The Psychobiology of Post Traumatic Stress Disorder (PTSD): Part I

—— Consideration of the adaptive role of symptom precursors & their later role in prolonging activation of the hypothalamic-pituitary-adrenal axis ——

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Abstract

A certain subset of people exposed to traumatic stress develop long-term changes in behavior and in their neurobiological systems. Symptoms may include dissociative flashbacks and intrusive memories, sleep disturbance, nightmares, avoidance reactions, abnormal startle reactions, and physiological hyperresponsiveness to reminders of the original trauma, etc.

Current evidence concerning the neurotransmitters and central structures which are likely involved in PTSD are considered along with the drugs which have been found to be effective in treating some of the symptoms of the disorder. The changes which initially occur during the traumatic experience and which set the stage for PTSD are discussed from the point of view of their being adaptive in the early stages of the crisis with abnormality developing over time if the vicious cycle of hyperarousal and further glucocorticoid secretion cannot be broken.

Introduction

Based on current DSM-IV criteria, the diagnosis of Post Traumatic Stress Disorder (PTSD) is applied when a person has been exposed to a traumatic event in which "the person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others". Also in response to this event, "the person's response involved intense fear, helplessness, or horror". In addition, the person has one or more symptoms of involuntary reexperiencing (symptoms shown in Table 1) of the traumatic event. There is also persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness (not present before the trauma), as indicated by three or more of the symptoms listed in Table 2. The person also experiences symptoms of increased arousal which were not present before the trauma as indicated by two or more of the symptoms listed in Table 3.

Table 1 Symptoms of reexperiencing of a traumatic event

1.	Recurrent and intrusive recollections of the event, including images, thoughts, or perceptions. Note: In young children, repetitive play may occur in which themes or aspects of the trauma are expressed.
2.	Recurrent distressing dreams of the event. Note: In children, there may be frightening dreams without recognizable content.
3.	Acting or feeling as if the traumatic event were recurring (includes a sense of reliving the experience, illusions, hallucinations, and dissociative flashback episodes, including those that occur on awakening or when intoxicated). Note: In young children, trauma-specific reenactment may occur.
4.	Intense psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event
5.	Physiological reactivity on exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event

from *Diagnostic Criteria from DSM-IV*, American Psychiatric Association, Washington, D.C., 1994, p. 209.

Table 2 Symptoms of avoidance of stimuli associated with the traumatic event

1.	Efforts to avoid thoughts, feelings, or conversations associated with the trauma
2.	Efforts to avoid activities, places, or people that arouse recollections of the trauma
3.	Inability to recall an important aspect of the trauma
4.	Marked diminished interest or participation in significant activities
5.	Feelings of detachment or estrangement from others
6.	Restricted range of affect (e.g., unable to have loving feelings)
7.	Sense of a foreshortened future (e.g., does not expect to have a career, marriage, children, or a normal life span)

from *Diagnostic Criteria from DSM-IV*, American Psychiatric Association, Washington, D.C., 1994, p. 210.

Table 3 Symptoms of increased arousal present since the traumatic event

1.	Difficulty falling or staying asleep
2.	Irritability or outbursts of anger
3.	Difficulty concentrating
4.	Hypervigilance
5.	Exaggerated startle response

from *Diagnostic Criteria from DSM-IV*, American Psychiatric Association, Washington, D.C., 1994, p. 210.

In order for the diagnosis of PTSD to be applied, the person's symptoms must have persisted for more than 1 month and the symptoms need to have been the cause of clinically significant distress or impairment in social, occupational, or other important areas of functioning. The syndrome is given the label of *acute* if the duration of the symptoms is less than 3 months, *chronic* if the symptoms have persisted for 3 months or more, and *delayed onset* if the onset of symptoms is at least 6 months after the stressor.

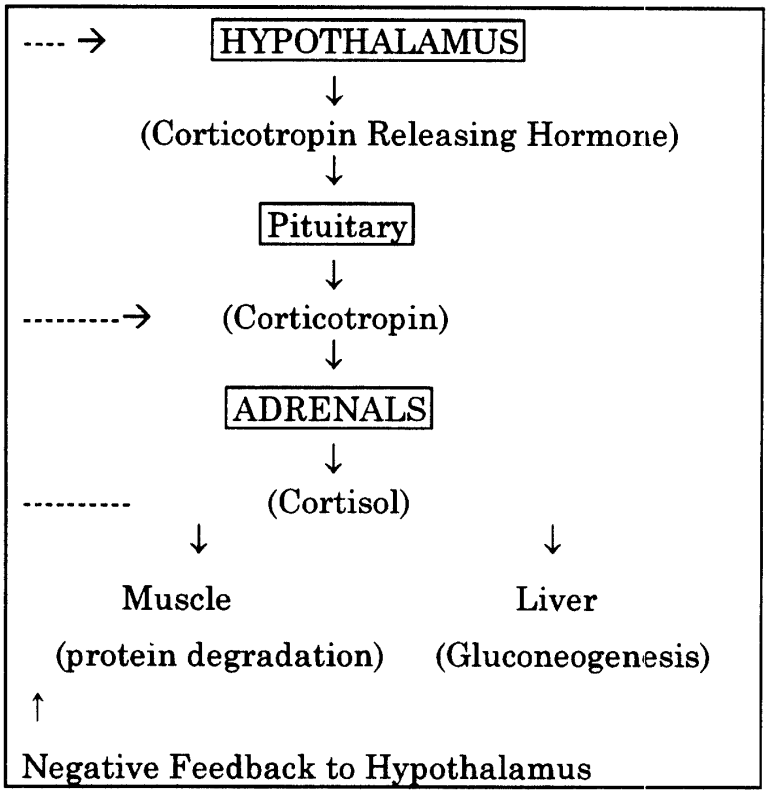

Fig. 1 The Hypothalamic-Pituitary-Adrenal Axis

The Consequences of Extreme Stress

More and more research is elucidating the mechanisms underlying the physiological consequences of extreme stress. Attention has focused on the Hypothalamic-Pituitary-Adrenal (HPA) Axis (Fig. 1) and the secretion of glucocorticoids. The most important glucocorticoid physiologically is cortisol (hydrocortisone) and physiological glucocorticoid effects are mainly cortisol effects. Research has shown that stress causes increased cortisol concentrations.

Glucocorticoid release is regulated by the HPA system. In the case of decreased cortisol, Corticotropin Releasing Hormone (CRH) release from the hypothalamus stimulates Adrenocorticotropic Hormone (ACTH) release from the pituitary. This stimulates glucocorticoid release in the adrenal cortex.

During stress the brain responds by increasing the expenditure of energy (catabolism) and by suppressing physiological functions which are unnecessary in the short-term. Some of the effects of cortisol as well as the possible adaptive value of the response induced by cortisol are shown in Table 4. Though necessary for the immediate responding of the organism, these can become maladaptive if they continue for a prolonged period. The third column of Table 4 lists some of the side effects of glucocorticoid administration and prolonged stress. For example, increased blood glucose levels and glycogen formation in the liver may lead to diabetes, suppression of the immune system can increase the risk of infection, and a lowering of the seizure threshold may result in epilepsy.

Table 4 The effects and possible adaptive value of cortisol secretion during stress and the side effects of glucocorticoid adminstration

EFFECTS OF THE GLUCOCORTICOID CORTISOL	POSSIBLE ADAPTIVE VALUE OF RESPONSE	POSSIBLE SIDE EFFECTS OF GLUCOCORTICOID ADMINISTRATION (or PROLONGED STRESS)
Stimulates gluconeogenesis from proteins by increasing protein degradation (catabolic effect)	Provides necessary energy to respond by fleeing or fighting	Atrophy of muscle, skin and fat tissue due to catabolic effects
Increases blood glucose levels and glycogen formation in the liver (diabetogenic effect)	Provides necessary energy to respond by fleeing or fighting	Diabetogenic effects
Decreases the renal threshold for glucose		
Inhibits growth in children in high doses	Suppression of immediately unnecessary function	Stunted growth
Blocks inflammatory processes independent of their origin by inhibiting leukocyte exit from the vascular system, leukocytic phagocytosis, bacteriolysis and antibody formation (antiinflammatory effects)	Suppression of immediately unnecessary function	Increased susceptibility to disease
Suppresses fibroblast formation and collagen synthesis (antiproliferative effect)	Suppression of immediately unnecessary function	Wound healing is delayed
Reduces the *function* of *lymphatic tissue* which causes transient lymphopenia and formation of smaller lymphocytes (immunosuppressant effect)	Suppression of immediately unnecessary function	Increases risk of infection
Decreases ACTH and *gonadotropin* secretion in the anterior pituitary and *inhibits gonadal function*	Suppression of immediately unnecessary function	Reduced sperm count, Impotency
Decreases the number of *esosinophilic granulocytes* in blood and *increases* the number of *thrombocytes*	Increased ability of blood to clot in case of injury	Risk of thrombosis (stroke) is increased
Increases excitability of brain tissue and *lowers seizure threshold*	Acts to make organism more responsive to incoming sensory information & decreases motor response time	Latent EPILEPSY can be manifested
Has *psychotropic euphoric*, but also *depressive effects*	Possibly results from increase in opiate secretion which intended to deaden pain to allow organism to respond even if injured	
Increases excretion of calcium ions by the kidney (Vitamin D antagonistic effect), mainly as result of *inceased calcium release from bone*		Osteoporosis due to degradation of mesenchymal bone matrix and vitamin D antagonistic effects; persons with limited motor activity particularly at risk
Suppression of digestion	Suppression of immediately unnecessary function	Ulcers in gastrointestinal tract can be reactivated
		Increased intraocular pressure which can cause GLAUCOMA & BLINDNESS

		Dermatological effects of striae and steroid acne
		Due to effect on CNS, there may be • Lack of sleep • Lack of impulse inhibition • Psychological alterations
(Mutschler et an, 1995, p. 283)		(Mutschler et al, 1995, p. 287)

Although the negative effects of prolonged stress on the body are becoming considerably clearer, the effects of prolonged stress and in particular, extreme stress on cerebral processes is still poorly understood. For example, a recent text on drug actions lists the CNS effects of stress as only euphoria (and also depressive effects), lack of sleep, lack of impulse inhibition, and psychological alterations (Table 4). The current paper will approach the issue of the psychotropic effects of extreme stress by reorganizing the DSM-IV diagnostic symptoms of PTSD in such a way as to view them as components of a response which may be initially adaptive, but which proves maladaptive when stress is prolonged either by external stimuli/circumstances or by internal stimuli.

PTSD-When an Initially Adaptive Response Becomes Maladaptive

The current paper will argue that the precursors of PTSD symptoms are initially adaptive in the situation of danger. However, the brain changes which occur set the stage for later dysfunction. Tables 5 through 9 list first the phenomena which occur at the time of the traumatic experience, this is followed by the PTSD symptoms which may arise as a result of this phenomenon. Next is listed the hypothesized short term adaptive function of the original phenomenon with this being followed by how the response can become maladaptive in the long term.

For example, the increased excitability of brain tissue which results during the Fight or Flight Response makes the organism more sensitive to incoming sensory information and allows the organism to respond more quickly. However, after the danger has passed, the person is left with a more sensitive nervous system. Following the traumatic stress, the person is likely to react to smaller challenges than before the event and thus is more easily thrown back into a state of hyperarousal. There is also a greater likelihood of spontaneous firing of neuronal networks, consequently flashbacks may occur spontaneously as well as in response to external stimuli. In addition, there is an increased likelihood of external stimuli related to the original traumatic event eliciting flashbacks, thoughts, or images of the experience with all of these resulting in increased secretion of catecholamines thus perpetuating the vicious circle (increased excitability → flashbacks → catecholamine secretion → increased excitability →).

The components of the Fight or Flight Response which are analyzed in this way are

Table 5 Extreme emotional memory potentiation - resultant PTSD symptoms, short-term adaptive function, and long-term maladaptive consequences.

FIGHT OR FLIGHT PHENOMENON	RESULTANT PTSD SYMPTOMS	ADAPTIVE FUNCTION	MALADAPTIVE IN LONG-TERM
EXTREME EMOTIONAL MEMORY POTENTIATION (extreme classical conditioning)	B-1 Recurrent & Intrusive: Images, thoughts, perceptions, repetitive play B-2 Dreams B-3 Flashbacks, reliving experience with illusions or hallucinations	1. Extreme emotional potentiation imprints details of event thus allowing organism to avoid recurrence 2. Extreme potentiation forces person to recall event - forced thinking may have survival value in forcing person to ruminate on the event with the consequence that the person may generate a new way of dealing with the threat (e.g., may motivate person to make home more earthquake proof or to install security system)	1. Recurrent & intrusive thoughts, dreams, and flashbacks act as internal stimuli which throw person back into hyperarousal with concomitant hypersecretion of glucocorticoids 2. Also interfere with daily life; person unable to concentrate on trivial day to day demands of living 3. High levels of emotion now paired with extreme sensory experience any of the elements of which can now elicit the emotional response

Table 6 Increased excitability of brain tissue - resultant PTSD symptoms, short-term adaptive function, and long-term maladaptive consequences.

FIGHT OR FLIGHT PHENOMENON	PTSD SYMPTOMS	ADAPTIVE FUNCTION	MALADAPTIVE IN LONG-TERM
INCREASED EXCITABILITY OF BRAIN TISSUE with concomitant INCREASED SENSITIVITY TO SUBSEQUENT STRESS	D-2 Irritability or outbursts of anger (Amygdala kindling) Inceased sensitivity to stress	1. Greater excitability of brain tissue at time of traumatic stressor makes organism more sensitive to incoming sensory information (vision, hearing, olfactory senses *more acute*); enhanced perception gives organism edge in survival 2. Another survival advantage stemming from increased excitability is that person is able to respond more quickly in case of another occurrence of the same or similar threat (e.g., creaking of window which woman heard but ignored prior to rape; after rape she responds with huge fight or flight response when hears similar sound)	1. Person more sensitive to subsequent stressors; likely to react to smaller challenges than he/she would have before the traumatic stress → easily thrown back into high state of arousal 2. May get spontananeous firing of neuronal networks resulting in outbursts of anger or in spontaneous flashbacks in absence of eliciting stimulus 3. Greater excitability increases possibility that similar external or internal stimuli may elicit flashacks, thoughts of event, or images

Table 7 Increased vigilance & arousal - resultant PTSD symptoms, short-term adaptive function, and long-term maladaptive consequences.

FIGHT OR FLIGHT PHENOMENON	PTSD SYMPTOMS	ADAPTIVE FUNCTION	MALADAPTIVE IN LONG-TERM
INCREASED VIGILACE & AROUSAL	D-1 Problems sleeping	Organism which sleeping when danger near not likely to survive	Person is deprived of Delta sleep&REM sleep which are necessary for physical & mental recovery
	D-4 Hypervigilance	When danger has occurred, it is of survival value to be vigilant for reoccurrence of that danger	Paranoia and suspiciousness may result which may impact negatively on interpersonal relations
	D-5 Exaggerated startle response	Greater excitability (sensitivity) of orienting response; each new stimulus in environment elicits attention so that it can be properly evaluated for its level of threat to the organism	Person overreactive to any sudden loud noise, etc.; easily thrown back into hyperarousal with further glucocorticoid secretion
	D-3 Difficulty concentrating (due to distractibility stemming from stimulus hypersensitivity)		Hypersensitivity to environmental stimuli disrupts concentration; here biological survival mechanism overriding attempt to get on with daily living
ANXIETY & FEAR	C-3 Inability to recall an important aspect of the trauma (fragmented memory with amnestic portions)	Well known in psychology that extreme levels of arousal impair memory (bell curve). May be that at these levels, brain may be processing at more primitive level which allows more rapid responding than cortical processing with its collation of various sensory information into unitary whole with conscious access	This level of processing may result in fragmented but extreme emotionally tagged memories which may replay spontaneously eliciting sympathetic arousal. Person may lack conscious access to the experience and thus is unable to use cognitive strategies to decrease the distress

Table 8 Analgesia & euphoria - resultant PTSD symptoms, short-term adaptive function, and long-term maladaptive consequences.

FIGHT OR FLIGHT PHENOMENON	PTSD SYMPTOMS	ADAPTIVE FUNCTION	MALADAPTIVE IN LONG-TERM
ANALGESIA & EUPHORIA	C-4 Decrease in interest or participation in significant activities	During danger, endogenous opiates are secreted to induce analgesia such that if the organism is injured, it will still be able to function despite pain; these opiates also secreted in areas involved in internal reward resulting in euphoria	Brain may adapt to this abnormal increase in opiate secretion by down-regulating with the consequence that in the post traumatic period the person may have lower than normal levels of opiate secretion or opiate receptor sensitivity resulting in decreased pleasure in normal activities (decreased functioning of internal reward system)

Table 9 Suppression of emotions-resultant PTSD symptoms, short-term adaptive function, and long-term maladaptive consequences.

FIGHT OR FLIGHT PHENOMENON	PTSD SYMPTOMS	ADAPTIVE FUNCTION	MALADAPTIVE IN LONG-TERM
SUPPRESSION OF EMOTIONS	C-6 Restricted range of affect (inability to express love)	Allows person to function in dangerous situation without being paralyzed by emotions (fear, anxiety, etc,)	1. Negatively impacts on interpersonal relationships 2. Leads to dissociation between experience & emotion; may result in denial of reality of event or one's participation in it
	C-7 Sense of foreshortened future	same as above	same as above
	C-5 Detachment or estrangement from others	same as above	same as above

Table 10 Changes in brain neurotransmitter and neurohormonal systems with stress.

Neurotransmitter	Acute Stress	Chronic Stress	Brain Regions Involved	PTSD SYMPTOMS
Norepinephrine	↑	↑ responsiveness of Locus coeruleus neurons	Hippocampus Hypothalamus Locus Coeruleus (in Pons) Cortex Amygdala	Anxiety Fear Hypervigilance Hyperarousal Irritability Encoding of traumatic memories
CRF-HPA axis Brain CRF	↑	↑/↓	Hippocampus Hypothalamus Cortex Locus Coeruleus Amygdala	Anxiety Fear Memory alterations Hyperarousal
-Peripheral ACTH	↑	↑/↓		
-Peripheral cortisol	↑	↑/↓		
Dopamine	↑	↑	Prefrontal cortex	Hypervigilance
			Nucleus accumbens	Paranoia Alterations in memory
Benzodiazepines (GABA)	↑	↓*	Hippocampus Hypothalamus Cortex Striatum Midbrain	Anxiety
Endogenous Opiates	↑	↓*	Midbrain Hippocampus	Analgesia Emotional blunting Encoding of traumatic memories

MB = Midbrain
Hipp = Hippocampus
Hypo = Hypothalamus
Cor = Cerebral Cortex
Amyg = Amygdala
Stria = Striatum

CRF = Cortiotropin-Releasing Factor
HPA = Hypothalamic-Pituitary-Adrenal Axis
ACTH = Adrenocorticotropic hormone
PFC = Prefrontal cortex
NA = Nucleus accumbens
LC = Locus Coeruleus (pons) site of majority of noradrenergic neurons in brain
*Decrease in receptor binding measured by B max

from Bremner et al, 1994.

extreme emotional memory potentiation (extreme classical conditioning) (Table 5), increased excitability of brain tissue (Table 6), increased vigilance and arousal (Table 7), analgesia and euphoria (Table 8), and suppression of emotions (Table 9). Detailed analysis of these can be found in the tables.

In a recent review of the neurobiology of PTSD, Bremner et al (1995) identified a number of intracerebral neurotransmitters and structures associated with changes

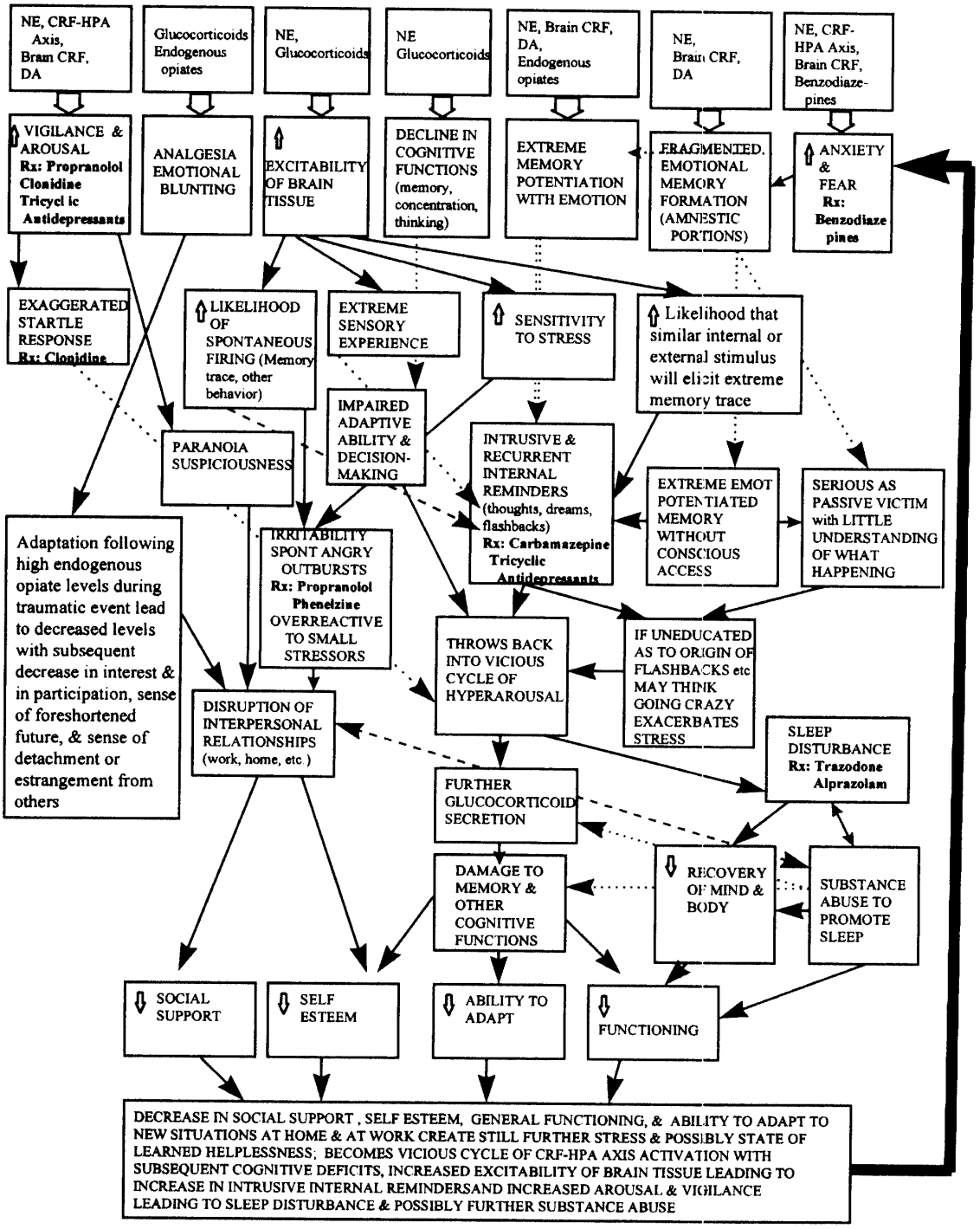

Fig. 2 Immediate and long-term psychotropic consequences of traumatic stress - drugs effective in treatment of individual symptoms and role in HPA axis hyperactivation.

during traumatic stress (Table 10).

When one considers the symptoms of PTSD and their relationship to neurochemistry, one must think in terms of phases. There is likely an initial extreme increase in certain neurotransmitters during the stage of acute danger. This may likely be followed by a rebound effect due to adaptation. Research has found high levels of various neurotransmitters during the acute phase frequently followed by decreased levels in the chronic phase (Table 10). For example, high levels of norepinephrine may initially result in high energy and strength but may later be followed by low energy and low strength. Similarly, the secretion of endogenous opiates which play a role in analgesia and euphoria in initial stages may be followed by dysphoria or anhedonia. The flowchart in Fig. 2 suggests how the different initially adaptive phenomena created by the traumatic stress may lead to later dysfunction. Information from Table 10 has been merged with the phenomena to show which neurotransmitters may be involved. Table 11 shows the drugs which current literature suggests as being useful in the treatment of PTSD symptoms. Information from this chart has been added at the appropriate place in Fig. 2 to show where intervention has been found to be effective. There is no one drug which has been found to be effective for all the symptoms of PTSD. Given the various neurotransmitters and systems involved, this is not surprising. Individual drugs have been found to be effective in treating specific symptoms. For example, Carbamazepin, a GABA-agonist with anticonvulsant activity has been used to treat persistent flashbacks. Propranolol (a β-noradrenergic receptor blocker & GABA-mimetic) and Clonidine (acts on presynaptic neurons and inhibits noradrenergic transmission at the synapse) have been used to treat the persistent anger, vigilance, and startle response. Benzodiazepines have proved of use in the treatment of anxiety and fear and Trazodone (a cyclic antidepressant) and Alprazolam (a benzodiazepine) have been used in the treatment of the sleep disturbance often found in PTSD. Drugs which block norepinephrine and serotonin reuptake (cyclic antidepressants such as Doxepin (Sinequan), Fluoxetine (Prozac), and Imipramine (Trofranil; a Selective Serotonin-Reuptake Inhibitor [SSRI])) have been used to treat flashbacks and the increased arousal found in PTSD.

One of the questions which has puzzled PTSD researchers is why only some people who experience the same traumatic event develop the disorder. It should be noted that PTSD occurs following a number of very different events, and the nature of the event can greatly influence not only the initial rate at which acute PTSD symptoms are experienced, but also the later development of chronic PTSD. For example, 94% of rape victims are said to initially show symptoms of PTSD (Rothbaum et 1992). This rate has been found to be much lower for natural disasters. There are, of course, differences in the reactivity of the nervous system which can combine with previous trauma or stress to make some people more susceptible to PTSD than others. Also following the trauma, a number of social factors can interact with the initial neurobiological changes and "feed" the vicious circle of hyperarousal and glucocorticoid secretion. For example, soldiers with traumatic experiences in Vietnam returned home

Table 11 DRUG TREATMENT OF PTSD

SYMPTOMS	DRUG	
Persistent anger Vigilance Startle	Propranolol Clonidine	**Propranolol**: a β-blocker; has membrane-stabilizing effect & GABA-mimetic activity Useful in controlling rage, violence, irritability & aggression: Beneficial for somatic or autonomically mediated symptoms of anxiety (e.g. tremor, palpitations); used in control of mania, antisocial behavior, anxiety, and schizophrenia **Clonidine**: a central & peripheral α-adrenergic agonist; acts on presynaptic neurons & inhibits noradrenergic transmission at the synapse - used in treatment of some anxiety disorders, ADHD, mania, & schizophrenia (decrease in psychotic symptoms)
Persistent flashbacks	Carbamazepine	DEF: GABA-agonist activity; Anticonvulsant activity (particular efficacy in temporal lobe (complex partial) through a "peripheral" type benzodiazepine receptor; effective in inhibiting seizures kindled from repeated stimulation of limbic structures;
Refractory & angry	Phenelzine Lithium	Phenelzine: MAOI (Irreversible) inhibits action of MAO-A and B enzymes that metabolize the neurohormones responsible for stimulating physical and mental activity (NE, serotonin, dopamine) Lithium: exact mechanism of action unknown, but postulated that it may stabilize catecholamine receptors, and may alter calcium-mediated intracellular functions and increase GABA activity
Sleep disturbance	Trazodone Alprazolam	Trazodone: Triazolopyridine (cyclic antidepressant) Alprazolam (Xanax): benzodiazepine (medium acting)
Significant distress on re-experiencing	Propranolol	**Propranolol**: a β-blocker, has membrane-stabilizing effect & GABA-mimetic activity; Useful in controlling rage, violence,irritability & aggression: Beneficial for somatic or autonomically mediated symptoms of anxiety (e.g. tremor, palpitations); used in control of mania
Anxiety	Benzodiazepine	Benzodiazepines mediate actions of GABA, brain's major inhibitory neurotransmitter; GABA inhibits firing of neurons by opening chloride channels on the neuronal membrane This causes a hyperpolarization that requires a greater depolarization to trigger an action potential
Positive sympotoms of PTSD (re-experiencing the past & increased arousal) affected more than negative symptoms (avoidance & withdrawal)	Dexepin Fluoxetine Imipramine	All 3 are Tricyclic antidepressants (TCAs) which block NE & Serotonin reuptake
taken in part from Jerrold S. Maxmen, *Psychotropic Drugs*, WW Norton & Co., 1991, p. 192		

to further trauma when, rather than being welcomed home as victorious heroes as the soldiers of World Wars I and II before them, they were cursed as "baby killers" and rejected by many in the society.

At a recent conference on the psychobiology of PTSD, it was suggested that psychotropic intervention might be useful immediately following a traumatic event. This intervention might consist of medication to block or weaken the extreme emotional memory formation which later feeds the cycle of HPA axis hyperarousal, cognitive deficits, hyperexcitability of brain tissue, etc. It was suggested that β-blockers might be useful in this regard.

In the event that immediate administration of such a substance were not possible, treatment might be conducted from the point of view of preventing acute PTSD from developing into chronic PTSD, and in this regard, the major objective might be the interruption of the vicious cycle previously described. This treatment would likely include medications to decrease arousal, anxiety, and the excitability of brain tissue.

The new discoveries being made in psychopharmacology may tempt some professionals into thinking that drug therapy alone will solve the problem. Although psychotropic medications may prove useful in helping the distressed individual override certain primitive biological mechanisms, effective treatment will likely continue to be based on a combination of techniques including education, psychotherapy, and social skills training. For example, education about possible symptoms which might occur following a traumatic event (e.g., flashbacks as being normal outcomes of traumatic events) is necessary to prevent the individual from feeling they are "going crazy". Significant others should be helped to understand the possible cognitive, emotional, and physiological repercussions of the traumatic event. It is unlikely that medication will be able to help the traumatized individual combine fragmented sensory images of the trauma into a whole which can be consciously accessed. It is also unlikely that pharmacology alone will be able to mend interpersonal relationship which have been disrupted through unexplained aggressiveness, paranoia, and alcohol abuse.

Conclusion

Our understanding of the role of extreme stress in mental dysfunction is as yet incomplete. Although the last two decades have seen tremendous progress in the treatment and understanding of a number of mental disorders, there is much that is only partially understood. We have only fragmentary knowledge about neurotransmitters, the pathways where they can be found, and the ways in which these pathways interact. There appears to be a specific pathway for anxiety, a separate pathway for internal reward, different pathways for attention and memory, etc.

Our comprehension of how these pathways mesh together is still extremely poor. However, one of the keys to understanding this may be the condition known as the Post Traumatic Stress Disorder. Here we may see in extreme relief a number of psychopathologies superimposed on each other (phobic disorder, depression, sleep disorder, paranoia & suspiciousness, anxiety, extreme anger, impulse control prob-

lems, etc.) yet they may have arisen from one specific extreme stressor. Careful study of this disorder will likely lead us to a clearer understanding of the human mind.

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