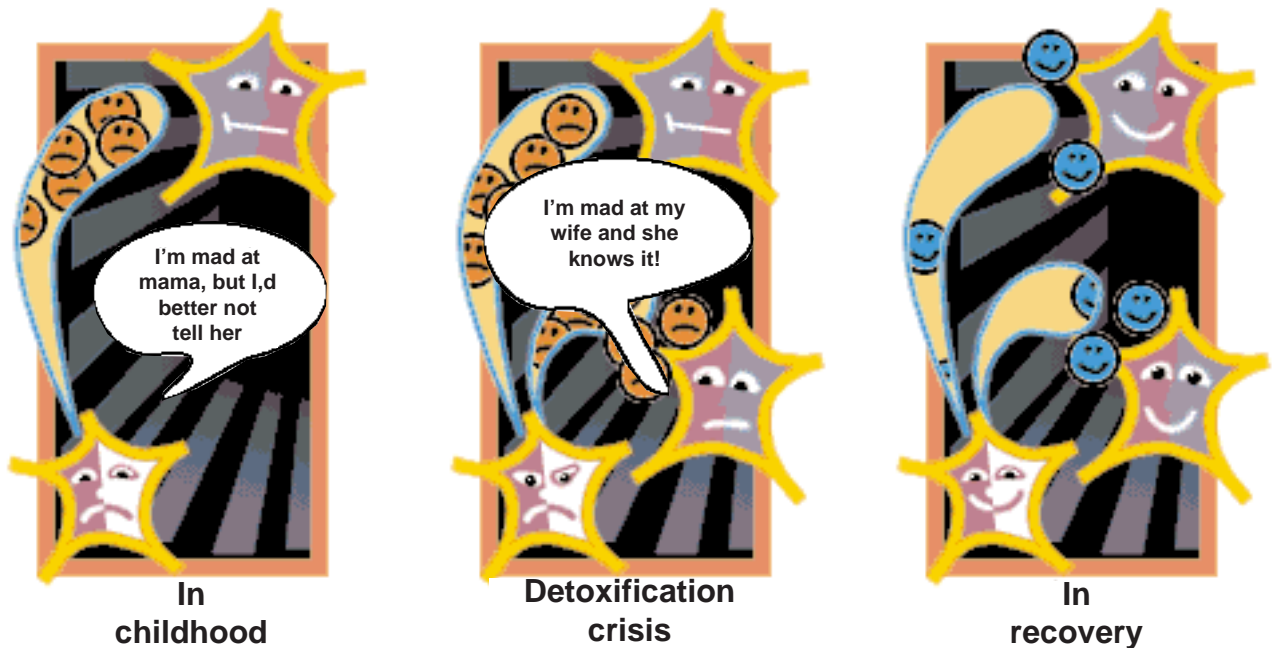
## MEMORY

Researchers have found a variety of receptors for each false neurotransmitter. Since receptors are not designed specifically for substances other than the true neurotransmitter, what then is the purpose of this variety? It is possible that the diversity of protein provides the mechanism for encoding specific memories. For example, a neuron may store memory for a particular shade of blue.

Based on genetic possibility and total number of brain cells there may be many cells with identical protein that facilitate memory for this shade of blue. There may be other neurons with slightly different proteins for other qualities of the color blue. Within the membrane spanning domains of adrenergic receptors the proteins are approximately 80% identical, whereas in other regions of the receptor they are much more divergent (15). This divergence may account for the storage and recall of specific memories.

Changes in electronic potentials related to short-term memory occur predominantly in superficial dendritic layers (8). Long-term memory may involve receptor areas in the older protein in deeper regions of the membrane. Norepinephrine is thought to be released after excitation (2), but perhaps the molecules remain bound, contributing to reverberation and short-term memory. As new receptor protein is formed on the superficial surfaces, sodium permeability would decrease, but the permanent binding of some of the neurotransmitter molecules may make the neuron more excitable and contribute to long-term memory. Routine lysosomal action to repair membranes may bring about the release of some molecules and account for the need for rehearsal. In enervated neurons the endogenous and exogenous toxins that remain bound would contribute to inhibition. This would impair memory. In Alzheimer's disease short-term rather than long-term memory would be impaired because, over time, the neurotransmitter is exposed to increasingly toxic superficial receptor sites. Unless the neurons have died, the action of lysosomes during detoxification crises would improve memory because some of the inhibitory substances would be released, and if thoughts and emotions are redirected, norepinephrine molecules would have access to the receptor sites.

Evidence for this theory is found in a number of physiological mechanisms. When afferent fibers to regions of the rat hippocampus are stimulated in proximity to postsynaptic neurons, there is a long-lasting increase in sensitivity of these cells (12). Long-term memory for a newly acquired behavior requires continuous protein synthesis. Long-term memory does not occur to a significant extent when formation of RNA or of protein is blocked (8). The genes in the nucleus of the human neuron control the synthesis of thousands of separate kinds of protein. Hormones, including neurotransmitters, function by controlling the activity levels of target tissues, which have specific kinds of protein (8). They may achieve this by direct action on genes to cause protein synthesis or by activating adenylyl cyclase and converting cytoplasmic ATP to cyclic AMP, which initiated synthesis of protein. But the functional characteristics of each cell are determined by the character of the cell itself (8).



**Fig. 1** The wrong neuron. This illustration is an anatomical oversimplification since **Mama** and **Wife** are stored as characteristics in many neurons, some of which are shared. When negative emotions are suppressed, toxic neurochemicals clog up the axon endings of neurons and interfere with neurotransmission. If nerve impulses are diverted during a detoxification crisis, neurochemicals flood other synapses, and angry feelings might be directed toward someone who reminds us of **Mama**. During therapy nerve impulses are redirected toward **Mama** and neural pathways are cleared. In recovery, when all the neurons have detoxified, relationships may be restored to harmony.

### VICARIOUS DETOXIFICATION CRISES

When negative emotions are suppressed, toxic neurochemicals clog up the neurons, and nerve signals may be diverted. The axon from one neuron may branch and terminate in as many as 200 000 synapses, and a single neuron may receive synaptic contacts from 200 000 other neurons (13). Because of the spatial nature of nerve transmission, messages may travel through alternate neurons causing distorted and compulsive thinking, delusions, hallucinations, psychosis, and unintended behavior. As a result of a vicarious elimination of toxins a person might direct rage inwardly as suicidal behavior or toward an innocent person in an aggressive assault. As an example, a man's conflict with his wife may trigger in him unconscious memories of childhood incidents with an abusive mother. There is no time regression in the brain, but experiences with wife and mother share common neural pathways. During the current conflict nerve impulses will travel through neurons that encode feminine characteristics shared by wife and mother. This man may have been justifiably angry with his mother but had to suppress his feelings. As a result of atrophy some of the neurons responsible for directing emotions toward his mother may have become clogged up and unable to transmit messages. Therefore, during a detoxification crisis he may direct angry feelings toward his wife or daughter instead.

How often we read of domestic violence during which a murderous act is directed toward an innocent person with no apparent motive. The drawing in Figure 1 is, of course, an anatomical oversimplification since many neurons rather than one are involved, and both presynaptic neurons and postsynaptic receptors become clogged up. But the drawing illustrates a vicarious detoxification crisis and is a useful concept for understanding persons in recovery who need to redirect their anger. Emotions need to be expressed in the current situation, but if they are intense they probably have to do with previous experience. Levels of toxin are reduced to some extent during a vicarious detoxification crisis, but many of the most toxic neurons, namely those neurons that would facilitate memories of past abusers, may not be able to release their toxins. To achieve detoxification of all neurons, thoughts and emotions must be continually redirected.

### THE EVIDENCE

#### Noradrenergic dysfunction

Much of the evidence for the toxic mind theory comes from the nature of symptoms. If symptoms are not caused by irreversible organic damage, they reflect the efforts of the nervous system to detoxify. Behavioral patterns associated with emotional experience comprise

subjective feelings and objective physical expressions. These expressions can be recognized as enhanced activity of the noradrenergic and sympathetic nervous systems (13). Symptoms include excessive mental activity, palpitations, blood pressure changes, and often reflect exaggerated fight or flight reactions. Rage is intense anger, and its expression depends on the release of norepinephrine and epinephrine. Epinephrine is not normally released from nerve endings, but excessive amounts released from toxic neurons and from the adrenal medulla during detoxification crises overexcite the heart and contribute to the pounding sensation associated with neurotic fear. Mania and many of the symptoms of psychosis resemble intense fight or flight reactions, whereas in vegetative states characteristic of depression this defensive system is largely repressed (8).

For close to fifty years researchers in biological psychiatry have provided statistically sound evidence that disturbances in noradrenergic function are linked to nervous and mental disorders, including schizophrenia, manic-depression, Alzheimer's disease, Parkinson's disease, and Tourette's syndrome. Also included are anxiety, panic disorders, depression, mania, autism, pervasive developmental disorders, attention deficit-hyperactivity disorders, post-traumatic stress disorders, addictions, aggression, and criminal behavior. In a computer search of Index Medicus for the years 1976 to 1983 alone, I found over 600 articles in which catecholamines were associated with nervous and mental disease. In most of these studies symptoms were correlated with abnormal body fluid levels of norepinephrine and in many cases with dopamine, serotonin, GABA, amino acids, peptides, and other metabolites. These studies provide unequivocal evidence that nervous and mental disease involves disturbances in noradrenergic function. Generally, levels of catecholamine were found to be increased in patients with disorders comprising mostly excitatory symptoms and decreased in depression. This was not the case in all studies, but the reason may have been that patients were exhibiting different types of symptoms at the time of testing and oftentimes were receiving drugs that adversely affected the results.

### Toxic neurons

Histological evidence for toxicosis is widespread. Lipofuscin granules, which are tertiary lysosomes, are commonly found in aging neurons (13) and reflect the cell's effort to repair itself. Pigment found in places where it has no function suggests toxicosis. Tyrosine, the amino acid precursor of norepinephrine, can be converted to melanin, which is often found in the locus ceruleus and substantia nigra. Fluorescence histochemical techniques developed in the 1960s allow neuroscientists to visualize

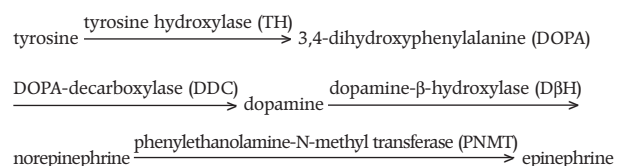
storage sites of excess norepinephrine. Small dense-core vesicles containing norepinephrine and dopamine are characteristic of peripheral postganglionic sympathetic neurons, whereas large dense-core vesicles are associated with noradrenergic endings in the central nervous system (13). In noradrenergic neurons much of the norepinephrine is not stored in these vesicles but is found in secondary pools. When noradrenergic neurons are excited, one might expect that some of the stores of norepinephrine would be diminished. However, it has long been known that endogenous levels of tissue norepinephrine are not influenced by the degree of sympathetic activity (2,12). Upon excitation of noradrenergic neurons it is the newly synthesized norepinephrine that is released (2). Furthermore, norepinephrine is found in vesicles along the axon and in areas of the cytoplasm where there are no synaptic contacts (19).

### Acetylcholine

Certainly, the continual suppression of emotions affects brain function dependent on cholinergic neurons and voluntary as well as involuntary motor function. Toxic levels of acetylcholine, choline, and other metabolites probably contribute to symptoms. For example, toxicosis in the parasympathetic system may prevent the release of tears and interfere with the expression of grief. Acetylcholine has been linked to a number of disorders, but there is more evidence for the role of norepinephrine in the development of symptoms of mental illness. As far as I know, sophisticated techniques are not available for determining the presence of excessive amounts of substances in the cytoplasm of cholinergic neurons. Therefore, I have focused on catecholamine metabolism as evidence for the toxic mind theory.

### Catecholamine metabolism

The pathway for the synthesis of catecholamines is as follows:



### The expression of genes

Studies on twins provide new insight into the mechanism of gene action and further support the toxic mind theory. In studies on monozygotic twins discordant for schizophrenia a gene was found with a seven-fold greater expression in the 'well' twin compared to the twin with symptoms (21). In these studies childhood traumas were

not explored, but if the 'well' twin was favored as a child, it is possible that the 'sick' twin was neglected or otherwise abused and was therefore more prone to toxicosis. While it is not the only possibility, the unexpressed gene in the 'sick' twin may be for regulating the synthesis of DDC. When the level of activity of sympathetic neurons is increased for prolonged periods of time, the amount of mRNA coding for TH and D $\beta$ H is increased in neuronal perikarya. DDC does not appear to be modulated by this process (12). Thus, the increased D $\beta$ H converts excess dopamine to norepinephrine, while DDC activity is not increased. This may constitute gene action to reduce toxic levels of dopamine. Cortisol mobilizes amino acids out of cells, so there is no need to reduce TH activity to avoid a build-up of DOPA. The possibility that this gene directs the synthesis of DDC is supported by the finding that this gene is expressed in areas of animal brain where levels of dopamine are normally low. Where dopamine levels are low, there is no need for gene action to suppress DDC activity. Cortisol stimulates PNMT activity (12), and excess norepinephrine may be converted to epinephrine. This variable enzyme activity appears to account for the notion that neurons are specific for dopamine or epinephrine.

It will be helpful if future studies on the expression of genes in psychiatric patients are correlated with symptoms at the time of testing, and it is possible that both twins were affected. Synthesis of monoamine oxidase (MAO) may eventually be inhibited in depression and stimulated in mania, accounting for the shift in symptoms of persons with manic-depressive disorder. This appears to be an innate biological mechanism that is mimicked by the use of MAO inhibitors as antidepressants. The gene for catechol-*O*-methyltransferase (COMT) may be variably expressed as well, depending on the need to degrade excess catecholamine. Abnormalities in lipid metabolism have also been reported in mental patients (22), and since lipids are important constituents of synaptic membranes, genes for the enzymes involved may be variably expressed as needed to repair toxic receptor sites.

### Methylated metabolites

When norepinephrine is deactivated by COMT, a number of other substances are methylated, accounting for the appearance of the toxic substance in the urine of schizophrenic patients (1). Methylation of catecholamines produces a number of derivatives not normally found as excretory products (23). Many of these methylated derivatives exacerbate symptoms when injected into animals (24). Melatonin, a methylated derivative of serotonin, has depressant effects. When the MAO inhibitor iproniazid, which is similar to drugs still used in the treatment of depression, was administered to rats, there was an

increased excretion of methylated metabolites (25). The use of iproniazid has been linked to relapses in schizophrenia, which is further evidence that toxicosis results in symptoms, in this case intensified by the administration of a drug.

### Wild animals

Convincing evidence for the toxic mind theory is found in studies of wild animals. As far as we know, wild animals do not suffer from psychiatric disorders, certainly not to the same extent as humans. But caged animals have learned to suppress the fight or flight reaction and occasionally exhibit bursts of abnormal excitatory behavior. In studies where domesticated and wild silver foxes were compared, levels of norepinephrine were significantly higher in the anterior hypothalamus of the domesticated animals (26). Silver foxes selected for tame behavior and no defensive reaction to human contact had higher serotonin levels in the midbrain and hypothalamus (27). When domesticated rats were under emotional stress, norepinephrine and serotonin levels in the brain were reduced to a lesser extent than in aggressive rats (28). Experimental enhancement of brain serotonin was found to block killing behavior in rats, mice, mink, and silver foxes. The suppressed killing behavior did not depend on the inhibitory effect of serotonin but was caused by the low tonus of the system activating predatory behavior (29). It is not surprising that caged laboratory animals are unreliable sources of information about neurophysiology and that researchers have entertained the notions there were neurons specific for dopamine, serotonin, and other substances. In my many years of laboratory work I seldom saw an aged rat that did not exhibit parkinsonian-like tremors.

### Pathology in the human brain

Unequivocal evidence for toxicosis in mental illness is found in the pathology of the human brain. Since endogenous amines are bound to receptor sites, the increased density of toxic receptors found in postmortem brain tissue of psychiatric patients (20) is evidence for the accumulation of these substances. In a group of psychotic patients diagnosed as schizophrenic, a significant increase in the dopamine concentration of nucleus accumbens samples was reported. In a larger group of more than 50 samples there was an increase in dopamine and norepinephrine concentration in the nucleus accumbens and the anterior perforated substance, a limbic forebrain area (30). The increased concentrations in schizophrenia were statistically significant by both parametric and non-parametric statistical procedures used. Increases in norepinephrine have also been observed in the bed nucleus of stria terminalis, ventral septum, and



mammillary body in postmortem brain tissue of paranoid schizophrenic patients (31).

### THE UNITY OF DISEASE

A careful study of what are described as distinct pathologies will illustrate the unity of disease. When toxins accumulate in regions of the brain that control specific activities, the symptoms observed will be related to those activities, giving rise to supposedly distinct disorders. Alzheimer's patients may have been forced to suppress emotions related to the learning process. Parkinson's patients often have mask-like faces and may not have released emotions through facial expression. Patients with Alzheimer's and Parkinson's disease usually have symptoms of other psychiatric disorders. Patients often have multiple diagnoses or are re-diagnosed many times throughout life. No disease possesses its own special symptoms, but in their nosological systems scientists classify and arrange symptoms as if they belonged to distinct syndromes. They begin to regard subjective taxonomic orders as objective realities of nature and, for example, classify symptoms in one part of the body as a certain disease separate from symptoms arising in another part of the body. But inflammation of the brain and inflammation of the stomach are the same disease. 'The brain can't vomit and the stomach can't become insane' (6). The Diagnostic and Statistical Manual of Mental Disorders (32), which undergoes constant revision, lists hundreds of mental disorders, each characterized by a group of symptoms. If the boundaries are unclear, a second or third diagnosis is superimposed upon the first.

Psychiatrist Judith Herman writes:

The mental health system is filled with survivors of prolonged, repeated childhood trauma. This is true even though most people who have been abused in childhood never come to psychiatric attention. To the extent that these people recover, they do so on their own. While only a small minority of survivors, usually those with the most severe abuse histories, eventually become psychiatric patients, many or even most psychiatric patients are survivors of child abuse. The data on this point are beyond contention ... Survivors of childhood abuse who become patients appear with a bewildering array of symptoms ... Perhaps the most impressive finding is the sheer length of the list of symptoms correlated with a history of childhood abuse (33).

### ADDICTIONS

Addictions to exogenous stimulants, chemical and psychological, commonly occur with psychiatric disorders. The fact that stimulants can trigger detoxification crises provides the physiological basis for 'craving.' It is

paradoxical that the very thing that can accelerate the detoxification process is itself toxic. This may explain homeopathy and the beneficial effects of psychological stimulation in therapy. It also explains why recovering alcoholics encourage active alcoholics to continue drinking until the detoxification crises are sufficiently painful for them to seek help. Physiologically speaking, addicts crave stimulation to initiate a detoxification crisis, which gives them a 'high' because of the increased synaptic norepinephrine. They crave sedation to terminate crises and relieve excitatory symptoms, but the sedation is followed by more excitatory symptoms during the withdrawal. That these are factors in 'craving' is supported by the observation of therapists that addicted persons in the kind of therapy that encourages the releasing and redirecting of repressed emotions gradually lose their craving for stimulants and sedatives (34).

### SLEEP DISORDERS

Much of the repair of neurons occurs during sleep. Hypersomnia and insomnia are conditions commonly suffered by psychiatric patients. Toxicosis accounts for dream paralysis and narcolepsy. Depressed persons often experience a prolonged and heavy drug-like sleep caused by toxicosis at postsynaptic receptor sites, and periodic detoxification crises account for nightmares and insomnia.

Two compatible theories of sleep exist. The first states that sleep is a passive process occurring when the neurons become fatigued, noradrenergic activity is diminished, and there is decreased excitability of the reticular activating system accompanied by a reduction in peripheral sympathetic activity. This type of sleep is characterized by slow delta waves and is normal and restful. According to the second theory, which developed along with the interest in catecholamines, sleep results from inhibitory signals transmitted into the reticular activating system. The basis for this inhibition lies in the biochemical milieu of brain stem neurons, a milieu that may consist of serotonin, GABA, peptides, and other substances. Lesions in the midline area of the brain stem where serotonin is often found cause insomnia. But after a period of insomnia brought on by chemical inhibition of serotonin, normal sleep patterns return despite the fact that brain serotonin levels remain below normal (7). Serotonin is associated with hypersomnia. Drugs that increase serotonin levels have an antidepressant effect probably because they also inhibit reuptake of norepinephrine and a sedative effect because serotonin is bound by noradrenergic receptors. Toxic presynaptic neurons, inadequate synaptic levels of norepinephrine, and the binding of endogenous and exogenous substances by noradrenergic receptors are factors that interfere with the normal arousal action of the noradrenergic system.

In normal sleep the nervous system rests, and as a result of anabolism various structures are restored. During the overlying and often extended drug-like sleep, generally toward morning when elimination is most active, the neurons appear to accelerate the detoxification process. Paradoxical sleep, during which emotional dreaming occurs, is thought to result from abnormal channeling of signals even though brain activity is not significantly depressed (8). Episodes of paradoxical sleep, also called REM sleep, are superimposed on slow-wave sleep in periods from 5 to 21 minutes every 90 minutes, the slow delta waves shifting to beta waves that are characteristic of the waking state. Paradoxical sleep is accompanied by irregular heart rate and other signs of increased sympathetic activity. Episodes of paradoxical sleep reflect detoxification crises during which noradrenergic and sympathetic activities accelerate. Dreaming probably occurs throughout sleep but is particularly emotional during paradoxical sleep. When the nervous system eliminates enough of the sleep-producing substances to allow norepinephrine to excite the reticular activating system, the drug-like sleep will end. If toxicosis is extensive, detoxification crises may recur frequently, and increased levels of norepinephrine will excessively excite the reticular activating system, contributing to insomnia. It is interesting that half of an infant's sleep is spent in the REM state (7). The nervous systems of infants whose neurons have not yet accommodated to toxins appear to actively cleanse themselves throughout the night.

### DREAMS AND FANTASIES

Dreams are patterns that are often combined with patterns of past experience. In everyday experiences specific characteristics are laid down in neurons along with characteristics that may have been a part of childhood experience. In the dream, therefore, current and early experiences are mixed together but appear as one scenario. Fantasies are similar to dreams, and the more toxic the mind the more distorted the dream or fantasy. Imagination is memory of actual experience – only the characters and scenery have changed. The brain cannot create new experience but designs new mosaics made up of bits of old experience. Because memories are often distorted, a 'false memory' syndrome has evolved. But there is no such thing as a false memory, only a distorted version.

Most of us are familiar with Freud's contribution that dreams facilitate the release of emotions. He defined dreaming as a means of discharge for unconscious forces stored up during childhood. His theory has a sound basis in physiology. The reticular activating system has a periodic excitability cycle occurring once every 90 minutes,

increasing and decreasing in activity throughout the 24-hour day. This excitability cycle reflects periodic detoxification crises that cause emotional dreaming at night and perhaps some other excitatory behavior during the day. Persons engaged in a fantasy world might be said to be 'day-dreaming,' and these periods of creating fantasies are influenced by the same physiological events that account for paradoxical sleep. Fantasies, like dreams, provide a stage for the release of emotions and are frequently attempts to re-enact childhood traumas. What Freud did not understand was that emotional dreams and fantasies are detoxification crises during which neurons are releasing toxic neurochemicals.

### PSYCHOSOMATIC DISORDERS

Because of toxicosis in the hypothalamus the activity of pituitary hormones may be altered periodically, adversely affecting a number of systems. The periodic shift from underexcitation to overexcitation in the autonomic nervous system contributes to a variety of psychosomatic disorders, better termed neurogenic. Fluctuations in parasympathetic activity affect the heart, digestion, and elimination. Because the entire sympathetic system is usually excited at the same time, periodic changes in its activity affect most of the visceral organs. The sympathetic system increases cellular metabolism, which accelerates the release of toxins throughout the body. When this system is repressed, the body cannot efficiently carry out the daily process of detoxification. Tumors can occur anywhere in the body where toxins are being walled-off, but enervation in the central and autonomic nervous systems is likely to contribute to cancer. Increased levels of dopamine and its metabolites are associated with gangliogliomas and neuroblastomas (35). Excess catecholamine in the adrenal gland is found in pheochromocytoma. Women with metastatic breast cancer were shown to live longer when they entered therapy for the release of repressed emotions, and patients who died more rapidly were less able to communicate dysphoric feelings, particularly anger (36).

During detoxification crises the sympathetic system is overactive, and there is an increased release of catecholamines, which, in persons prone to outbursts of anger, has been linked to coronary heart disease (37). Decreased hypothalamic activity or increased tissue metabolism as a result of overexcitation of the sympathetic system may cause the thyroid to become hypoactive. People generally see a doctor when they are having symptoms, namely detoxification crises that involve both the central nervous system and peripheral organs, and they may be diagnosed with hypothyroidism when there is no actual pathology in the thyroid gland. In recovery, hypothyroidism usually disappears, and body temperature, blood pressure, and

pulse rate tend to normalize (34) as the activities of the sympathetic and parasympathetic systems stabilize.

## VIOLENT BEHAVIOR

Acts of violence are committed by persons under the influence of drugs and by drug-free persons diagnosed as mentally ill. Violent crimes are often committed by persons who have been quiet and depressed. The courts are filled with defendants whose actions are the subject of much debate over whether the accused was mentally ill at the time of the crime. What the courts do not understand, assuming the accused person actually committed the crime, is that violent behavior is a physiological response to toxicosis. Murder may be the result of a vicarious detoxification crisis and as much a symptom of disease as the sneeze is a symptom of the common cold. It is not my intention to propose this as physiological evidence for innocence and certainly not to silence the justifiable anger of victims of violence. Victims who suppress their anger will release it eventually, perhaps as revenge. Hopefully, the toxic mind theory will affect the kind of rehabilitation given to violent offenders. Until the toxins are removed, violent persons will be compelled to continue some form of aggressive behavior toward themselves or others. Unless the vital powers of the body have been diminished to the point of exhaustion and ultimate death, the neurons will continue to repair themselves. The cure for violent behavior is in eliminating the toxins.

Whether we have conscious control over behavior initiated by unconscious activity in the brain probably depends on the degree of enervation and the extent of the toxicosis. If the detoxification crisis is sufficiently strong, conscious thought may not be able to override it. Furthermore, when we do express emotions, we may not be able to control how they are expressed. This is the reason many cannot explain why they committed violent crimes. The anger is justifiable, but the detoxification crisis is usually vicarious, and there is often no remorse. Guilt, which is anger turned inward, may be felt, but true remorse is possible only in recovery, and even then it is not likely to be for past sins. The New Testament word for sin, *hamartia*, comes from the sport of archery and literally means 'missing the mark' (38) – wrong neuron. This condition of health or sickness in the neurons may provide the physiological basis for the exercise of free will. Whether we can control an exaggerated fight or flight reaction is the subject of moral appraisal and the frequent debate of ethical and religious thinkers. In every court of law it demands reflection by judge and jury as they consider the oftentimes violent behavior of the accused. It may be that free will is best exercised in a decision to embrace measures for recovery.

As we have seen, persons with toxic minds have a craving for stimulants because stimulants can trigger

detoxification crises. Abused children are attracted to violent TV programs for this reason. All of us have toxic neurons to some extent and crave stimulation. Many of us could not turn off the TV during the Gulf War. Some sociologists speak of man as having a need for enemies. This need comes from unconscious cravings that bring about the release of repressed anger. In its extreme this is what motivates cult leaders, terrorists, dictators, all who wage war, and all those who follow along in their paths of destruction. That there might be conspiracies behind acts of violence is because other individuals with toxic minds have the unconscious need to tag along and release their own pent-up anger. This explains why an eleven-year-old boy needed to go along with his thirteen-year-old friend on a murderous spree in Jonesboro, Arkansas. As soon as the lives of those who have committed violent acts are investigated, we see the truth in headlines, 'In the End, the Oklahoma Bombing May Be the Work of 2, Not a Major Conspiracy,' and 'New Defendant in Trade Center Blast Is Described as Shy and Apolitical' (39). The weapons amassed by David Koresh, Timothy McVeigh, Shoko Asahara, and Saddam Hussein were probably for the purpose of releasing anger stored up as toxic neurochemicals in the nervous systems of those individuals and had little to do with the purposes for which they were ultimately used. Adults who were abused as children are likely to continue to fill the arsenals of the world with nuclear bombs.

## THE END OF MENTAL ILLNESS AND VIOLENCE

The toxic mind theory, by providing an understanding of the physiological effects of toxicosis on behavior, will have a positive influence on the way people deal with emotions in everyday life, on the development of therapeutic methods, and on measures taken by society to eliminate violence. When a theory is found that can help prevent and relieve suffering by explaining the causes of disease, a decision to embrace such a theory is ultimately a decision to support life itself. An understanding of the biology can provide the basis for therapy and self-help measures that will alleviate a wide variety of disorders. Hopefully, the toxic mind theory will provide knowledge useful to everyone – abused children, parents, the mentally ill and all addicts, therapists, physicians, educators, religious leaders, government officials, the courts, prisoners, and those in charge of rehabilitation.

Proper nutrition is essential to prevent deficiencies and toxicosis. Exogenous toxins are particularly likely to accumulate in the hypothalamus and in some cases may be the primary cause of symptoms. Dietary changes are known to alleviate symptoms of nervous and mental disease (6,40,41), and it is well known that when the nutrition of prisoners is improved the likelihood of violence is

diminished. Nutrients in excess of bodily needs and nutrients that have been altered chemically by processing and cooking contribute to toxicosis. Diets high in raw foods are better able to provide nutrients the neurons can utilize and will facilitate the release of toxins, both endogenous and exogenous. Persons who are willing to detoxify their nervous systems of exogenous toxins from food and other environmental sources, and who are willing to do the work of releasing repressed emotions, are the most likely to recover fully.

There are times when symptoms become intense, and drugs and/or confinement are necessary. Since all drugs are toxic and will prolong the detoxification process, their use should be short-term. Persons with toxic minds are prone to addictions to drugs, food, and stimulatory activities. Alcoholics Anonymous (42) and other 12-step programs encourage the detoxification process, but members of these groups transfer their addictions to other members. This is commonly called co-dependency (43), which is the underlying addiction. Most members do not recognize the importance of releasing negative emotions, which is essential for recovery from co-dependency. One of these groups, Adult Children of Alcoholics, which might be better named Adult Children with Repressed Emotions, encourages the release of anger and is a place where a redirecting of emotions often begins. When the detoxification process is completed, these programs are no longer needed. Thousands are recovering in these programs and in experiential therapies that encourage the releasing and redirecting of emotions. Their stories would provide further proof of the toxic mind theory, but because of anonymity they are not available for statistical analysis. Perhaps final proof will be in the theory's prediction that violence will end.

Mental health depends on the ability of an individual to respond to stress with a healthy fight or flight reaction. Abused children, young or old, need to direct angry feelings toward all those who have abused them or caused them to suppress emotions. This might include teachers, bosses, partners, religious leaders, or any persons in authority. Experiential psychotherapy such as that provided by the Caron Foundation in Wernersville, Pennsylvania, which is not just talk therapy but encourages the releasing and redirecting of repressed emotions while re-experiencing childhood traumas, can facilitate the detoxification process. In primal therapy a patient may release angry cries like those of a newborn child. Therapists are most effective when they help patients recognize that the anger needs to be directed toward early abusers. Since there is no actual time regression in the brain, it is not necessary to re-experience the childhood traumas in detail. When emotions are being released, the neurons are detoxifying, and consciously redirecting the emotions toward past abusers allows neurons that may have been clogged up since childhood to clear.

Therapy need not be long-term. An awareness of the relationship of current symptoms to childhood traumas can make the use of self-help measures effective. Excitatory symptoms may appear as anxiety, neurotic fear, low self-esteem, guilt, paranoia, compulsive thoughts and behavior, revengeful thoughts, or misdirected anger. Or there may be cravings for food, alcohol, activity, or people. These are signals that the nervous system is trying to detoxify. An understanding that the symptom is the beginning of a detoxification crisis and that anger is trying to emerge can allow one to consciously redirect the anger toward all past abusers and clear neural pathways that may have been clogged up for years. If emotions in a current relationship are intense, they were probably emotions suppressed during past experience and can be redirected at the first sign of a symptom. This is frequently fear caused by excess epinephrine. An example might be the pounding sensation that often accompanies the action to confront someone who has been abusive in a current situation. One might first bang with one's fists on a bed and direct thoughts toward all past abusers. Sometimes direct confrontation of past abusers brings relief, and if spoken calmly, may restore relationships if those confronted are open to the truth.

Full recovery is undeniable to anyone who experiences it. This is because the detoxification process is like a periodic opening of flood gates. When the flood is gone, recovery is virtually complete. The fight or flight reaction is no longer exaggerated, anger can be expressed in non-violent ways, and symptoms of nervous and mental disease disappear. Post-primal therapy patients have been observed to recover from a variety of physical as well as mental disorders (34). Cleared neural pathways throughout the brain enhance memory, intelligence, and creativity. Neurotic fear, anxiety, and depression do not return. Norepinephrine levels at synapses fluctuate only slightly, and euphoria, best defined as 'freedom from anxiety and distress' (19), is permanent.

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