Gates, States, Rhythms, and Resonances: The Scientific Basis of Neurofeedback Training

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This paper presents a set of electrophysiological and neurophysiological processes as bases for the efficacy of neurofeedback training (NT) for attention deficit/hyperactivity disorder (ADHD), depression, obsessive-compulsive disorder (OCD), and schizophrenia. It then suggests neurophysiological commonalities between these disorders to explain the observed efficacy of NT for depression and OCD, and to suggest the possibility of adapting it to treat schizophrenia.

I. Introduction

The treatment of attention deficit hyperactivity disorder (ADHD) is a challenging endeavor for both clinicians and researchers. ADHD is one of the most puzzling and pervasive disorders of childhood, and, unfortunately, frequently persists into adulthood. Estimates are that ADHD affects between 5 and 15% of the population (Rie & Rie, 1980). As defined in DSM IV, it is characterized by a persistent pattern of inattention, hyperactivity, and impulsiveness, though it can present with or without hyperactivity (APA, 1994). Attentional disorders impose a great burden on the individual, strongly disrupt family functioning, and drain an enormous amount of talent and energy from society. Their effects discourage and demoralize a significant percentage of its sufferers too often leading them away from productive activity and into antisocial lifestyles, drug abuse, and crime. Advances in the understanding and treatment of these disorders, therefore, are likely to produce significant gains for all of society. Fortunately, pharmacological treatment, primarily with stimulants and tricyclic antidepressants, has been found effective in the treatment of ADHD (Barkley, 1990). Recently, neurofeedback has also begun to look effective for treating attentional disorders; of major clinical importance is the fact that it appears that its results persist well after treatment. Unfortunately, the medication and neurofeedback treatments are sometimes considered mutually exclusive; cooperation between the proponents of the two treatment modalities has not flourished.

Motivated by these circumstances, this paper explores the physiological phenomena that underlie neurofeedback treatment of ADHD. Because more is known about neurofeedback work with ADHD than with other conditions, the emphasis in this paper will be on ADHD; other conditions are discussed in the context of conclusions drawn about ADHD. No distinction is made here between ADD and ADHD. Emphasis will be on commonalities in the neurophysiological mechanisms subserving the two treatment approaches-commonalities somewhat underemphasized both in practice and in the literature. It will emerge from this approach that the existence and efficacy of the different treatments can be used, not to force a choice between them, but rather to suggest useful avenues for understanding the neurophysiological aspects of a range of psychiatric disorders and of the mechanisms underlying their successful treatment. Ideally, this understanding can suggest, for example, how the two modalities can be optimally combined. A number of neural mechanisms will be suggested for the finding of long-term

efficacy of neurofeedback for ADHD. Since the mechanisms generating field potentials, however, are themselves still incompletely understood, any discussion of procedures utilizing them must involve a degree of uncertainty, especially in the anatomical and physiological details involved. Nonetheless, the utility of such suggestions can transcend the uncertainties of their details by stimulating research to explicate these details, as well as to unravel other aspects of brain function and dysfunction. This paper presents a synthesis of observations to date with the aim of enhancing understanding of brain function in both normal and pathological functioning. It will be suggested throughout that for ADHD, operant conditioning by neurofeedback rests on the same well-established neurophysiological principles that mediate the effects psychotropic medication. Generalization to other psychiatric conditions will follow in Section IV.

II. Neurophysiological Processes Relevant to Neurofeedback Treatment

To assume that normalizing an ADHD patient's power spectrum, within a single session or over tune, will automatically normalize his symptoms would be fallacious. On the other hand, it would also be incorrect to assume that because a correlation between brainwave normalization and behavioral normalization is not necessarily true, that it is therefore not true. What must be done instead is to complete the relevant observations and then to identify (and integrate conceptually) neural mechanisms that can explain the efficacy of neurofeedback training (NT).

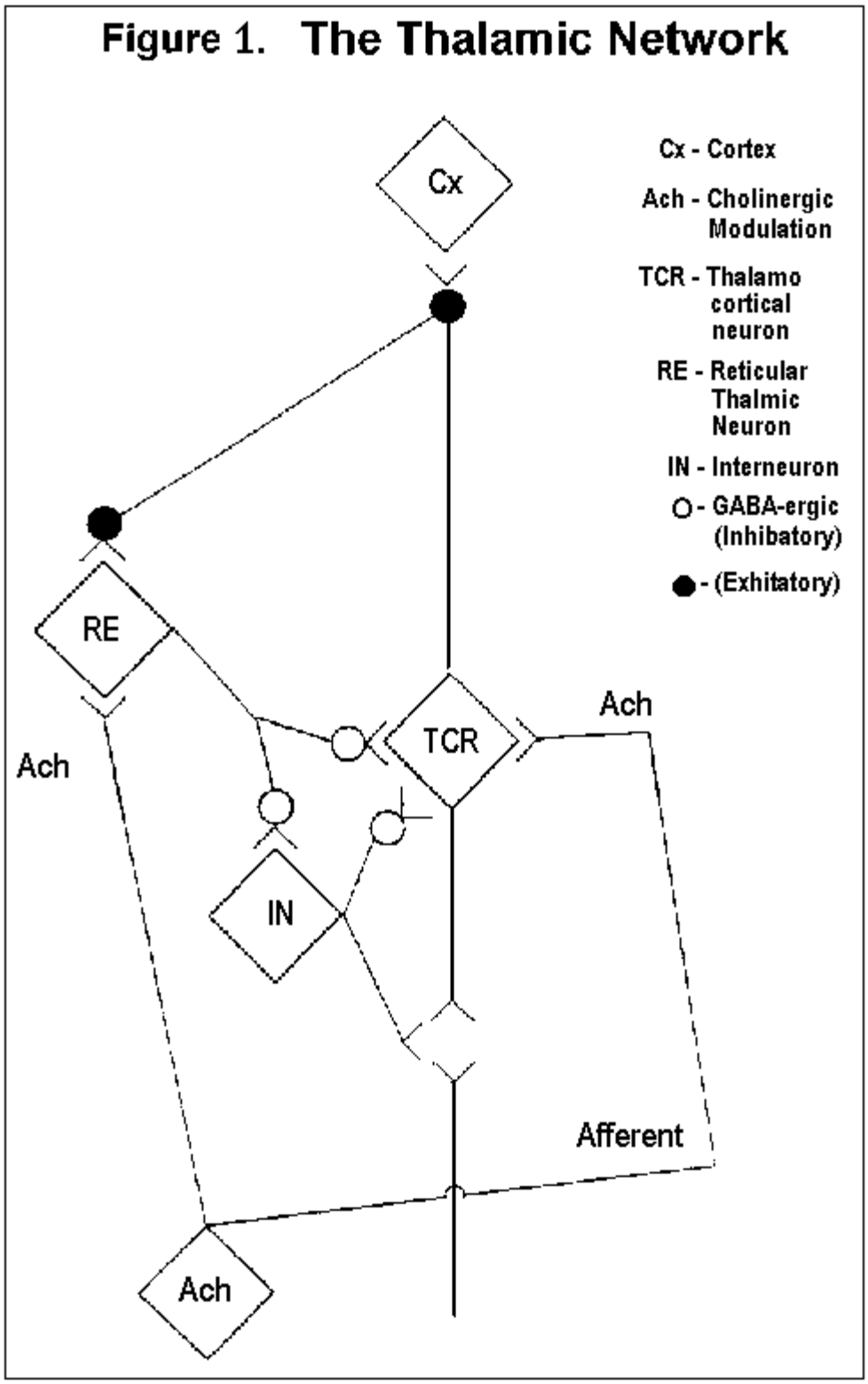
Explanations for the efficacy of NT for ADHD are offered here at three levels. The simplest is empirical: an elevated theta/beta (or theta/SMR) ratio correlates empirically with the presence of ADHD symptoms, reduced theta/beta (or theta SMR) ratios correlate empirically with the resolution of these symptoms. On a somewhat deeper level it can be suggested that in NT, the patient learns to exert neuromodulatory control over the circuitry mediating the attentional process. Over time, long term potentiation in the circuitry involved consolidates an optimization of the attentional system. In terms of network theory it can be said that during NT the system is neuromodulated into an attractor state, a stable equilibrium point for the system (Cohen & Servan-Schreiber, 1992). At this level of explanation, one can analogize what happens in NT to learning a motor task like riding a bicycle. As a child practices the skill, sensory and proprioceptive input initiates feedback regulation of the motor circuits involved (in sensorimotor cortex, basal ganglia, etc.); over time practice automatizes the skill. The parallel to NT can be visualized by imagining a child working with a specific NT paradigm, like the raising of a balloon on a visual display, as an index of a decreasing theta/beta ratios. As the balloon rises, the child watches) and "feels" himself moving it; he feeds these perceptions and "feelings" back to whatever circuitry decreases theta/beta ratios (and which therefore increases attentional competence). Over time, practice automatizes the improved attentional capacity. A third level of explanation seeks to explain how theta beta ratios and attentional competence are mediated and how they relate to one another. As noted earlier, physiological or anatomical explanations at this level must involve a degree of uncertainty because of uncertainties about the processes generating field potentials or regulating the attentional process.

Despite formidable difficulties in reaching precise formulations for the relation ships of EEG rhythms, neural mechanisms, and behavioral competencies, recent advances in neurophysiology and electro-physiology are beginning to allow a more direct access to the processes mediating attentional phenomena; these include improved understanding of oscillatory modes, eventrelated potentials, long term potentiation (LTP), and neuromodulation. What is learned about the anatomy, physiology, and treatment of attentional processes and their treatment by NT can help clarify the even thornier issues of the neurophysiology and treatment of mood and thought disorders (see Section IV).

1. Generation of Cortical Potentials

Despite a good deal of recent progress, the neural mechanisms generating theta, SMR, and beta range scalp potentials remain controversial. Some of the details, however, are being clarified (Steriade et al, 1990; Lopes da Silva, 1991). Oscillatory activity is best understood in the brainstem-thalamus-cortex axis, especially in the case of alpha spindles, though even here there is some controversy (Vanderwolf, 1988; Vanderwolf & Stewart, 1992).

In both the thalamus and the limbic system, certain neurons display oscillatory behavior; this intrinsic activity is significantly affected by inputs from other neurons. Thalamic neurons in vitro tend to oscillate in the 6 to 10 Hz range. There are three types of neurons in the thalamic relay system 1) thalamocortical neurons (TCR), 2) reticular nucleus neurons (RE) that provide inhibitory (hyperpolarizing) feedback control to the TCR neurons, 3) local interneurons that help coordinate the interactions between the first two (see Figure 1). The TCR neurons function in two distinct modes: 1) as relay cells that depolarize in response to input volleys, thereby transmitting (and to some extent integrating) ascending sensory input; 2) as oscillatory cells that fire in a collective rhythm, thereby blocking input to the cortex. Which modality appears depends or. how close the RE and TCR resting membrane potentials are to their firing thresholds. The resting potentials in turn are determined by neuromodulation from brainstem centers. This modulation does not supply information to be relayed to the cortex, but rather provides either depolarizing or hyperpolarizing influences to thalamic neurons by adjusting thalamic membrane permeabilities to ion flow. This process adjusts the firing characteristics of the TCR and RE cells, therefore establishing either the relay or oscillatory state.



Alpha spindle generation is the example best understood (Lopes da Silva, 1991). If brainstem cholinergic modulation is withdrawn from RE and TCR neurons, the oscillatory mode appears. If cholinergic modulation is increased, the relay mode appears.

If noradrenergic modulation from the locus ceruleus increases, the neuronal firing rates increase, and the signal-to-noise characteristics of the circuits are enhanced. Alpha spindle production during the transition from wakefulness to sleep is the prototypic example of brainstem modulatory control. About one second before the onset of sleep, there is a decrease in the firing rate of the cholinergic input to the thalamus. This establishes the oscillatory mode in the TRC neurons, thereby shielding the cortex from input as sleep ensues. The TCR cells transfer the alpha rhythm to the cortex which in turn generates the potentials measured on the scalp EEG.

For frequencies out of the alpha range, understanding is less complete. In a recent review, Sterman (1994) relates the generation of field potentials at scalp level to the influence on the thalamus of three integrative activities of the brain he calls 1) vigilance, 2) sensorimotor integration, and 3) cognitive integration. The vigilance system involves diffuse networks and specific centers in the brainstem and their ascending influence on thalamic, subcortical and cortical centers. The sensorimotor system involves the ascending touch and proprioceptive pathways and their projections to thalamus and on to sensorimotor cortex, and the efferents from this cortical area. This system generates the sensorimotor rhythm (SMR), the 12 to 14 Hz rhythm over the sensorimotor strip. Cognitive integration involves a range of centers that process and integrate sensory inputs and motor responses.

Sterman relates the generation of SMR, alpha, and theta rhythms to the presence or absence of input from these systems on the thalamic oscillatory generators. Specifically, the different oscillatory modes in the thalamus appear when influence of combinations from the three modalities is withdrawn from it; as noted above, the prototypic example involves initiation of alpha rhythms by the withdrawal of brainstem cholinergic activity from the thalamus. If sensorimotor inputs are withdrawn, the SMR rhythm appears. If cognitive processing is withdrawn (as in relaxed states without cognitive activity), alpha appears. If vigilance is withdrawn (as in states of inattentive drowsiness), theta appears. Thus the presence of these rhythms on the EEG indicates the underlying brain states of vigilance, cognitive processing, and sensorimotor integration. If it is assumed that attentiveness intrinsically accompanies states of SMRassociated stillness (including frequencies between 15 to 20 Hz), the connection between Sterman's scheme and what is observed in NT for ADHD becomes clear: the combination of higher activity in the beta or SMR range and lower activity in the theta range associates directly with states of increased stillness, attentiveness, and decreased drowsiness and other cognitive disturbances associated with theta activity. Sections II.5 and III will elaborate these arguments.

Sterman's synthesis leaves unspecified whether intrinsically oscillatory activity in the limbic system also contributes to the generation of cortical field potentials, perhaps by influencing or complementing thalamic activity. It would seem that there is sufficient hippocampal-cortical circuitry to allow hippocampal-generated oscillations to generate scalp-measured field potentials (see, for example, Miller, 1991), but there is little support for this in the literature. It will be assumed in what follows, therefore, that the thalamus is the main generator of scalp-level field potentials. This assumption, however, does not

affect the major premises of this paper. Since a good deal of work implicates the limbic centers in attentional processes (see reviews by Sieb, 1990, and Pribram & McGinniss, 1992), it is reassuring that Sterman's scheme is consistent with a number of observations on limbic contributions to attentional capacity (see below). To pursue matters beyond the (relatively) familiar confines of the thalamus, however, further details about neuromodulation and about the gating function of oscillatory states will be needed.

2. Neuromodulator Control

If NT is to make effective and lasting changes in neural circuitry mediating attentional functions, those circuits must be adjustable by feedback control as well as able to maintain those adjustments over time; that is, the systems involved must be sufficiently plastic. Two mechanisms subserving such neuronal plasticity are neuromodulation and long-term potentiation. Though historically these processes were introduced in different contexts (LTP in hippocampal circuitry, neuromodulation in ascending brainstem systems), their actions are not altogether independent. For convenience, however, they will first be presented separately (here and in Section II.4). Section III then will discuss how they combine to mediate the effect of NT on the attentional circuitry.

Neurotransmission, the process by which the electrical properties of a neuron change as a result of synaptic or hormonal stimulation, can be separated into two sub-types: fast acting neurotransmission proper (usually involving fast Na+ and Cl- channels), and neuromodulation (usually involving slower K+ and Ca++ channels). In neuromodulation, the adjusted ionic flows act to change the membrane potential on the post-synaptic neuron such that firing characteristics are changed. Acetylcholine or noradrenergic alpha-1 receptors, for example, act by closing K+ channels, thereby raising membrane potentials. In this way, firing rates of individual neurons can be adjusted, and the group characteristics of neuronal circuits can be changed (state changes). Another mechanism of neuromodulation is the flow of Ca++ into cells; this influx can change membrane potentials directly as well as precipitate intracellular chemical and structural changes so that the firing characteristics of the post-synaptic neurons are changed.

Neuromodulation is best understood in the ascending modulator control from the brainstem. There are four major brainstem systems: the locus ceruleus (noradrenergic), the nucleus basalis and surrounding areas (cholinergic), the raphe nuclei (serotonergic), and the central tegmental area and substantia nigra (dopaminergic). These centers respond to incoming stimuli and discharge to higher centers; they react to global aspects of incoming stimuli, like novelty or intensity (Derryberry & Tucker, 1990). Noradrenergic discharge from the locus ceruleus, for example, follows the perception of unexpected, intense, or aversive stimuli - situations requiring rapid attention and response. Higher centers are thereby adjusted to suppress extraneous activity and to attend to the aversive stimuli while ignoring others. The dopaminergic system responds to a range of motivationally arousing cues, thereby facilitating activity in higher centers during stressful encounters. It facilitates a number of prepackaged motoric responses that are useful in situations requiring a "flight or fight" response. Thus the dopaminergic and noradrenergic centers respond to cues relevant to functions impaired in ADHD. This

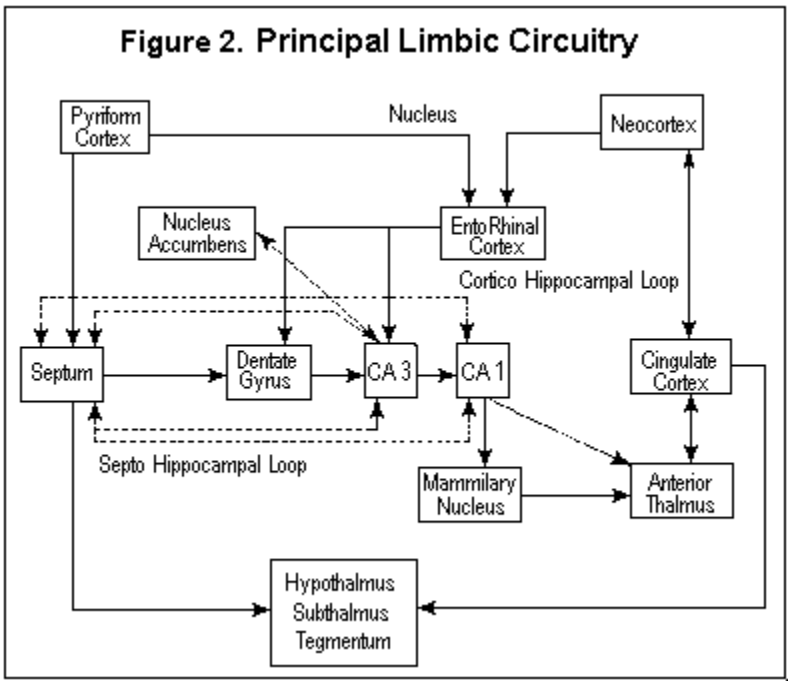
circumstance is consistent with the effectiveness of noradrenergic and dopaminergic agents for ADHD.

Neuromodulation is central to the mechanisms subserving NT. Ascending brainstem modulation of thalamic and limbic centers affect switches between states, rates of group oscillations, and other changes in (mainly thalamic and limbic) circuitry necessary to optimize attentional capacity. At the same time, limbic centers exert neuromodulatory control over several centers (Derryberry & Tucker, 1990; Isaacson, 1980).

3. Rhythmic Oscillations, Brain States, and Information Flow

Section 1 introduced the idea of relay and oscillatory states of the thalamic centers. The change to the oscillatory state from the relay state can also be described as the closing of a gate that blocks information flow (or as the opening of a switch, to use a circuit analogy). The switching of brain centers between different states, and the gating of the information flow are two important functions of oscillatory activity (a third, resonance, will be discussed in Section III).

A similar, if more complex, set of circumstances appears in the limbic centers. As will be detailed in Section III, these centers contribute significantly to attentional processes; thus, details of the gatings and state changes effected by oscillators in the limbic system will be discussed here in some detail. Figure 2 shows the main limbic oscillatory generators and pathways. The septal nuclei and hippocampus comprise the main pacemakers of the system, though cells in the dentate and entorhinal cortices also generate oscillatory modes (Bland & Colom, 1993). Ascending brainstem modulation projects to pacemakers in the septal nuclei and, to a lesser extent, to those in the hippocampus directly. The major circuitry in this area involves the septalhippocampalseptal loops and the trisynaptic circuit from entorhinal cortex to dentate through the hippocampus, and back to the entorhinal cortex (see Figure 2). There are three main patterns of hippocampal field potentials: 1) theta or RSA (rhythmic slow activity), between 3 and 11 Hz (depending on species); 2) LIA (large amplitude irregular activity) in a broad range between 0.5 and 25 Hz; 3) beta, fast waves between 20 and 60 Hz. Rhythmic inputs can entrain oscillations in the hippocampus across a range of frequencies. There are (at least) two neurotransmitter systems in the septal innervation of the hippocampus: cholinergic and GAGA-ergic. The balance between these inputs, themselves under brainstem modulation, determines whether LIA or RSA predominate in the hippocampal field potentials (Bland & Colom, 1993).



A study of these rhythms across a range of animal species shows that each rhythm can be correlated with particular behavioral states, each of which relates to attentional processes. In comparing the species studied (including man), a pattern emerges that helps elucidate the role of the limbic centers in attentional processes. In a number of species RSA appears during activities of particular survival value for (and therefore characteristic of) each species, and in the memory storage of what was learned during those activities (Winson, 1972, 1990; Miller, 1991). In the rat, for example, RSA occurs with exploratory behavior; in the rabbit, in active scanning of the environment; and in the cat, in stalking behavior. The behavioral correlates across species of LIA is less well documented, though for a range of species, studies have connected it to the maintenance of immobile posture (Vanderwolf, 1992). This finding is reminiscent of Sterman's finding that a 12 to 14 Hz rhythm over the sensorimotor cortex of the cat was correlated with immobile vigilance, and that this rhythm could be produced by the cat during operant conditioning experiments (Wyrwicka & Sterman, 1968; Sterman, Wyrwicka, & Roth, 1969). The higher frequency beta components have been correlated with focused attention in a number of species.

In addition to survival-related activity, animal studies have defined broad classes of behavior that correlate to both RSA and LIA. For example, in the rat, so-called type 1 behavior (motor acts like walking, jumping, swimming) is correlated to RSA; type 2 behavior (waking immobility along with patterns of licking, chattering the teeth, grooming) is correlated with LIA (Vanderwolf, 1992). Experimental limitations make the extrapolation of animal studies to man difficult; extension of animal results to man must be done cautiously (for some time even the existence of human hippocampal theta was questioned). A few studies, however, are available; these have taken advantage of unusual clinical opportunities to study human hippocampal EEG directly. They do seem to establish both the existence of hippocampal theta as well as the correlation of specific

behavioral states with specific rhythms - thereby suggesting that the relationship in lower animals between specific rhythms, behavioral patterns, and gatings of information flow also apply to man (Meador et al, 1992; Arnolds et al, 1980). The behaviors involved are more subtle than those with other animals; changes in rhythm relate less to motor activity and more to verbal behavior.

It appears, then, that frequencies in both theta and beta ranges exist in human hippocampal circuitry, and relate to state changes and gatings of information in the same way as does the thalamic circuitry, further, they follow the same general pattern of correlation to behavioral states as with the lower animals. The extrapolation from thalamic to hippocampal studies is therefore more reliable -as is the extrapolation from patterns in lower animals to man. This circumstance will be useful to a discussion of human attentional capacity in Section III.

4. Long Term Potentiation

As noted above, it is important clinically that data is emerging to suggest ongoing remission of ADD symptoms after discontinuation of neurofeedback treatment. In terms of what has been presented, it is likely that the marked plasticity of neurons in the limbic system contributes to this circumstance; specifically, these neurons respond to repetitive afferent signals by increasing the efficacy of their synapses in rapid and long-lasting fashion. This process is called long-term potentiation (LTP), and has been studied intensively during the last two decades (see reviews by Bliss & Lynch, 1988; Lynch et al, 1990, Doyere et al, 1993; Massicotte & Baudry, 1991; and Teyler & DiScenna, 1987). LTP is defined formally in terms of laboratory measurements; it is a stable and relatively long-lasting increase of synaptic response to a constant afferent volley following brief high-frequency stimulation of the same afferents (Teyler, 1989). The relationships between tetanic stimulation by implanted electrodes, LTP, and conditioning have been established as follows. LTP is observed in conjunction with behavioral conditioning in the absence of tetanic stimulation by implanted electrodes (Thompson et al, 1983; Weisz et al, 1984; Laroche & Bloch, 1982; Ruthrich et al, 1989). The reverse is also true: that is, hippocampal LTP, induced by high-frequency stimulation of the perforant pathway, can lead to an increased rate at which animals learn in subsequent classical conditioning experiments (Berger, 1984). Further, electrical stimulation of the midbrain reticular formation enhances LTP at perforant path synapses, prolongs its duration (Bloch & Laroche, 1985), and facilitates behaviora1 conditioning (Bergis, Bloch, & Laroche, 1990; Bloch & Laroche, 1981; Laroche, Falcou, & Bloch, 1983).

LTP was first studied in the trisynaptic circuit of the hippocampus (Bliss & Lome, 1973; Bliss & Garner-Medina, 1973). Within the limbic system, the effect of LTP is optimized when the frequency of incoming volleys is within the RSA range (Larson & Lynch, 1986; Larson, Wong, & Lynch, 1985)-a reassuring result in light of the central role of RSA in limbic processing. Since these early studies in the limbic system, LTP has been studied extensively in the neocortex (Tsumoto, 1990). A comparison of hippocampal and neocortical LTP (Teyler, 1989) shows differing magnitudes, temporal and developmental aspects, numbers of afferent pathways required, and possibly receptor types; nonetheless,

the process is basically the same in all areas - increased synaptic efficacy by repeated afferent stimulation, whether by electrode or rehearsal. It is found in the cat, for example, that for motor cortex LTP to occur, afferent stimulation from both the VL thalamus and the sensory cortex is required (Iriki et al, 1989). In these processes, LTP does not occur in the thalamus itself (Lee & Ebner, 1992); presumably, this stability preserves its capacity as an unchanging relay and gating station. For each area (neocortical or limbic), LTP has a characteristic time course during development. In the auditory and visual cortex, for example, there are early critical periods during which LTP is at a maximum (Tsumoto, 1990); following this, there is a significant diminution of potentiation throughout life. There is a corresponding process of long-term depression (LTD), in which synaptic strengths are diminished by repetitive afferent stimulation (Tsumoto, 1990); presumably LI'D, by adjusting synaptic efficacies down rather than up, complements the role of LTP in the development of plasticity in neuronal circuitry.

Recent reviews of neuronal plasticity and LTP suggest a number of component processes (Wolff et al, 1995; Weiler et al, 1995; Voronin, 1995). These include changes in the arrangement of synapses, in the size of synapses, in the numbers of so-called concave and spinule synapses (that increase synaptic efficiency), as well as in synapse formation and elimination. Work has shown (summarized in Wolff et al, 1995) that there is continuous turnover of synapses throughout life. This turnover includes changes in the number of synaptic junctions per axon terminal, and in the branching patterns of dendrites and terminal axons. The changes occur on the order of days to weeks. In some cases, the remodeling and elimination of synapses can lead to irreversible modification of networks (this corresponds to the concept of attractor states mentioned earlier).

LTP in the prefrontal cortex is of particular relevance to ADHD and its treatment. A number of studies (reviewed in Doyere et al, 1993) find that in behaving animals, electrical stimulation mimicking short bursts of action potentials at hippocampal sites induce LTP in the prefrontal cortex. In one study (Laroche et al, 1990) facilitation by paired pulses stimulating the CA1/subicular hippocampal field was effective in inducing LTP in the prefrontal cortex. Interpulse intervals between 40 and 200 ms (corresponding to 5 to 25 Hz) were effective; the range from 80 to 200 ms (5 to 12.5 Hz) was optimal. Thus, hippocampal stimulation in the range of both RSA and LIA induce LTP changes in the prefrontal cortex. Later, Doyere's group (1993) found that short high frequency bursts at 7.7 Hz induced LTP in prefrontal cortex, though only for one day. The same group measured the prefrontal cortex response in rats by stimulation of the CAl/subicular area before and after a classical conditioning experiment. Rats subjected to a paired conditioning paradigm showed a LTP response in prefrontal cortex to the stimulation, whereas pseudoconditioned rats showed a depression of postsynaptic potentiation of prefrontal responses.

The role of LTP in the neural mediation of NT assumes added clinical relevance in light of recent work (Wilson & McNaughton, 1994) showing that networks of hippocampal cells, correlated in their firing patterns during the learning of spatial behavioral tasks, are reactivated during slow wave sleep (SWS) with the same correlation patterns. Further, the hippocampal activity during SWS has been found to activate areas in the entorhinal

cortex (Chrobak & Buzsaki, in press); presumably the hippocampus is programming into cortical circuitry what was learned during the day. It has also been reported recently that perceptual tasks similar to those used to measure attentional capacity (and to diagnose ADHD) are found to be consolidated during REM sleep (Karni et al, 1994); hippocampal or cortical field potentials were not measured in this study, but the parallels to the Wilson and McNaughton study are compelling.

The above findings add support to the suggestion that the hippocampus can induce LTP in networks of cortical neurons in such a way that the cortical networks code information already processed in the hippocampus; in the example of Wilson and McNaughton, this involves learned motor behavior (cf. Miller, 1991). As detailed by Winson (1972, 1990), this process is mediated by the theta rhythm. Miller (1991) has calculated that this process involves transit times from hippocampus to neocortex to hippocampus on the order of 200 ms (corresponding to 5 Hz), thereby supporting a resonance at the theta frequency between the two sets of networks. This process, resonance, the facilitation of information exchange between brain centers resonating at the same frequency, is the third physiological function of group oscillations relevant to the present work (Lopes da Silva, 1991, 1992).

Though the time courses are different (LTP is a long-term change in synaptic efficacy, whereas neuromodulation is a short-term modulation of synapatic efficacy), neuromodulation and LTP are related both biochemically and functionally. Each process represents the influence of one neurotransmitter system on another, thereby allowing increased flexibility of synaptic activity. In the Schaffer/commisural synapses in CA1 (Lynch et al, 1990), for example, LTP involves two types of glutamate receptor (NMDA and AMPA); the NMDA receptor induces LTP by activating an inward CA++ current, thereby precipitating a number of chemical changes that modify the activity of AMPA receptors. These express the LTP effect. This can be compared to the neuromodulatory effect in the rat CA1 region (Brinton, 1990), for example, in which vasopressin acts as a neuromodulator for the noradrenergic receptor by effecting a Ca++ flow into the cell; the NE induced level cAMP (the second messenger in the NE system) is thus enhanced. In the mossy fiber-to-CA3 neurons (in guinea pig), Fisher and Johnston (1990) found that norepinephrine and acetylcholine affect LTP differently, with norepinephrine increasing it and acetylcholine decreasing it. Thus, changes in a range of neuromodulators from any one center can make a number of adjustments in a range of synaptic activity in other centers, thereby adding flexibility to the systems involved.

III. Neural Mechanisms Underlying Attention and NT

1. Anatomical Aspects

As noted above, Sterman's synthesis of the centers and processes subserving field potential generation in the context of attentional processes emphasizes the centrality of the brainstem-thalamic-cortical system. In addition, his conceptual organization of the systems of vigilance, sensorimotor integration, and cognitive processing influencing this axis provides a framework for filling in further details. In particular, a good deal of research suggests that the prefrontal cortex and several centers in the limbic system

should be included in any outline of attentional processes. In addition, clinical experience shows that the mood disorders, involving disturbances in limbic functioning, typically involve disturbances of attention and concentration (decreases capacity for each in depression, hyper-distractibility in mania), while attentional disorders, involving disturbances in prefrontal cortex functioning, typically involve depressed mood; both involve difficulties with memory, a function mediated through limbic centers. Further, animal studies of both prefrontal and hippocampal lesions reveal symptoms reminiscent of ADHD in humans (Pribram & McGuinness, 1992; Crowne & Riddell, 1969; Douglas & Pribram, 1969; Lopes da Silva, Witter, Boeijinga, & Lohner, 1990): hyperactivity, distractibility, and a tendency toward preoccupation with certain activities that verges on pathological undistractibility-distractibility (reminiscent of ADHD children's tendency to become mesmerized by television or video games). Recent reviews (Sprict, 1995, for example) emphasize the role of the hippocampus in terms of its widespread input for all sensory modalities, its reciprocal connections with the entire association cortex, its role as an integration center for sensory fields, as a center for comparing input with stored data, and, as such, a center to filter out irrelevant (that is, distracting) stimuli that might lead to maladaptive arousal responses.

A review and integration of attentional processes by Sieb (1990) suggests a way to include these regions within Sterman's framework. Sieb suggests that as sensory input reaches the brainstem, it processes and transmits these signals to the thalamus, and activates other centers, particularly septal nuclei, hippocampus, and frontal cortex. The hippocampus then orchestrates several components of the attentional process by selectively inhibiting a number of functions at a number of centers; these include orientation, alertness, awareness, and arousal. This orchestration facilitates the focusing of attention on only one set of environmental signals. By 300 ms after the initial stimulus, inputs from brainstem, mediodorsal thalamus, and several cortical centers converge on the prefrontal cortex. This area, in turn, processes the input and organizes a response to it. The response includes a major signal to the septal nuclei (which Sieb relates to the P300 evoked potential wave); this signal induces the hippocampus in turn to release its earlier inhibition of the several functions mentioned above. Thus for Sieb, the prefrontal-septal-hippocampal axis is a major linchpin of the attentional process. Further, he suggests that the initial inhibitory action of the hippocampus is mediated by an oscillation in the theta range, and that the prefrontal signal to the septal nuclei induces a beta rhythm in the hippocampus which blocks the theta inhibiting signal. The suggestion that the hippocampus and prefrontal cortex exert selective inhibitory actions on a number of centers presumably corresponds to the withdrawal of combinations of cognitive processing and vigilance functions in Sterman's scheme; these withdrawals acting to generate oscillatory thalamic modes. However accurate in its details, or however consistent it is with Sterman's scheme, Sieb's concept of pairs of balanced processes (theta vs. beta oscillations, hippocampal inhibition vs. activation) introduces an important view of attentional processes that will appear repeatedly throughout this discussion.

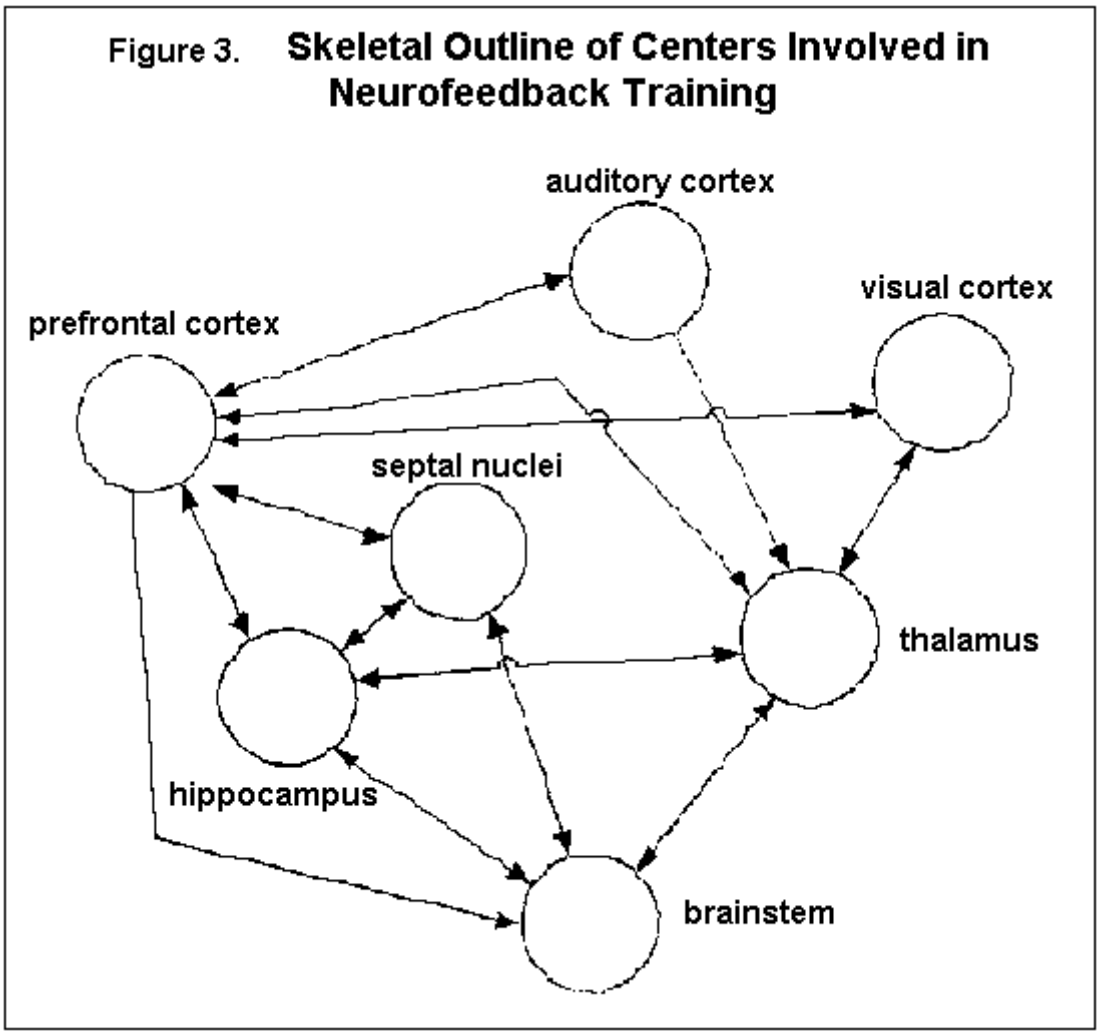


Figure 3 represents a skeletal outline of the processes suggested by Sterman and Sieb. The characteristics of the circuitry shown that are most relevant to NT are its levels of adjustability and of stability. The adjustability is provided by the collaborating mechanisms of neuromodulation and LTP that operate at each juncture in the network. It is well known, for example, that brainstem centers neuromodulate thalamic centers (Lopes da Silva, 1990; Sterman, 1994), and can induce LTP in the hippocampus (Doyere et al, 1990). Stimulation in the hippocampus, in turn, has been shown to induce LTP in prefrontal cortex (Laroche et al, 1990; Doyere et al, 1993). Further, hippocampal and other limbic centers can neuromodulate centers in the brainstem (Derryberry & Tucker, 1990). LTP has been shown in motor neurons stimulated simultaneously by thalamic and sensory cortical neurons (Iriki et al, 1989), motor cortex stimulated by polysynaptic cortical stimulation (Sutor & Hablitz, 1989), and sensory cortex stimulated by VM thalamus (Lee & Ebner, 1992). Finally, stimulation in basal forebrain can induce cortical LTP (Lee & Ebuer, 1992).

The stability of the attentional system adjusted by neurofeedback is of central importance clinically, but a thorny problem theoretically. If the system is in a stable attractor state, small imbalances at any point in the system will tend to be damped out by the functioning

of the system as a whole. If it is not in such a state, small imbalances at any juncture will be maintained or amplified. The next sections suggest that NT adjusts the attentional system into a stable attractor state through the action of its multiple self-adjusting feedback loops.

2. Balances in the Attentional System - A Hypothesis

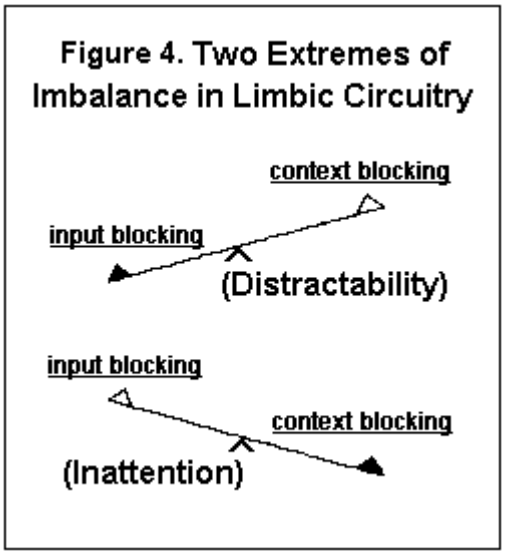
As noted above, the motif of pairs of balanced functions recurs repeatedly in observations and conceptualizations of the attentional system. Studies in the rabbit (Krnjevic, Robert, & Casullo, 1988; Brazhnik et al, 1993; Vinogradova et al, 1993a, 1993b, 1993c), for example, suggest a balance between the GABA-ergic and cholinergic septal-hippocampal signals. The GABA-ergic signal is more immediate, and seems to "reset" the hippocampal circuitry before processing a new set of input. The cholinergic signal is slower in onset, and serves to filter out cortical input of information coded during earlier signals. When performing correctly, these operations lock the hippocampal circuitry onto only one set of inputs at a time, thereby facilitating selective attention to only one set. In similar manner, a number of anatomical and functional balances have been suggested for the prefrontal cortex (reviewed in Fuster, 1989). In primates this area is composed of two general regions: dorsolateral, and ventromedial. These differ phylogenetically, ontogenetically, in their pattern of connections with other brain centers, and in their roles in attentional processes. In man, for example, dorsolateral lesions lead to a decreased awareness of the environment, whereas ventromedial lesions lead to hyperactivity and distractibility (that is, increased and indiscriminate attention to the environment).

Pribram and McGuinness (1992) discuss a pair of attention-related functions (and centers that subserve them) that will be useful in considering the relationship between hippocampal and cortical field potentials. Their discussion is based on earlier work in the cat (Macadar, Chalupa, & Lindsley, 1974; Lindsley & Wilson, 1976) that identified two systems of neurons affecting theta synchronization and desynchronization in the hippocampus. Madacar et al. locate these systems in the brain stem. One is medial, producing desynchronization of hippocampal theta (presumably leaving LIA and beta); the other is lateral, and produces synchronized hippocampal theta. These authors associate the first system (which synchronizes theta) with exploration of more or less familiar territory, and the second (which desynchronizes theta) with generalized orienting with immobility when food is encountered. These observations correspond to the behavioral correlates of hippocampal RSA and LIA presented in Section II. 3. These studies found that, to a good approximation, when the first system synchronizes theta in the hippocampus, it desynchronizes theta in the cortex, and vice versa for the second system This circumstance will be useful below for interpreting theta/beta ratios in scalp level field potentials.

This extended dialectic of paired functions and processes leads to an integrative hypothesis: that imbalances in one or more of these pairs can lead to deficits in attentional capacity (including ADHD). These imbalances can be in the timing of signals, intensity of potentials, amplitude of frequency components, balances between neuromodulator inputs, and so on. The suggestion is that in attention-disordered patients

there are a number of possible imbalances between the myriad signals and counter-signals, processes and counter-processes, that amount to a coarseness or imbalance in the "tuning" of the circuitry, this coarseness of control causes an attentional disorder marked by excessive attention to either external or internal stimuli, or both. This hypothesis can be correlated with clinical experience in several ways.

Since the centers shown in Figure 3 are so densely interconnected, any imbalance at any one center or in any one connection can lead to imbalances in the system as a whole. Because of the central role of the septal-hippocampal inputs, however, a consideration of imbalances in that system, whether primary or as a result of its connections to other centers, is particularly useful in extending the above hypothesis to clinical experience. Specifically, the septal-to-hippocampal input determine the RSA/LIA balance of hippocampal rhythms; it, in turn, is regulated by brainstem, prefrontal, and hippocampal afferents. Consequently, imbalances in any of these centers can lead to imbalances in the septal signal. From the suggestions of Vinogradova's group (that the cholinergic/GABA-ergic balance determines the balance between hippocampal resetting and cortical input blocking), an imbalance in this system can be correlated directly with one of the seminal characteristics of ADHD in the following way. A too early cutoff of the hippocampus from cortical input (the cholinergic function) makes it lock onto subsequent inputs without connecting them to prior input and trains of thought. This corresponds to a too selective attention to each input without adequate integration into the background context of observation and thought; in other words, it leads to distractibility. On the other hand, the reverse circumstance, too much blocking of inputs with respect to blocking of prior contexts (the GABA-ergic function) leads to a general inattention to inputs-clinically represented by the daydreaming or generally inattentive behavior characteristic of ADHD children, including becoming "lost" to the environment when watching television or playing computer games. Figure 4 schematizes the two clinical patterns.



[This model also raises the possibility that psychotic or autistic states may represent an especially exaggerated instance of an (input)/(internal context) imbalance; it is of interest, therefore, that during acute psychotic episodes, patients do show ADHD like profiles in

the power spectral analyses of their evoked potential signals; this pattern resolves with the resolution of the psychosis (Koukkou, 1980).]

3. A Synthesis of Neural Processes in NT

Earlier an analogy was suggested between a child learning to ride a bicycle and learning to move an object on a display screen which indexes his theta/beta ratio. When the child is given the instruction to lower the balloon, he experiences a period of internal experimentation during which signaling along various internal paths are tried until the right combinations are found to lower the balloon. During this process the prefrontal cortex monitors the level of balloon through afferents from the visual cortex, and signals the septal-hippocampal system (and possibly the brainstem and/or the thalamus directly). From the pathways shown in Figure 3, there are a number of feedback loops (from brainstem, thalamus, and hippocampus back to the prefrontal cortex, from the hippocampus back to the septum, from brainstem, thalamus back to the hippocampus, from hippocampus, thalamus, prefrontal cortex back to brainstem, and so on) available to neuromodulate the prefrontal activity, it can therefore regulate the frequency distribution of the thalamus (directly, through hippocampus, through the brainstem, or perhaps through all three and more) to produce a decreasing theta/SNR (or beta) ratio. Rehearsal of these activities during ongoing NT sessions (and possibly during slow wave sleep) can then stabilize the system through LTP.

These mechanisms show that the various centers can adjust and stabilize the capacity to adjust theta/SMR or theta/beta ratios. As noted earlier, arguments extending this to the capacity to regulate the attentional process range from the concrete observation that low theta/beta ratios correlate with good attentional capacity, to a number of inferences and extrapolations from clinical and neurophysiological studies of animals and humans. Sterman's work with the SMR rhythm, for example, provides a rather direct correlation between a specific EEG rhythm and the attentional processes involved in motionless vigilance. More specifically, the broad range of event related potential (ERP) studies illustrate that specific components of perceptual and attentional processes can be reproducibly correlated with specific EEG wave forms (see, for example, Hillyard, 1985, 1987; Oakley & Magnum, 1990). Further, the effect of attention directed to the left or right visual field can produce specific changes in ERP's (in strikingly asymmetrical visual evoked potentials in left or right hemisphere). The P300 wave, as another example, has been associated with activity in prefrontal/hippocampal/amygdaloid activity (Sieb, 1990; Hillyard, 1985), and has been found during brain surgery in humans to relate to activity in hippocampus and amygdala (Halgren et al., 1980).

The findings presented in section II.3 of consistent correlation across species (including man) of hippocampal rhythms with specific components of attentional processes (RSA with active explorations, LIA with immobile attention) reinforce these arguments, and help guide interpretations of specific rhythms in humans. These results lead one to associate theta mediated activities with a general attentiveness to the environment, and LIA with those subserving immobility. This general scheme is supported by the speculation that the 4 to 7Hz frequency range of RSA corresponds to the sniffing and

whisking rates first evolved in lower mammals (and supposedly conserved through mammalian evolution); studies in the rat and hamster (Macrides, 1975; Macrides et al., 1982) have found that hippocampal RSA tends to be phase and frequency locked to theta range sniffing and whisking activity in the animals. At first glance it seems paradoxical, however, that cortical theta activity should correlate inversely with the adequacy of a process associated with increased attentiveness. It is possible, however, that the reciproca1 activation of hippocampal RSA and cortical theta (mediated by basal brainstem activity discussed by Macadar et al, 1974) indicates that decreased cortical theta actually measures increased RSA activity in the limbic circuits. If true, this circumstance argues against direct hippocampally generated cortical theta activity.

IV. Relevance to Psychiatric Disorders

1. Clinical Findings

The original stimulus for this work was the reported efficacy of both NT and medication for both mood and attentional disorders, as well as the observation that NT often lowers the levels of medication required to treat ADHD and depression. Recent electroencephalographic research on these and other psychiatric disorders suggests that a range of psychiatric disorders should respond to some form of NT, and in fact clinical experience confirms this. This work includes power spectrum analysis (PSA) patterns reported for schizophrenia (S. Schneider & Pope, 1992), ADHD (Mann et al., 1991), alcoholism (Peniston & Kulkosky, 1990), and PTSD (Peniston et al., 1993). It also includes double stimulus experiments with depressives which have found specific patterns in cortical slow potentials (CSPs), which are slowly changing negative DC changes in scalp field potentials with anticipation of motor or cognitive tasks (F. Schneider, 1992a), alcoholics (F. Schneider, 1993), and schizophrenics (F. Schneider, 1992b). Normal controls, as well as depressed and schizophrenic patients appear to regulate their PSA's and CSP patterns differently. Depressed patients can be trained to normalize their CSP's, but schizophrenics cannot (F. Schneider et al., 1992; F. Schneider et al., 1992). Both normal controls and schizophrenics can change their PSA's, but controls can maintain the changes between NT sessions, whereas schizophrenics cannot (S. Schneider & Pope, 1982).

Beyond these results, a number of clinical observations raise the possibility that gating, switching, and resonance phenomena may be involved in the etiology of mood and psychotic disorders. The case is clearest with the mood disorders. Patients who respond to antidepressant medication, for example, often report feeling more "bulletproof"; that is, after recovery, they feel emotional pain from losses, reproaches, or humiliations much less intensely. Their descriptions are reminiscent of patients treated with opiates: they still perceive the pain, but don't seem to care about it anymore. One can imagine that with recovery from depression, information flow in limbic circuitry is rerouted such that input to certain "psychic pain" centers (analogous to thalamic and cortical centers for the experience of physical pain) is rerouted by oscillatory gating. Alternatively, the states of such centers may be adjusted to be less receptive or less fragile. One can also imagine oscillatory frequency changes such that resonances between areas are facilitated or suppressed. Further, the mysterious switches between manic and depressed states may

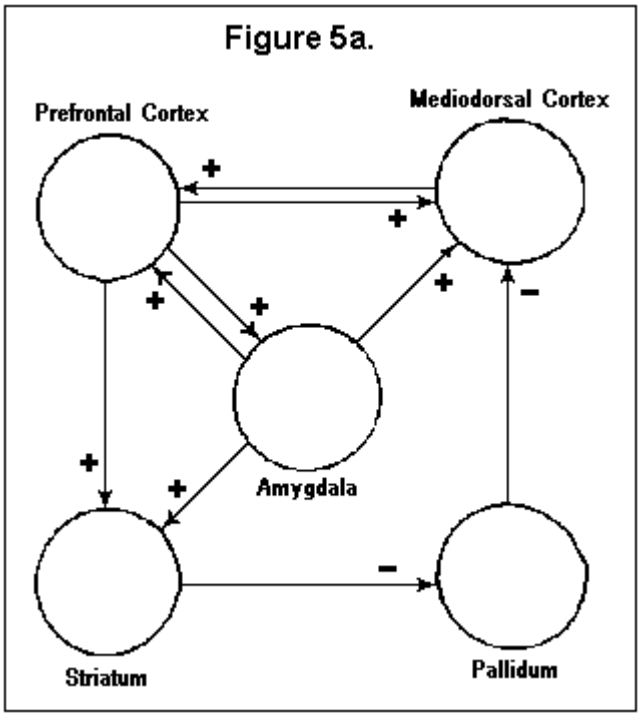
involve oscillatory switching controlled by ascending or descending neuromodulation that initiate switches or gatings that cause state changes in relevant brain centers. One must wonder, too, whether the antimanic effects of anticonvulsants like carbamazepine, valproic acid, and clonazepam are related to these neurophysiological processes (Kaplan & Buggino, 1989). Electroconvulsive treatment (ECT), for example, relies on the induction of seizure activity for a critical amount of time (Wiener, 1989); it may be that, in the same way that theta frequency optimizes LTP in limbic circuits, the seizure oscillations affect limbic pathology in such a way as to change states, reroute information, and so on. The new psychotherapy technique of eye movement desensitization training (Shapiro, 1991) in which rapidly alternating lateral gaze changes seem to mobilize affect-laden memories, may involve similar mechanisms; in fact, since the pontine gaze centers project strongly to the septal nuclei, it may be that the oscillatory signals from the repetitive gaze alternation induce changes in septal-hippocarnpal activity, thereby remobilizing memories previously phase or frequency locked out of consciousness.

2. Major Psychiatric Disorders as Generalized Attentional Disorders: Circuit Theories

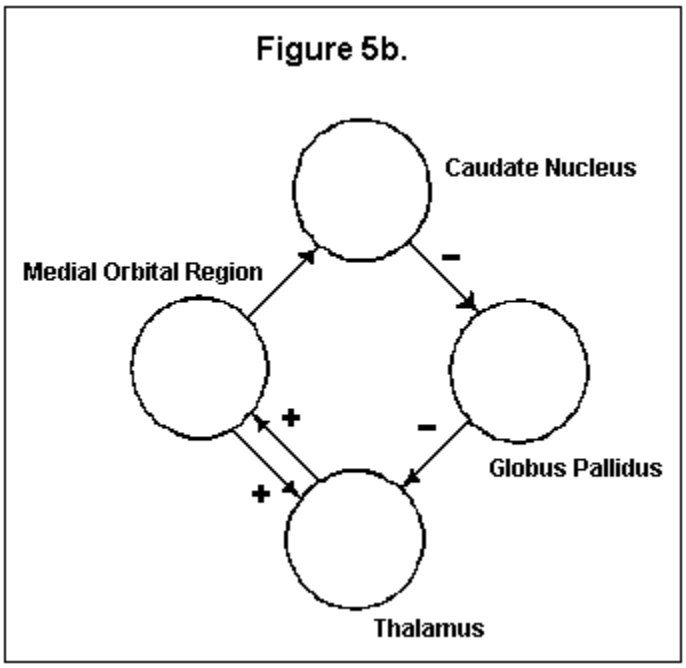
A number of recent studies as well as the theoretical constructions based on them are beginning to support such clinical speculation. Recent regional blood flow studies for depression (Drevets et al., 1992; Drevets & Raichle, 1992), OCD (Baxter, 1994), and schizophrenia (M. Carlsson & A. Carlsson, 1990a, 1990b) when combined with several decades of neurophysiological study, do suggest the existence of sets of balanced circuits (themselves regulated by balances of neuromodulators) in similar fashion as those suggested here for ADD. Work as early as 1937 (Papez, 1937) proposed that reverberations through the limbic system were responsible for generating emotional activity. Drevets proposed, based on PET scan regional blood flow studies with depressed patients, that abnormal activity in a pair of circuits was responsible for the symptoms of depression. The blood flow studies found that actively depressed patients, not depression prone individuals not currently depressed, had increased blood flow in the left prefrontal cortical areas (specifically, an area extending from the left ventrolateral prefrontal cortex onto the medial prefrontal cortical surface); this suggests that increased prefrontal blood flow is a state marker--present, that is, only with active depression. The left amygdala had increased blood flow in depressives whether or not they were actively depressed (though the differences from control were significant only in the actively depressed group). The data suggests, then, that the increased left amygdala blood flow was a trait marker--its presence indicating a depressive disorder, whether or not it is active. In addition, there is increased blood flow in the mediodorsal thalamus, decreased flow in the left medial caudate nucleus, and other changes in a number of related areas.

Combining these findings with other neurophysiological data, Drevets and his coworkers suggest that abnormal functioning in the pair of interacting circuits shown in Figure 5a. Specifically, they suggest that the prefrontal-amygdala-medial dorsal thalamic circuitry in depressed patients is overactive, and that this generates a number of symptoms of depression. These would include the perseverative negative ruminations, the ongoing and

repetitive negative self-evaluations, and so on. Further they suggest that in depressives the amygdala-striatal-pallidal-medial dorsal thalamic circuitry, normally inhibitory to the PAM circuit, is underactive, thereby disinhibiting the first circuit. They suggest that neuromodulation with dopamine, norepinephrine, and serotonin adjusts these circuits, and that antidepressant medication, by normalizing these systems, can restore normal function to the interlocking systems.

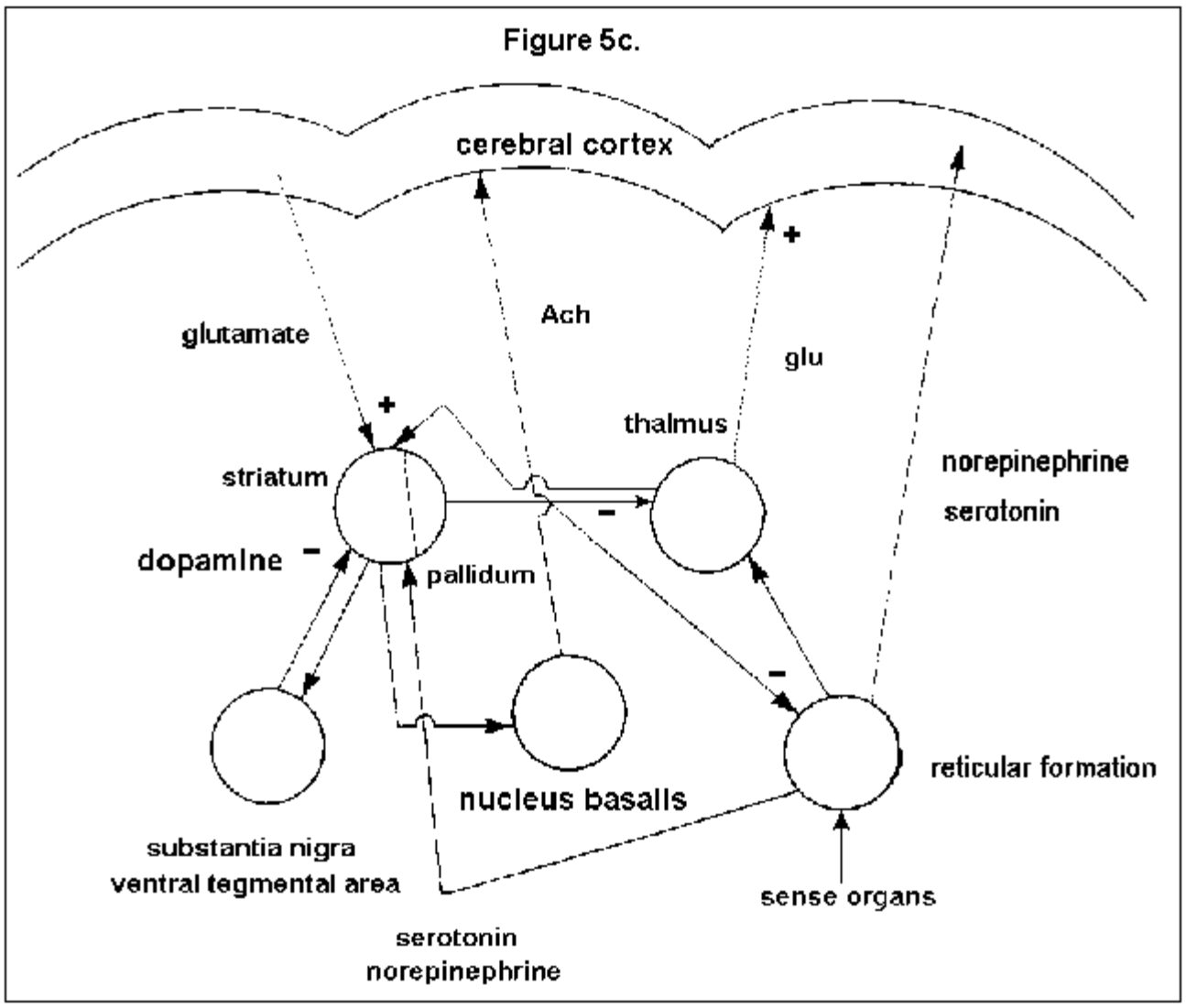


The active depressive state is postulated to involve self-sustaining activity in the prefrontal cortex-amygdala-mediodorsal thalamic circuit. Ordinarily the inhibitory influence from the pallidum to the thalamus suppresses overactivity in the circuit.



In the symptomatic obsessive-compulsive state, orbital frontal cortical input to the caudate drives proposed OCD-related circuits in the caudate. This increases inhibitory output to the globus pallidum, reducing its inhibition of thalamic activity. Thus, the prefrontal input is unsuppressed, and self-sustaining circuit loops result. If the orbital input is blocked to the caudate, there is less inhibitory effect on it, and therefore more inhibitory input to the thalamus; thus the circuits do not became self-sustaining.

Recent regional blood flow studies show similar finding for obsessive-compulsive disorder, in this case with changes mainly in the orbital prefrontal cortex and the caudate nucleus (Baxter, 1994). Baxter suggests that inadequate sensory information gating allowing self-sustaining loops (see Figure 5b). He suggests that overactivity in the loop drives prepackaged behavioral routines. He suggests further that the orbital cortex, in conjunction with neostriatal and thalamic centers, normally helps animals modulate these behavioral packages in responses to specific stimuli. He argues that the circuitry normally mediates the balance between potential distractibility and the engagement of these behaviors, that is, hypo- and hyper-distractibility from such balances.



The Carlssons suggest that the cortico-striatal-thalamo-cortical loops modulate cortical input from the thalamus. If, however, inhibitory dopaminergic input to the striatum decreases its inhibitory influence on the thalamus, the thalamo-cortical activity is unmodulated and can increase to the point of flooding the cortex. This flooding is postulated to lead to the cognitive disorganization found in the active schizophrenic state.

Figure 5c illustrates the 1990 suggestion by Maria and Arvid Carlsson about schizophrenia. They propose that two circuits function abnormally in schizophrenia, and that the balance of dopamine, glutamate, and GABA regulate their activity. The relevance of these circuits to schizophrenia, they suggest, is that they modulate thalamo-cortical signaling, with inadequate modulation of these pathways, the schizophrenic is flooded with incoming information. This process has been associated for many years with the cognitive experience of the schizophrenic. The Carlssons offer it as an explanation of the activity of dopaminergic antagonist medication. Specifically, they suggest that it is the cortical-striatal-thalamo-cortical feedback loop that protects the cortex from the overload of thalamic input. In this circuit glutamatergic cortico-striatal neurons are excitatory, GABA striato-thalamic neurons are inhibitory, and glutamate/aspartate thalamo-cortical

neurons are excitatory. Conversely, they suggest that the mesostriatal dopaminergic pathways act in the opposite direction, widening the thalamo-cortical filter and increasing information flow to the cortex. Based on these considerations, the Carlssons suggest that glutaminergic agonists might be useful supplements for treating schizophrenia, and that glutaminergic antagonists might be useful for treating Parkinson's disease.

For each of these disorders, then, it has been suggested that imbalances in sets of circuits result in psychopathology. Each of the diagrams in Figure 5 can be compared to the scheme suggested for ADD. In each case one can suggest intuitive connections between the malfunctioning of the circuits and the clinical symptoms. In schizophrenia the patient's experience of overwhelming censorial flooding is the result of an inadequate modulation by the basal ganglia centers of the thalamocortical signals. For depression and OCD, the overactive circuits represent autonomous and exaggerated activity of prefrontal or basa1 ganglia circuits that code for negative imagery of self and the world (for depression), or of fixed behavioral or ideational circuitry (OCD). [One can visualize these circuits as mediating abstract mental operations that have developed from more concrete motor functions (in the Piagetian sense that increasingly abstract mental functions develop from more concrete ones). Alternatively, since mental functions in neurological disorders tend to parallel the neurological symptoms (for example, mental perseveration in Parkinson's Disease as a parallel to bradykinesia), the symptoms of depression or OCD can be seen as the psychological parallels of certain childhood motoric activities. Specifically, one can suggest that in depression the sense of badness and the generalized inhibition are abstract parallels of the (currently disinhibited) childhood functions of turning the head away from the breast- an action that involves both inhibition (of sucking) and the judgment that it is bad (more milk causes pain). The symptoms, then, result from an overactivity (disinhibition) of the circuits mediating the more abstract (further evolved) experiences of badness or inhibition.

In general then, each of the conditions involves either the inability to attend to external input compared to inner ideas, inability to filter external inputs, or both. Thus, in the same way that it has been suggested here that neurofeedback can retune circuitry and reroute information flow in ADD, the observed efficacy of neurofeedback in OCD and depression (and perhaps at some point in schizophrenia) results from similar retuning and rerouting of neural circuitry.

V. Summary and Conclusions

This paper suggests that the effects of neurofeedback techniques can be understood in terms of well-known neurophysiological mechanisms. It is suggested that neural networks mediating attention processes can be adjusted through neuromodulation and stabilized through long term potentiation into stable (attractor) states; it is further suggested that during NT for ADHD, the patient consolidates an enhanced capacity to regulate state changes and gatings of signals between brain centers such that attentional capacity is enhanced. It is argued that this process yields long lasting results compared to stimulant medication treatment of ADHD because it employs the same sort of neuromodulatory control and LTP that with practice indelibilizes such sensorimotor skills as riding a bicycle.

Further suggestions are offered to elaborate the details of this process. A streamlined review of some neural underpinnings of the attentional process is presented in order to identify connections between the theta, SMR, and beta field potentials employed in neurofeedback for ADHD, and specific neural processes in a number of brain centers. Several schemes are offered, but it is suggested that the most likely process involves thalamic generation of theta, SMR, and beta waves under modulation from a number of cortical, limbic, and brainstem centers that regulate various checks and balances in the component functions of the attentional process; LTP then makes these changes persistent through practice NT sessions. It is suggested further that the attentional disorders represent coarseness in the limbic control of attentional processes; neuromodulation during neurofeedback work can fine tune this control, and long term potentiation over the course of treatment can make the changes permanent.

It is suggested that neurofeedback results are more persistent than those with stimulant medication because neurofeedback and stimulants may operate at different locations with different receptivity to long-term potentiation by neuromodulation. Finally, it is suggested that there is a commonality of mechanisms in ADD, OCD, depression, and schizophrenia which 1) lets us conceptualize each of these as variants of a disorder of attention, and 2) suggests a basis for the positive neurofeedback effects with ADD, OCD, and depression (and perhaps someday schizophrenia).

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