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# CENTRAL AND PERIPHERAL MECHANISMS IN THE NEUROPHYSIOLOGY OF DEPRESSION

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Our purpose is to review two directions in the study of depression; central and peripheral theories. Central theories focus on the central nervous system, that is, the brain and spinal cord. Peripheral theories, in contrast, focus on the body soma, that is, on the peripheral nervous system, the visceral organs, the muscles, the skin and the special organs of reception, eyes, ears, nose and mouth.

What causes depression -- the central nervous system or the body soma?

Most clinicians tend to advance a theory that is exclusively central or peripheral, since each theory favors an alternative treatment approach. Central theories, for example, favor a pharmacological approach; peripheral theories, in contrast, favor a body-oriented psychotherapeutic approach. Our hope is to show that both central and peripheral processes can lead to depression, and that these two sets of processes can be integrated within a single model.

## Central Theories of Depression

At the beginning of this century, the James-Lange peripheral theory of emotions, which states that emotions emerge from the perception of body changes, was the predominant medical model. Then an important paper

by Walter Cannon (1927) showed the insufficiency of the James-Lange theory and substituted for this a centralist theory. Cannon placed the seat of emotions in the thalamus. (The thalamus is the main relay station reached by nerve impulses stemming from contact with the environment and from voluntary muscle tonus, that is, from perception and proprioception, before these impulses reach the cerebral cortex.) It is important to note that visceral feedback is not directly relayed to the thalamus but follows an alternative pathway that will be described subsequently.

Cannon's hypotheses concerning the thalamus as the seat of emotions was then replaced by James Papez' (1937) model in which he describes a circuit that connects various nuclei -- hippocampus, amygdala and septum -- all located in the diencephalon, that is, just below the cortex. Papez proposed that the circular arrangement of this circuit could explain how an emotion, once triggered, could continue by means of its own self-repeating propensity. Papez called this circuit "the visceral brain."

Papez' model was then substantiated by Paul MacLean (1949), who relabeled this organization of subcortical nuclei "the limbic system", because it is situated on the "limbus" (or frontier) of the temporal lobe of the cerebral cortex.

It is now accepted that emotions are primarily regulated by the limbic system. The limbic system, in turn, exerts a direct effect upon the hypothalamus. The hypothalamus represents the final integrator of motor, visceral, hormonal and probably immunological responses. After hypothalamic integration, each type of response is directed by means of separate pathways into a different part of the body soma. In other words, the hypothalamus is the final integrator before outputs separate into different directions, and the limbic system is the main regulator of this final output box. Therefore, when we speak of depression, or of any other emotional disorder, our first task is to examine how the limbic system and hypothalamus are involved.

#### Biochemical Models of Depression

The most well-known mechanism of depression involves a lowering of the neurotransmitter, norepinephrine. Norepinephrine facilitates the synaptic transmission of nerve impulses, and it is found, especially concentrated within the limbic system. The major support for the norepinephrine hypothesis is that most antidepressive medications used today exert their effect by increasing norepinephrine levels within the limbic system.

In fact, this raising of norepinephrine levels can be accomplished in two different ways: the monoamine oxidase inhibitors (MAO inhibitors) such as phenelzine prevent the destruction of norepinephrine after it has crossed the synaptic barrier. The tricyclic antidepressants, in contrast, such as amitriptyline (Elavil) and imipramine (Tofranil), prevent the reuptake of norepinephrine at its presynaptic origin. (Schildkrant, 1972). Both types of medication increase the concentration of available norepinephrine and are thus understood to resolve the problem of depression through this action.

More recently, it has been suggested by De Montigny and Aghajanian (1978) that these same antidepressive agents work in another way: Rather than increase norepinephrine levels, they may influence serotonin metabolism. This is supported by the fact that while the

time interval for norepinephrine to act is rather short, the time interval for the serotonin effect is two to three weeks; this is the same time interval needed for these medications to exert their clinical effect. Whatever neurotransmitter is increased by the antidepressives, it is clear that the allopathic physician who treats depression by prescribing pills will put his "scientific weight" behind the central theory of depression.

#### The Limbic-Hypothalamic Pathway in Depression

Two other central theories of depression which might interest the clinician are the Laborit and Gellhorn theories. These theories look at the nerve pathways that underly the depressive reaction. Before describing Dr. Gellhorn's contributions, we will review the limbic-hypothalamic pathways that have been uncovered in recent years: James Olds (1954) had shown that "pleasure-oriented" reactions are mediated by the median forebrain bundle (MFB), which links the hippocampus and septum with the hypothalamus, and then runs down into the tegmental and central gray regions of the mesencephalon. It is in these mesencephalic loci that subcortical pathways descending from the limbic system may be integrated with ascending pathways from the lower brain Nucleus Solitarius (Nauta, 1972). (The Nucleus Solitarius is the principal nucleus for receiving visceral afferent impulses coming in through the vagus nerve.) This mesencephalic connection is therefore a major constituent of our "impulse system" in which viscerally-based "drives" are connected to limbic-regulated and hypothalamic-controlled appetite centers. MacLean (1972) suggests that conditioned reflexes are mapped out in the limbic system since these regions permit receptor-organ afferents stimulated by the environment to meet directly visceral afferents.

Following Old's discovery of the pleasure response, DeMolina and Hunsperger (1962) showed that defensive reactions of fight or flight are mediated by another limbic-hypothalamic-mesencephalic circuit, the periventricular system (PVS) situated in proximity to the fourth ventricle. Thus the MFB and PVS both represent active responses --plea-

surable or defensive--when the living creature faces the environment.

#### Dr. Laborit's Theory: Inhibition of Action

Dr. Henri Laborit (1979) has demonstrated the presence of response-inhibiting pathways between the limbic system and hypothalamus. He named these pathways the Action Inhibition System (AIS). While the active response systems previously described can be compared to stepping on the gas pedal to accelerate the car engine, the Inhibition System is like stepping on the brake to stop the vehicle (or ourselves) on a dime. This is a life-saving mechanism when an animal in the heat of action -- running, climbing, pouncing, eating -- receives a new signal, "Danger!", and must reorient his action. The trouble is that a prolonged period of action inhibition, as frequently occurs under civilized conditions, creates a functional disturbance.

In more picturesque terms, it is as if we are stepping on the brakes of the car while our other foot is still pressing down on the gas pedal. We hear the squeal of tires and the grating of metal parts jamming, and this is how the body reacts: disequilibrium, anguish, thoughts of helplessness and poor coordination. For Dr. Laborit, the action inhibition mechanism serves as the basis for both psychosomatic and neurotic illnesses.

We might note that Dr. Laborit's work clarified a previously confusing set of findings within neurophysiological research: Stimulation of certain limbic system sites, such as the amygdala or septum, tended to give contradictory results, in that their stimulation brought the experimental animal to become, at times, more aggressive or active, and at other times, less so. Dr. Laborit's research clarified the dilemma: Each of these limbic sites contains two different neuroanatomic regions, one that stimulates action, and another that inhibits it. Specifically, it is the dorsomedial part of the amygdala that stimulates action and the lateral part that inhibits action. Likewise, in the septum, the lateral part stimulates action and the medial part inhibits it.

The fact that these important subcortical centers work by a "dialectical relation" of facilitation-and-inhibition might eventually help to understand the brain's internal circuitry and the dialectic control of both our behavioral and psychological functions. (We will also see that this dialectical principle functions within the autonomic nervous system.)

#### Dr. Gellhorn's Theory: Sympathetic/Parasympathetic Non-Reciprocity

Dr. Gellhorn's theory (1967) focuses upon processes within the hypothalamus and their effect upon autonomic nervous system functioning. Let us remember that the automatic nervous system, as opposed to the voluntary motor system, controls visceral processes that are automatic, that is, over which we have no direct voluntary control. This includes heart-rate, bronchial dilatation, peristalsis, gastrointestinal secretions, blood distribution between voluntary and non-voluntary muscles, and so on. To perform these functions, the hypothalamus is divided into two regions -- one that produces sympathetic responses linked to motor discharge and energy-consuming metabolic processes needed for vigorous action, and another region that produces parasympathetic responses linked to rest and energy-recuperating processes needed for digestion and sleep.

Dr. Gellhorn's research shows that these two components--the sympathetic and the parasympathetic--should become active at different moments. When the sympathetic component needed to sustain "active" metabolic processes is on the increase, the parasympathetic component needed to regenerate energy (increase ATP reserves) should decrease. And, at another moment, vice versa. Such alternative firing is called a "reciprocal" or seesaw arrangement.

Trouble crops up when this reciprocal arrangement is disturbed, that is, when both sympathetic and parasympathetic components fire at once. Dr. Gellhorn shows a number of vegetative and behavioral symptoms that seem to be associated with such a derangement. In summary, Gellhorn's hypothesis is that depression comes from sympathetic and para-

sympathetic discharge losing their reciprocal relation and being replaced by a simultaneous or "additive" relationship.

#### An Integrated View

The author's position is to combine Dr. Laborit's and Dr. Gellhorn's theories (see Boadella and Liss, 1986). The neuroanatomical organization underlying these two theoretical positions readily lends itself to this type of integration: First, the action inhibition pathway, which connects the emotional-regulating limbic system to the emotional-discharging hypothalamus, is fired for an abnormally prolonged period; this creates chronic action inhibition despite the provoking effect of stress, as Dr. Laborit pointed out. Second, the sympathetic and parasympathetic components of the autonomic nervous system which are organized by the hypothalamus as a to-and-fro reciprocal relation, goes out of kilter. In fact, not only is the autonomic nervous system response disturbed, but other hypothalamic-dependent processes, such as hormonal and motor responses, also become abnormal. The most evident hormonal abnormality is excessive secretion of norepinephrine and corticosteroids. These two "stress hormones" create abnormal visceral responses: excessive norepinephrine leading to hyper-tension, excessive corticosteroids causing a diminished immunity response and therefore a predisposition toward infectious diseases or else tumor-formation.

At the same time, another phenomenon crops up which serves as a key mechanism for understanding depression: feedback! That is to say, the norepinephrine and corticosteroids circulating in the bloodstream and acting upon the body soma turn back to act upon the central nervous system by passing the blood-brain barrier. And at what level do they cross the barrier? At the level of the limbic system. More precisely, they become concentrated within the action inhibition centers and prolong the action inhibition. In other words, these two hormones, norepinephrine and the corticosteroids, (though not adrenalin, which is linked to action liberation), return to reinforce the limbic centers that initiated their secretion. The re-

stimulation of these limbic centers prolong the paralyzing effect.

Though Dr. Laborit does not suggest any other peripheral-to-central feedback mechanisms, body-oriented therapists could easily offer further possibilities: chronic muscle tension from an unceasing "preparation for action that is never executed", reduced breathing, peristaltic disturbances, sexual dysfunctions, sleep difficulties and skin disorders. These are but some of the symptoms of depression which we claim create feedback effects upon the central nervous system and prolong the vicious cycle. In fact, even "mental symptoms", such as confusion, suicidal ideation, the failure complex, unworked through grief and the self-negating thoughts -- "I'll never succeed, I'm worth nothing to anyone" -- also derive their force from the grinding motor of action inhibition, and they too feed back their effects toward their central nervous system origins so that the depression becomes solid like granite. (The work of Quarti and Renaud, 1972, offers interesting observations and interpretations, based on EEG data, of the connection between thalamic "diffuse" functioning in stress and the breakdown of cortical associative processes that may be associated with mental symptoms.)

Thus, the depressed person is in a vicious circle: Once the depression is set off, the physiological feedback mechanisms originating from the body periphery and directed toward the central nervous system reinforce the pathological process. To say to a depressed person, "It's all in your head!", is no longer valid. Brain and body interact to close off the person in a physiological two-way street of depression. This can help us understand the physiological depth of our emotional depression and can encourage both physician and client to confront the problem with patience and persistence, accepting gradual relief as the important indicator that the vicious circle is being reduced, that is, that the therapeutic intervention is effective.

#### The Peripheral Theory

The peripheral theory claims, as we have already said, that depression is due to pathological processes in the body soma. Let us first examine the socio-economic aspects of this theory, as we previously did when we described the central theory of depression, which is upheld by drug-prescribing medical doctors. The peripheral theory is especially supported by those non-medical psychotherapists who base their treatment approach upon the notion that the body is deeply involved in depressive disturbances. We must remember that these non-medical therapists cannot prescribe medications, since that is the exclusive domain of medical doctors. On the other hand, these psychotherapists (most often psychologists) have so far maintained, in face of medical opposition, the legal right to directly approach the body soma by means of massage, stress positions, play fighting, respiration exercises and screaming. In other words, we have the body-oriented psychotherapies -- Biosystemics, Biosynthetics, Bioenergy, Organismic Therapy, Vegetative Therapy, Primal Integration, Rebirthing, Arica Training, Neo-Reichian Massage, etc. Their purpose is to alter the somatic body processes, sometimes by means of emotional discharge, sometimes by direct vitalization (Rebirthing and Arica Training).

#### Origins with Reich

The father of the body-oriented therapies, Wilhelm Reich, differed from his psychoanalytic colleagues by directly regarding how the body functions at the same time that the patient verbalizes his problem. Reich put his finger on the muscular armour, that is, upon chronically tight muscles, as the basis of the emotional problem; the muscular armour inhibits emotional experience and expression. Reich especially noted that the emotionally disturbed patient shows an incapacity to hit out aggressively, scream, breathe deeply or reveal feelings with facial expression; all these signs give evidence of the muscular armour, since the blockage primarily involved the voluntary muscle system.

#### Neo-Reichian Developments: I. The Theory of Three Embryonic Layers

David Boadella (1986) has focused on disturbances of various organic systems as the key factor in emotional disturbances. Boadella first points out that our adult body emerges from the three layers of embryonic development -- endodermal, mesodermal and ectodermal. The endodermal layer leads to the development of our visceral organs, the mesodermal layer to our voluntary muscle system and the ectodermal layer to our nervous and skin systems. Boadella suggests that all of these somatic levels can participate simultaneously in emotional disturbance. Thus, depression can be conceived as a pathological alteration that can involve various organs: decreased visual and auditory perception and absence of skin contact, (ectodermal), voluntary muscle inhibition (mesodermal), liver, kidney and digestive tract disorders (endodermal).

#### II. Blocked Peristalsis

Gerda Boyesen (1970) has demonstrated that peristalsis is severely impaired in depression and can be effectively treated by massage methods applied to specific skin areas; the result is a return of peristaltic movements. (This is verified by constant monitoring of bowel sounds with a stethoscope).

#### III. Venous Stasis and Decreased Metabolic Exchange

Still another proposed mechanism is venous stasis in the visceral organs, especially in the gastrointestinal tract. Venous stasis interferes with drainage of waste products and may create other metabolic disturbances. A related mechanism is connective tissue stasis (Oleson, 1971), with decreased exchange of metabolites at the capillary level, once again diminishing normal energy exchange processes; for example, the decreased oxygenation in connective tissue stasis can lead to decreased ATP (adenosine triphosphate) production. ATP has been called the basic energy packet for all cellular activity, therefore its reduced concentration can also act as an important mechanism in the depressive spiral.

## Emotions and the Skin.

"Why does the body-oriented therapists touch their patients?" First we have the psychological impact of touch. Direct touch in a professional setting immediately opens up the possibility of trust and direct communication: An arm on the shoulder or a hand that guides the abdominal breathing results in the therapist resembling a trusting parent, and the patient can permit the intimate emotions of hurt, vulnerability and disappointment to come to the surface. More vigorous "catalytic" touching (rubbing the shoulders and back, pushing one another chest to chest, shaking the arms and legs, etc.) stimulates both play and play-fighting, and thus gives the patient permission to show his aggressive energies within a context of emotional security and acceptance. Thus the therapist's introduction of touch contact, which the client can accept or refuse according to his desire, establishes a basic working relationship between the two people that is favorable for the therapeutic process. Let us examine in more detail the skin and its physiological relevance for our emotional life:

1. The galvanic skin reaction (GSR) shows important variations of bio-electrical potential during emotional stress. (Lader, 1975)
2. There is evidence that skin stimulation can alter gamma system discharge, with the gamma system altering muscle tone and thus, muscle tension. (Lethin, 1977)
3. Soft skin stroking produces a generalized parasympathetic response while vigorous skin stroking produces a generalized sympathetic response. (Gellhorn, 1967)
4. Skin touch can alter peristaltic movements. (Boyesen, 1970).
5. The acupuncture meridians surface to skin level at particular sites, and thus stimulating these points permits effects at distant organs. (Sussman, 1972).

6. Skin areas overlying the chakras have a special sensitivity which may permit these areas to act as "doors" for incoming or outgoing body energies. (Pierrakos, 1977).

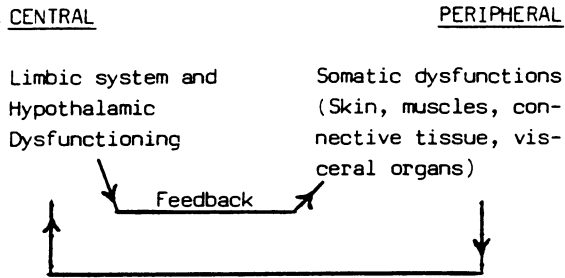
## Scientific Progress and the Socio-Economic Barrier

Each of these mechanisms supports the idea that touching the skin is an important, and sometimes essential, therapeutic method. Touching the skin produces local changes immediate under the healing hands, stimulates organs at a distance and introduces feedback stimulation that can calm the CNS "search for an optimal stimulation". Nevertheless, these mechanisms need to be verified not just by clinical experience, but by the physiological laboratory. But here we run up against another socio-economic barrier: Academic physiologists are unwilling to accept these "somatic hypotheses" because they are derived from clinical observations that are carried on outside of traditional medicine and are therefore not endorsed by today's medical authorities. The outcome is that the therapeutic impact of direct touch has not yet been investigated. Therefore, while body-oriented therapists continue to develop their methods on an empirical basis, their theories remain unintegrated with the physiological models of modern science. It is hoped that the barriers which prevent scientific advancement will be overcome in the future when clinicians and physiologists begin their dialogue.

## Systems Theory and Circular Processes

In conclusion, our proposal is that the various "peripheral" somatic disturbances in the previous section -- chronic tension, blocked peristalsis, venous stagnation, connective tissue edema, alteration of the skin bio-electric capacity, inhibitory stress hormones, and so on -- can be understood as due to disturbed central nervous system processes involving the limbic system and hypothalamus. (The theories of Laborit and Gellhorn.) These peripheral processes then feedback

their effect to create a circular interaction with the central nervous system.



The point is that whether we start from the center or the periphery, we can recognize the interaction of all processes. General Systems Theory (Liss, 1985) suggests, as an overall model for the life sciences of biology, ecology, economics and psychology, that we avoid reducing mechanisms to "first causes", but that we develop, instead, a more comprehensive model that emphasizes, 1) interaction among all systems and 2) the circularity of processes that repeat themselves over time.

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