On the Integration of Objective and Subjective Components During the Schizophrenic Experience

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Introduction

The life experience has long been recognized to somehow integrate objective mechanisms which can be scientifically measured with conscious processes of which we are subjectively aware.

This was quite clearly expressed by C. Judson Herrick[1] in 1956: "Psychology is a biologic discipline, but it should be a psy-chobiology and not merely a subdivision of physiology. What we must now do is to bring together these artificially separated domains of experience, the subjective and the objective, and build a coherently integrated psychobiology."

This paper presents the conclusions and a neuro-physio-logic discussion of the paper by Drs. Miyata and Buckley, presented to the First International Congress of Psychosomatic Medicine in Guadalajara, Mexico, December, 1971.

Limbic System Responses Related to Aberrant Behavior and Subjective Awareness

A correlation of culturally aberrant feeding drive behavior has been found to be significantly correlated with an increased state of tonus of the trophotropic (parasympathetic) response system among schizophrenics in Kobe, Japan.

During the past five years Keiichi Mi-yata[2] has found not only that these autonomic and primary drive responses are abnormal among newly admitted Japanese patients but that as the patients recover and become ready for discharge both of these responses improve until the findings cannot be distinguished from the normal population.

Since primary drive behavior in humans is accompanied by a sense of subjective awareness and intention we have found a way to begin the integration of the subjective and the objective domains of experience which Judson Herrick proposed as being essential for the development of a "coherently integrated psychobiology."

These findings focus attention upon limbic system centers and circuits which extensively influence the way the autonomic system affects the "tuning" or equilibrium of the central nervous system. The hypothalamus has been called the "hub of the limbic system"[3] and activity here not only influences limbic system circuits but also affects ascending pathways to the neocortex and descending circuits of the autonomic system.

Some of the extensive studies of Jose Delgado and Jules Masserman shall be reviewed in order to place emphasis upon limbic system responses and their relation to aberrant behavior and subjective awareness.

Stereotactic Stimulation of Limbic System Centers

The studies of Jose Delgado[4] and associates at Yale in the past 20 years have focused attention upon behavioral and social responses which can be activated by stereotactic stimulation of limbic system centers which influence primary drive behavior. This is most pertinently illustrated in his account of the defensive-aggressive behavior of a female monkey, "Lina," in three different monkey colonies where she had quite different social status.

A stereotactic electrode had been implanted in the posterolateral nucleus of her thalamus. When this center was activated in social situations (by a subcutaneous radio receiver) a consistent stereotyped automatism was followed by varied socialized activity in her monkey colony. When she was stimulated here for five second each minute, she ran across the cage, vocalized, climbed the wall and then would be attacked by or assault other monkeys. This defensive-aggressive behavior was determined by her current social status.

In the first colony where she was lowest in the social scale she attacked only once and was attacked or threatened 24 times. The study was discontinued as she became a member of another colony where she had a much higher status. Thalamic activation now resulted in attacks upon other monkeys 24 times and she was only threatened or attacked three times. In a subsequent colony where she was the second monkey in social status, thalamic activation caused the automatism to be repeated, following which she attacked 79 times and was not threatened even once.

Behavioral Responses to Brain Stimulation

The variable which determined Lina's social behavior was the recent experiences which determined her social role. Delgado[4] concludes that *both* neurophysiology and sociology must be considered during attack behavior, since "electricity cannot determine the target for hostility nor direct the sequences of aggressive behavior."

These findings by Jose Delgado in regard to social behavior following electric brain stimulation (EBS) confirms the conclusions of Jules Masserman and associates of Northwestern University of Chicago. They had developed techniques for the induction of apparently neurotic behavior in experimental animals and then studied their postoperative behavioral changes following lesions to the limbic system.

Pechtel and Masserman[5] have summarized their conclusions in the title of one paper "Cerebral Localization: Not Where But In Whom?" They found that neurotic traits were not only maintained but were even accentuated by certain cerebral lesions. In this instance the animal could become a "caricature" of his presurgical neurotic self. This was found to occur particularly when the neurotic behavior included excessive caution, dependency or belligerence. We can then conclude that both stimulation and lesions to the limbic system can influence precedent patterns of behavior such that behavioral responses depend upon the social role and/or expectations of the particular subject.

This would be illustrated if we could perform an "anthropomorphic" interview of members of the first and third colonies which Lina belonged to. Members of the first colony where she had low social status would probably report that her dependent behavior "invited attack," whereas monkeys from the third colony would probably say that a previously domineering female had become "even more aggressive."

Yet the intensity and location of the thalamic stimulation was the same and only her social status had changed. This supports the editorial conclusion of Masser-man: "Cerebral Localization: Not Where But in Whom?" When a defensive-aggressive limbic system response is activated, the behavior can be dependent upon expected responses within the sociocultural mileau.

Neurological Inhibition and Psychological Repression

That emotional responses based on past personal experience can be associated with neurophysiologic seizure discharges has been reported by Groethuysen et al.[6] A 46-year-old woman had spent 21 years in a Minnesota state hospital with catatonic schizophrenia. She was being evaluated for a lobectomy and depth electrodes were placed in or near the amygdaloid nucleus of her left temporal lobe. The electrical response here was normal during the first part of a structured interview.

It was suspected on the basis of family history that she had experienced a sexual relationship with her father during a three month period just prior to her first hospitalization at the age of 21. When this topic and her angry but repressed feelings toward her father were consistently dealt with during the structured interview, the depth electrode revealed the development of a seizure response within eight minutes. This activity continued and in 15 minutes she experienced her first grand mal epileptic seizure in 40 years. She had experienced several febrile convulsions during childhood

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diseases, but her last previous seizure was at the age of six.

The similarity of the process called "repression" by Sigmund Freud and "inhibition" by Hughlings Jackson was discussed by Roy Grinker[7] in 1939. He concluded that the same logical principles were the basis for these concepts although both Freud and Jackson insisted that these "subjective" and "objective" areas of conjecture be kept separate.

As a result of the findings of Groethuysen[6] we can propose that the deliberate confrontation of this woman's long repressed fury with her father had somehow disrupted **a** neurologic inhibition of amygdaloid and/or periamygdaloid seizure activity. The resultant grand mal seizure was followed by a behavioral change in which she became more overtly aggressive and destructive.

A Descending Ergotropic Pathway from the Amygdala to the Hypothalamus

Stimulation of certain limbic system centers, particularly in the amygdala, thalamus, hypothalamus and the brain stem reticular formation will extensively influence central nervous system function. In particular stimulation of the same point can consistently activate both autonomic responses which can be objectively measured, and primary drive behavior which can only be observed and subjectively experienced.

Fernandez-DeMolina and Hunsperger[8,9] have studied the organization of subcortical systems which influence "fight or flight" behavior and dominance of central nervous system tuning by the ergotropic (sympathetic) response system. They found descending circuits from the amygdaloid nucleus of the temporal lobe to the lateral hypothalamus and from there to the central grey matter of the reticular formation of the mid-brain which activate defensive-aggressive behavior. These findings provide important information regarding limbic system descending pathways which influence both autonomic and behavioral activity.

These findings provide support for the proposal by Miyata and Buckley[2] that limbic system responses in the hypothalamus are involved in alterations of both primary drive behavior and autonomic responses which prepare the body for primary drive behavior. They have proposed that a disruption of normal integration mechanisms for regulating autonomic responses can account for the correlation of aberrant behavior and paradoxical autonomic responses in schizophrenic patients.

The Phylogenetic Brain Model

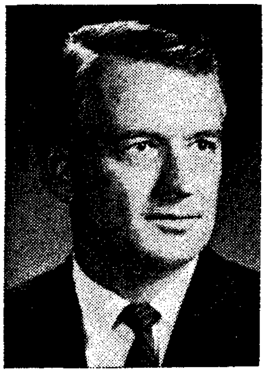
In order to place this correlation of objective and subjective events in a more coherent psychobiologic perspective, we shall review proposals regarding the organization and integration of central nervous system activity. Almost a century ago Hugh-lings Jackson[10] proposed that the association areas of the neocortex which were the last to develop during evolution imposed inhibition and direction upon primary drive behavior which can be activated by centers of the brain stem.

Yakovlev[11] in 1948 proposed a tri-partite phylogenetic brain model, composed of an endopalium, a mesopalium and an ecto-palium. By 1962 Paul MacLean[12] had proposed that man's brain was composed of three superimposed and integrated brain systems: a reptile brain, an early mammal brain and a primate brain. He had previously described the "reptile" brain stem and spinal cord as constituting a "neural chassis for behavior." With the development of the hypothalamus of the early mammal brain (or limbic system) evolution had added a "driver at the wheel of the neural chassis."

The hypothalamus has also been called the "head ganglion" of the autonomic system by John Fulton in 1946, and the "hub" of the limbic system by Gellhorn and Loof-bourrow.[3] In 1939 Roy Grinker[13] concluded that the hypothalamus served as a "con-denser," which influenced brain responses to incoming stimuli. He proposed that schizophrenic patients had a disruption of hypothalamic function.

By 1941 Grinker and Serota[14] had investigated this disruption of hypothalamic function by the activation of an intranasal electrode placed in the basal bone of the skull. They found that recurrent bursts of excitation of cortical neurones were significantly different in schizophrenic and normal patients, and hypothesized that abnormal hypothalamic responsiveness represented a basic biologic deficit in schizophrenia. With defective autonomic homeostatic mechanisms, the responses to frustration, trauma and rejection will be more devastating to the schizophrenic who must then either attack or withdraw from the environment.

Manfred Sakel[15] has speculated that the schizophrenic had an intensified tonus of the parasympathetic nervous system, blockading the nerve cell and fostering anabolic forces at a central site, the hypothalamus. The hypothalamus has also been called a "central switchboard relay center"[16] since it has such an extensive influence upon ascending pathways to the cortex and descending circuits which activate the peripheral autonomic system. The hypothalamus has received so many descriptive



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labels because it participates in such a vast variety of autonomic, behavioral and endocrine responses.

Hypothalamic Tuning

The well-nigh appalling complexity of responses to hypothalamic activation have been quite usefully organized as Gellhorn integrated Hess's proposals regarding a trophotropic and an ergotropic response system with his extensive studies of autonomic integration mechanisms.[3,18]

When the anterior hypothalamus is activated, descending circuits cause the parasympathetic system to dominate autonomic responses while ascending pathways alter the EEG as sleep does. This has been called the "trophotropic" response system. When the posterior hypothalamus has been activated, descending circuits influence the cardiovascular centers of the medulla as well as the peripheral sympathetic division for adrenaline secretion. Ascending pathways alter the EEG as awakening and arousal do. This has been called the "ergotropic" response system.

In the concept of hypothalamic tuning Gellhorn has integrated two principles which contribute to autonomic homeostatic equilibrium. The "reciprocal inhibition" principle indicates that when the ergotropic response system is dominant it has an inhibitory influence upon the trophotropic system. When this period ends the "post-inhibitory rebound" principle prevails and a transitory increase of trophotropic responsiveness will occur.

These principles describe typical autonomic function during normal activity. Under the influence of stress a sufficiently intense activation of ergotropic responses can result in a "spill-over" of activation such that descending parasympathetic circuits of the trophotropic response system can be paradoxically activated rather than inhibited.[19] This "spill-over" contributes to the development of duodenal ulcers and other psychosomatic disorders.

Rapidly alternating mood shifts, which are clinically termed "emotional lability," can be attributed to a neurophysiologic state of autonomic instability. Such states are part of the prodrome of emotional distress occurring in many schizophrenics before the acute psychotic episode.

Gellhorn explains this as follows: "It is therefore in principle understandable that under the influence of exertional strain (emotional or otherwise), and favored by a constitutional lability, the balance of the hypothalamus may be altered temporarily or permanently. The former is thought to be associated with the reversible autonomic instability syndrome; the latter may lead to permanent changes in the hypothalamic-cortical relations which appear as psychosis. It will be our task to see whether other investigations support these tentative statements."[3]

Autonomic Tuning in the Schizophrenic

When Miyata[2] studied the autonomic responses of Japanese schizophrenic patients he used the methacholine (Mecholyl) and noradrenaline tests which Nelson and Gellhorn[20] found to indicate decreased sympathetic system responsiveness with increasing age in both the normal and the schizophrenic population. Deviant autonomic responses also were found to be seen more frequently in neuropsychiatric patients than in the normal population when age categories were held constant.

Funkenstein, Greenblatt and Soloman[21] found that when a subjective improvement in psychological state occurs (regardless of whether apparently due to psychotherapy, electroshock or spontaneous remission), a change in the response to the methacholine test in the normal direction will occur. Gellhorn[3] has found that autonomic responses are aberrant in both manic and depressive disorders and that upon recovery these measures return to normal.

It was found that the newly admitted and seriously disturbed Japanese schizophrenic patients were primarily interested in withdrawing from social contact. They preferred to stay in the ward on their beds and were reluctant to go to the cafeteria. In consequence they chose to be at the end of the line for food. They ate quickly however and were among the first to return to the ward. As they improved they chose positions closer to the front of the line for food and had more social interaction at meals. Work productiveness improved as they became ready for discharge.

An important aspect of this study was obtained when the "time required at table" (TRAT) was determined.

The TRAT of schizophrenics was midway between time spent eating by hospital personnel who were on a busy and physically stressful schedule, and when this normal population was on a "leisurely" schedule.

In particular, the TRAT of schizophrenics was significantly different from either "busy" or "leisurely" scheduled normals. Hospitalization itself was a stress situation for the patients who were themselves on a comparatively "leisurely" schedule, at least as far as social demands are concerned. In consequence they ate more quickly and withdrew from the social scene of the cafeteria than leisurely normals. When normal subjects were under stress they appear to have been more effective in eating quickly.

That the accelerated eating of these schizophrenics in the course of recovery from their disorder was the result of the social stress of hospitalization itself was confirmed by this finding that the TRAT while eating at home with family members was significantly longer than when eating at the hospital. The patients felt more "relaxed" and subjectively comfortable when at home, and in consequence would spend a longer time conversing and consuming at lunch.

This quality of tension response indicates an increased ergotropic (sympathetic) system responsiveness to the social scene while eating. Yet their response to the methacholine (Mecholyl) test reveals that the trophotropic (parasympathetic) response system is dominant in their response to the acute hypotension which follows I.M. Mecholyl administration.

We must then conclude that the schizophrenic experience involves a disruption of the typical "reciprocal inhibition" and the "post-inhibitory rebound" principles which usually regulate autonomic homeostasis in the normal population. It can be proposed that a disturbance of hypothalamic tuning during the schizophrenic experience basically involves a trophotropic (parasympathetic) system dominance, but that the patient is also prone to increased ergotropic (sympathetic) responses when under social stress.

Hypothalamic Tuning And Responses To The Methacholine And Noradrenaline Tests

The cardiovascular centers of the medulla oblongata are significantly influenced by "buffer nerves" which send impulses from baro-receptors in the aorta and carotid sinus to the brain stem.[3]

The methacholine and noradrenaline tests give a reliable indication of central (hypothalamic) sympathetic and parasympathetic reactivity. When the baro-receptors are inhibited by the acute hypotension following the I.M. injection of 10 mg. of methacholine, measurements of pulse and blood pressure for 25 minutes will reveal the level of sympathetic reactivity. When the baro-receptors are activated by the acute hypertension following the I.V. injection of 0.04 mg./60 kg. of body weight of noradrenaline, measurement of the pulse and blood pressure responses for 15 minutes will reveal the level of parasympathetic reactivity.

The selection of a place in the feeding line by schizophrenic patients is significantly correlated with their sympathetic responsiveness as shown by the methacholine test. The time spent while eating correlated with their parasympathetic responsiveness as shown by the noradrenaline tests. Statistically significant variations were found between normal subjects and newly admitted schizophrenic patients. Moreover, as the patients recovered and became ready for discharge their abnormal autonomic responses became typical of those seen in the normal population group.

The Hypothalamus And Primary Drive Behavior

The observation by Paul MacLean that the hypothalamus became the "driver at the wheel of the neural chassis" is both poetic and pertinent to the influence which it has upon primary drive behavior. As the "early mammal brain" evolved, the hypothalamus integrated incoming olfactory sensations with feeding centers already present at the top of the brain stem.

Indeed, these structures became known as the rhinencephalon or "nose brain" because the primary drives which they directed were so influenced by the sense of smell. MacLean[22]-[23] has extensively discussed the participation of the limbic system in psychosomatic disturbances and primary drive behavior.

The hypothalamus contains centers which are related to feeding and satiety. The "satiety center" in the central hypothalamus has been identified as the glucoreceptor mechanism of the ventromedial and arcuate nuclei, and when it is activated by acute hyperglycemia it acts as a negative feed-back center to inhibit some but not all ergotropic system responses. When the glucoreceptor mechanism is inhibited by acute hypoglycemia the person is likely to experience hunger, tachycardia, gastric hyperacidity and an alien anxiety.

Disruptions in normal hypothalamic function have been proposed to occur during the schizophrenic experience by many investigators, including Grinker and Serota,[14] Sakel,[15] Gellhorn,[3, 18] and Buckley.[24] This does not infer a simplistic "cause and effect" phenomenon where a hypothalamic disorder is the direct cause of disturbed function elsewhere.

Indeed, Fernandez de Molina and Hunsperger[8,9] have demonstrated that an ergotropic "defensive-aggressive" response can be elicited by pathways from the amygdala to the lateral hypothalamus and from there to the mesencephalic reticular formation. A disruption of hypothalamic activity can *reflect rather than cause* disturbed function elsewhere.

The changes in primary drive behavior which Miyata has reported are also reported in studies of the pattern of weight gained by schizophrenic patients as they improve. Holden and Holden[25] conclude that "variations in appetite, motor activity or agitation were not consistently associated with changes in weight. Significant relationships were found between increases in weight and improvement in psychotic symptomatology and decreases in weight and worsening of symptomatology." Singh, De Dios and Kline[26] found that drug induced changes in 14 male schizophrenics showed a fairly consistent relationship with clinical responses, with "significant weight gains (over 10 kg. in 6 months) being associated with a relatively good response and small weight gains or no weight gain at all being associated with a poor response."

These findings indicate that as the schizophrenic reaction improves, the feeding drive behavior becomes more normal and the person gains weight. When we recall that Funkenstein et al.[21] found that the methacholine test response returns to normal as the patient improves, the weight gain found by Singh, De Dios and Kline[26] provide confirmatory evidence for Miyata's[2] observations.

Autonomic responses which can be objectively measured are influenced by the variety of hypothalamic tuning which the individual is currently experiencing. The degree of trophotropic or ergotropic response system dominance which is reflected in the hypothalamic tuning concept will influence primary drive behavior which can only be observed and subjectively experienced.

It is proposed that the hypothalamic disturbance which Gellhorn and Grinker hypothesized to occur among patients with schizophrenic disorders is supported by these studies by Miyata. The proposal is not validated or proved by those findings however, and further study of the integration of autonomic responses, primary drive behavior and subjective experiences is indicated.

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