

1989 Eleanor Clarke Slagle Lecture

Neuroscience and Occupational Therapy: *Vital Connections*

Shereen D. Farber, PhD, OTR, FAOTA

Occupational therapy practitioners have embraced concepts from diverse origins that are prerequisites for our theoretical foundations. The philosophical base of occupational therapy has evolved by weaving relevant views into technology (Henderson, 1988). During the last decade, we have witnessed a technological revolution in some of our foundation sciences, especially neurobiology, that has resulted in the modification of theories and methodology. The continuous integration of new neuroscientific concepts into occupational therapy theory and practice has thus become mandatory.

My clinical, research, and teaching experiences have led me to formulate the following hypothesis: In-depth knowledge of the neurosciences serves as a common denominator that can enhance our ability to interpret all aspects of human behavior. Because occupational therapy encompasses heterogeneous practice areas, three widely divergent practice disciplines are presented to test the hypothesis: Neuroimmunomodulation (the relationship that exists among several body systems, including the central nervous system [CNS], immune system, and endocrine system); organic bases of psychopathology (as they apply to schizophrenia specifically); and traumatic brain injury (particularly, factors that influence reorganization of the CNS after injury). Current neuroscientific findings in each of these areas are described along with associated treatment and research questions. A neurobiology curriculum philosophy is incorporated to present main concepts important to the lifelong neuroscientific education of occupational therapists.

Neuroimmunomodulation

Neuroimmunomodulation describes the developing interdisciplinary practice that investigates the relationships among participating body systems and associated basic sciences. The term is considered more inclusive than *psychoimmunology* or *neuroimmunology* (Pierpaoli & Maestroni, 1988). A functional knowledge of neuroimmunomodulation will assist

occupational therapists in understanding how and why persons become ill. Therapists may then counsel patients to gradually modify maladaptive life-styles that contribute to either immunosuppression or overactive immune reactions.

Figure 37.1 presents a simplified overview designed to emphasize the overlapping of the endocrine, immune, and central nervous systems. These three systems may share common structures, receptors, regulatory methods, and substances (Blalock, Bost, & Smith, 1985). Bone marrow is the site of the precursor stem cells that give rise to immune cellular components (Pierpaoli, 1985). The two divergent cell lines situated in the bone marrow are the non-lymphoid and lymphoid stem cells (Cohen, 1988; Stein, 1986). The nonlymphoid stem cells differentiate into granulocytes and monocytes; monocytes further differentiate into macrophages, which are immunocompetent cells that secrete interleukin-1 (IL-1) (Calabrese, Kling, & Gold, 1987; Farrar, Hill, Harel-Bellan, & Vinocour, 1987). IL-1 is known to facilitate the differentiation of the precursor lymphoid stem cell into B cells and T cells. B cells mature in the bone marrow and then migrate to a variety of lymphoid tissues such as lymph nodes, Peyer patches, spleen, appendix, and tonsils, thus becoming part of humoral immunity (circulating antibody-antigen reactions) (Calabrese et al., 1987). The cells migrate from the bone marrow to the thymus, where, under neuroendocrine influence, they subdivide into helper, killer, and effector cells. T cells are considered part of cell-mediated immunity (cell-antigen reaction). Helper T cells produce interleukin-2 and other mediators that facilitate B-cell maturation. Plasma cells arise from B cells and produce antibodies, also known as immunoglobulins. Each of these immunoglobulins has a specific function. Suppressor T cells can block the production and secretion of immunoglobulins (Calabrese et al., 1987). The many interactions of the immune system are quite complex and beyond the scope of this presentation. Simply stated, immune system components of a normal, healthy person are in delicate balance.

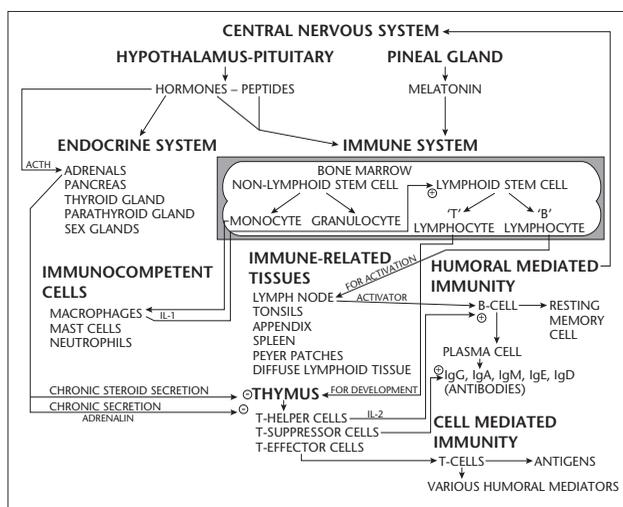


Figure 37.1. An overview of interactions between the immune, endocrine, and central nervous systems. (ACTH = adrenocorticotrophic hormone; IL-1 = interleukin-1; IL-2 = interleukin-2).

Various immune elements, as shown in Figure 1, can cross the blood-brain barrier and interact with the CNS. In turn, several CNS sites send regulatory messengers to interact with multiple body regions. Neuroendocrine products (peptides, hormones, releasing factors) from the hypothalamic-pituitary axis influence the function of the body's endocrine, immune, and nervous system structures. For example, consider the relationship between the pituitary gland and hypothalamus and the adrenal glands. Adrenocorticotrophic hormone, when released into the circulatory system,

stimulates the adrenal cortex to secrete corticosteroids (Blalock, 1988). Additionally, the posterior hypothalamus (the location of regulatory neurons for the sympathetic division of the autonomic nervous system) may stimulate the adrenal medulla to produce adrenalin. In small amounts, corticosteroids and adrenalin can be used to fight an acute stressful situation. In chronic situations, such as depression or long-term stress, corticosteroids, adrenalin, or both are known to suppress T-cell competency (Schleifer et al., 1984; Stein, 1986). This explains, in part, why our health is compromised when we experience chronic stress. The autonomic nervous system is known to innervate numerous immune-related structures, thus further influencing immune function (Bullock, 1987).

The pineal gland, located in the epithalamus, is said to participate in circadian fluctuations of hormones. Melatonin, one of its secretions, has been found to improve immune competency; chronic stress is said to reduce pineal function (Pierpaoli & Maestroni, 1988).

Opiate hormones (beta-endorphins and enkephalins) are produced in diverse places in the CNS. One known function of these natural opiates is to modulate pain perception (Pinchot, 1984). Moderate exercise releases endorphins and can produce a sense of well-being, whereas extreme exercise, such as overtraining and running in a marathon, may actually compromise the immune system (Mackinnon, 1989; Sforzo, 1988). "All things in moderation" appears to apply to exercise.

Patients with cancer have been taught to visualize their lymphocytes attacking cancerous cells located within their bodies. It was reported that those patients who used visualization to supplement chemotherapy survived longer than those who received chemotherapy alone (Simonton, Matthews-Simonton, & Creighton, 1978). Although these investigations contain important ideas, such as patients assuming responsibility for appropriate aspects of their treatment, serious flaws in the research designs of these imagery studies prevent the validation of imagery as a therapeutic modality (Laszlo, 1988). There is little evidence suggesting that patients can will their immune systems to kill cancer cells. After a complete review of Simonton et al.'s (1978) research, Laszlo said,

It is easy to make lofty claims, but when lives and costs are at stake it is imperative that investigations be careful and follow the "rules." If anything, studies that are inadequately set up or are misinterpreted to make a point (no matter how well intentioned) ultimately serve only to undermine confidence rather than contribute to supportive strength. (p. 266)

Eventually, imagery may be considered a useful adjunct to traditional therapy for those with disturbances in immune function, but only after well-designed experimentation validates it as a legitimate modality.

Rabin, Ganguli, Cunnick, and Lysle (1988) suggested that in some cases of schizophrenia there may be an underlying autoimmune abnormality. This would suggest that components of the immune system attack the CNS as though it were an enemy. Recently, Stein and Nikolic (1989), both of whom are occupational therapists, reviewed the use of relaxation techniques in schizophrenia. In their single-subject study, the subject demonstrated marked improvement on a standardized state-trait anxiety inventory after relaxation therapy. A

logical follow-up for Stein and Nikolic would be to collaborate with an immunologist on a prospective study. The investigators could conduct behavioral testing and collect blood samples to evaluate immune competency before and after relaxation therapy. Such a study would allow the immunologist to determine if there is a relationship between relaxation training and immune function in schizophrenia, while the occupational therapists could determine if immune function correlates with performance on the state–trait anxiety inventories. Such a collaboration has the potential to substantiate whether schizophrenia is at least in part an immune disorder.

Occupational therapists often use biofeedback and other methods of relaxation training in realistic environments rather than in an isolated laboratory. Once a patient masters the basic relaxation methods in a sensory controlled environment, the monitoring of his or her ability to perform functional activity in an occupationally relevant setting seems essential to facilitate a transition from laboratory performance to adaptive functioning in real-life situations.

As we age, we experience a decrease in immune system competency (Kelley et al., 1987; Solomon et al., 1988). It is encouraging to note that geriatric patients who have received relaxation training have improved T-cell competency (Kiecolt-Glaser, Glaser, & Williger, 1985). Many older people have not achieved a balance between health-promoting relaxation and unhealthy inactivity. Older people often become immobile, which may contribute to immune incompetency. Occupational therapists, who, by their training, consider all aspects of an older person's performance, can assist with planning the appropriate amounts and types of activity and environmental modifications to enhance occupationally relevant behavior.

Much work has been done to measure the immune competency of depressed patients. Persons with depression have been shown to have altered immune responses compared with normal control subjects (Schleifer et al., 1984). Conversely, emotional well-being can enhance immune function (Borysenko, 1982). As occupational therapists plan treatment programs, activities for both the mind and the body should be addressed. For example, moderate exercise, because it stimulates endorphins, can result in a sense of well-being.

The use of placebos is controversial; however, responses of numerous patients revealed that expectations affect their autonomic nervous system and body chemistry (Cousins, 1983). We must examine whether occupational therapists with positive, supportive attitudes influence patients in a manner that improves immune competency. We must also examine how therapists present treatment techniques. For example, one therapist declares to the patient, "I am going to try a new treatment technique. I have never done it before; I just learned it in a workshop last weekend and I am not sure I can do it correctly." Another, more confident, therapist says, "I am now going to use a treatment approach that is designed to help strengthen your arm muscles." The second therapist makes no promises but seems more likely to gain the patient's confidence and respect. It is possible that some of our modalities have a placebo effect; regardless, many physicians consider placebos to be a legitimate form of therapy.

Pearsall (1987) said that "superimmunity is the capacity to think and feel in ways that can protect us from disease, heal us when we are sick, and help us attain new levels of wellness . . .

far beyond the mere absence of symptoms” (p. xi). We as occupational therapists, because of the nature of our holistic interaction with patients, are in a perfect position to foster the development of enhanced immunity. We can encourage patients to establish positive attitudes (empowerment) and reduce helplessness and hopelessness. This action might improve the patient’s immune function.

The prevalence of AIDS should mandate that we be aware of the characteristics of those who are considered long-term AIDS survivors, that is, those who live longer than 3 years after their condition is diagnosed (Solomon, 1987). Fifty percent of persons diagnosed with AIDS live for 1 year or less. These statistics are changing with the widespread use of azidothymidine (AZT) and other new forms of therapy. Solomon, Temoshok, O’Leary, and Zich (1987) investigated the personal attitudes of long-surviving patients compared with those who succumbed rapidly. The long-term AIDS survivors

1. Had realistic attitudes, accepting their disease but believing in life
2. Possessed a fighting spirit
3. Modified their life-styles and left maladaptive situations
4. Were assertive
5. Attended to their personal needs
6. Talked freely about their illness
7. Assumed responsibility for their own health and considered themselves part of the treatment team
8. Helped others who had AIDS.

Solomon et al. (1987) proposed that further investigation of these attitudes and behaviors in AIDS survivors may yield some understanding of the mediators of relationships among cognitive, emotional, autonomic, and immunologic phenomena.

It is appropriate in concluding the section on neuroimmunomodulation to reflect on the philosophy espoused by Norman Cousins (1983) that we must focus on the possibilities of life instead of the limitations. Norman Cousins embodies the spirit of occupational therapy.

Organic Bases of Schizophrenia

During the last 100 years, various neurologists and neuroscientists, including Kraepelin, Alzheimer, Brodmann, Nissl, and Gaupp, theorized that mental illness was the result of brain pathology (Kraepelin, 1919). Unfortunately, these pioneers lacked the critical tools necessary to decipher the neuropathological substrata of mental conditions (Andreasen, 1988; Roberts & Crow, 1987). In the early 1900s, mental health personnel developed a classification system that separated mental disease into two categories: organic mental disease and functional mental disorders (Lishman, 1983). New technology has continuously evolved to examine both organic diseases and neurological conditions, whereas functional mental disorders were studied by Freud and his followers. The Freudians explored the wishes, intents, dreams, desires, and affects of their patients, thus providing valuable behavioral insights but yielding little understanding of the neuropathology involved in mental illness (Lishman, 1983). In the mid-1970s, a landmark study was conducted with the use of computerized tomography (CT)

scanning to compare the ventricle size of schizophrenic subjects with that of control subjects (Johnstone, Crow, Frith, Husband, & Kreel, 1976). This experiment validated early pneumoencephalography investigations that suggested that at least one subgroup of schizophrenic persons had enlarged ventricles, fissures, sulci, and decreased amounts of cerebral cortex (Shelton et al., 1988). Conclusions of earlier pneumoencephalography studies were poorly received due to research and methodology flaws (Seidman, 1983). Many CT studies have been published subsequently, verifying the results of Johnstone et al. (1976) and demonstrating that the ventricle–brain ratio is not related to length of illness, race, or sex (Seidman, 1983; Shelton & Weinberger, 1986).

It is now a common assumption that the disturbances of thought and affect seen in schizophrenia are due to changes in brain morphology, metabolism, or neurochemistry (Hornykiewicz, 1986). This conclusion has been based on studies employing magnetic resonance imaging (MRI), positron emission transaxial tomography (PETT), CT scans, and electroencephalography, all of which allow continuous, noninvasive analyses of mental state (Seidman, 1983). Preliminary work with the PETT scan, a relatively new experimental tool, indicated that persons with schizophrenia demonstrated abnormal use and regulation of glucose, particularly in the frontal lobes and basal ganglia, and decreased neuronal activity. PETT scan researchers have postulated that there is a relationship between length of illness and impairment of glucose metabolism. Chronic schizophrenic persons also show decreased cerebral blood flow (Lichtigfeld, Sandyk, & Gillman, 1988).

Schizophrenia is unlikely to be a simple deficit in a given neurotransmitter. Problems in neuroregulation among various neurochemicals and receptors are more plausible in this heterogeneous syndrome. Researchers, using labeled chemicals in MRI studies, have described dopamine and noradrenalin abnormalities in the CNS of some schizophrenic persons. It is unclear whether the neurotransmitter pathology is an outcome of the condition or is secondary to treatment with various pharmacological agents (Hornykiewicz, 1986). Numerous investigators have examined the neurochemical correlates and brain dysfunction or atrophy in mental illness (Andreasen, 1988; Goetz & van Kammen, 1986; Lohr & Jeste, 1988; Stevens & Casanova, 1988). It is clear that we have much to learn about neurotransmitter interactions in both normal and abnormal populations. Deficits in inhibitory neurotransmitters can result in sensory overload or sensory saturation commonly seen in schizophrenia. Carol North, a psychiatrist and recovered schizophrenic, heard voices and saw visual interference patterns from the time she was 6 years of age. Her behavior often became more adaptive when environmental demands and stimulation were controlled. North (1989) presented vivid descriptions of her personal experiences and perceptions as a person with schizophrenia during periods of excessive multisensory stimulation.

Figure 37.2 depicts dichotic listening, a noninvasive tool used to assess one aspect of brain function. Dissimilar auditory stimuli are simultaneously delivered to both ears of a subject. The speech center is located in the left hemisphere in 95% of the population. When auditory stimuli are presented to the right ear, they project to the left hemisphere. Therefore, when a normal person's right ear is stimulated with a verbal stimulus, it would be more

likely to register in the left cerebral hemisphere than if a nonverbal stimulus were presented to the same ear. Normal persons seem to be more generally attentive to verbal stimuli compared with nonverbal stimuli. In contrast, a subgroup of schizophrenic persons demonstrated a left ear advantage for verbal stimuli, thus suggesting that their speech center may be located in the right hemisphere. Right cortical activation, improved speech comprehension, or both are even more pronounced in schizophrenia when paired stimuli are substituted for a simple verbal stimulus presented to the left ear or to one ear at a time (Green & Kotenko, 1980; Lishman, 1983). Occupational therapists need to be aware of their position in space around a schizophrenic patient and its potential effect on the patient's speech comprehension.

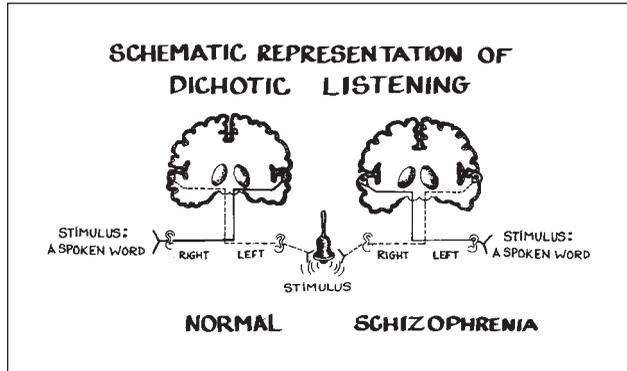


Figure 37.2. Dichotic listening in normal and schizophrenic persons.

Investigators have identified the following sites of CNS damage in schizophrenia: (a) reticular formation, (b) vestibular system, (c) cerebellar vermis, (d) oculomotor system, (e) basal ganglia, (f) thalamus, (g) frontal cortex, (h) prefrontal cortex, (i) left hemisphere, (j) corpus callosum, (k) insular cortex, and (l) reversal of the normal left-right symmetries (Andreasen, 1988; Crosson & Hughes, 1987; Falkai & Bogerts, 1986; Golden, 1981; Hornykiewicz, 1986; Lishman, 1983; Lohr & Jeste, 1988; Ornitz, 1970; Patterson, 1987; Roberts & Crow, 1987; Stevens & Casanova, 1988). Patterson suggested that some persons with schizophrenia may suffer from an ontogenetic deficit in both the limbic and thalamic nuclei that can interfere with frontal lobe development. Schizophrenic patients are less able to create behavior on the basis of prior experience; hence, their behavior becomes progressively inappropriate.

The concept of positive and negative signs in neurological diseases was first presented by John Hughlings Jackson (Andreasen, 1988). Negative signs relate to a loss in function, whereas positive signs represent a distortion of function (Andreasen, 1988). The negative signs commonly reported in schizophrenia include decreases in affect, attention, ability to experience pleasure, emotional attachments, ability to initiate and persist in tasks, postural mechanisms, postrotatory nystagmus, and oculomotor responses. Schizophrenic persons with a predominance of negative signs tend to demonstrate enlarged ventricles (Andreasen, 1988). The positive signs in schizophrenia include hallucinations, perceptions of nonexistent sensations, sensory flooding or saturation, faulty neurointegration, and increased delta waves on an electroencephalogram (Andreasen, 1988; Lishman, 1983; Morihisha, Duffy, & Wyatt, 1983).

Because neuropathology has been documented in the CNS of numerous psychiatric patients, a neurorehabilitative approach may serve as a useful adjunct to traditional occupational therapy intervention designed to promote adaptive behavioral responses. King

(1974), a pioneer in this area, used sensory integrative therapeutic intervention with the schizophrenic population. The following suggestions, summarized from the literature, may prove beneficial in a comprehensive treatment program in mental health:

1. Therapists should design the therapeutic environment with flexibility so that extraneous sensory stimulation can be minimized.
2. The occupational therapy profession must actively recruit more therapists to work in mental health, thus enabling us to reduce the size of the patients' treatment groups.
3. When using sensory input with a sensory saturated patient, the therapist should simplify the stimulus to a single sensory modality (unisensory modalities) instead of applying complex multisensory input (Farber, 1982). Ritvo (1969) found that autistic children showed improvement in the length of postrotatory nystagmus (an adaptive response) when they were tested in a darkened rather than a lighted room. Whereas the normal control subjects tolerated the combination of visual-vestibular input received during rotation in a lighted room, the autistic children produced marked reductions in postrotatory nystagmus under control conditions. Ritvo postulated that multisensory input may be overstimulating for the autistic child.
4. Relaxation training has been shown to improve the T-cell competency of older patients, and it enhanced performance on an anxiety-state-trait test in one single-subject study with a schizophrenic patient. Because one etiological theory of schizophrenia is autoimmune dysfunction, it seems logical that persons with schizophrenia might benefit from a regimen of relaxation activities.

In summary, the principles of neurorehabilitation may well complement the traditional psychiatric occupational therapy program. One might hypothesize that we are most likely to help psychiatric patients improve their functional performance when we address all aspects of their being, both mental and physical.

Traumatic Brain Injury

Plasticity refers to the integrated ability of the brain to remodel its connection in response to development, environmental changes, learning, stimulation, nutrition, and injury. The degree of plasticity that an organism possesses correlates inversely with its age (Cotman & Nieto-Sampedro, 1984; Lenn, 1987; Stein, Finger, & Hart, 1983). There are countless processes, substances, or factors that contribute to CNS plasticity. One example is *neurotrophic substances*, defined as factors, chemicals, hormones, and peptides that induce adaptive changes in the CNS by encouraging cells to respond to neurotransmitters. Nerve growth factor is one type of neurotrophic substance known to be released after an injury to specific cell types in the CNS (Hart, Chaimas, Moore, & Stein, 1978). It has been suggested that neurotrophic substances may be injected into a damaged brain at critical times to enhance recovery (Stein et al., 1983). After lesions, neurotrophic substances seem to be released to help in neural reorganization (Cotman, 1983; Cotman & Nieto-Sampedro, 1984; Skaper, Barbin, Longo, & Varon, 1982). Neurotrophic activity decreases with age, although diet, hormonal activity, and environmental conditions have positive effects on neurotrophic activity (Stein

et al., 1983). *Neurotoxic substances* are also present in the brain and are capable of killing brain cells. Some neurotransmitters (e.g., dopamine) modify their molecular structure when exposed to ischemia by forming oxygen radicals, which are volatile molecules toxic to cells. The current medical treatment for ischemia may include the use of a class of drugs called oxygen radical scavengers.

Another plastic process is reactive synaptogenesis. When a target in the CNS suffers input deficits, it can receive substitute input from alternative sources. If one cell dies within a cell pool, the remaining cells can sprout and innervate the target; however, should the entire pathway be eradicated, reactive synaptogenesis cannot restore the connections. Scientists are unsure if reactive synaptogenesis always enhances functional behavior, but it does seem to be important in the brains of elderly persons, in persons with neurodegenerative disease, and in persons with minor traumatic brain injury (TBI) (Cotman & Anderson, 1988). *Synaptic turnover* is a normal housekeeping function in the CNS used to remove discontinued, nonfunctional synapses (Cotman & Nieto-Sampedro, 1984). The rate of synaptic turnover is also influenced by environment and aging (Cotman, 1985).

When a person suffers a TBI, a typical sequence of events occurs within the CNS. After the insult, the CNS goes into shock and synaptic activity is decreased. Cerebral edema results as cells die and dump their intracellular contents into the extracellular spaces. This action elevates intracranial pressure and compresses small blood vessels that deliver oxygenated blood. Edema makes ischemia worse, which in turn exacerbates edema by killing more cells. At this point, physicians often attempt to decrease the patient's CNS metabolic demands and intracranial pressure by administering barbiturates, reducing body temperature, or using osmotic agents (Trauner, 1986). Both neurotoxic and neurotrophic substances are released after injury (Skaper et al., 1982). Ultimately, the connections reorganize and progress can continue for decades (Stein et al., 1983). Persons with TBI may enjoy significant recovery, but they seem less tolerant of environmental perturbations or demands.

Another factor that influences the outcome of TBI is the rate of injury. Persons who have slow-growing lesions, such as tumors, demonstrate more plasticity but have persistent sequelae, whereas those who have acute injury generally show less plasticity, but sequelae do not persist as long (Joynt & Benton, 1964; Stein et al., 1983).

Environmental stimulation after the trauma is of great interest to occupational therapists. Unfortunately, the majority of studies in this area have been conducted with laboratory animals. One cannot generalize animal findings to human beings, but the results are of interest in the elucidation of potential mechanisms that may also occur in human brains. Whether or not an animal benefits from an enriched environment depends on the lesion site, the amount of environmental exposure, and the specific behavior being measured (Kelche, Dalrymple-Alford, & Will, 1987; Will, Rosenzweig, Bennett, Herbert, & Morimoto, 1977). Many environments housing patients with TBI are highly stimulatory with continuous multisensory input. I do not believe that this practice should be considered environmental enrichment or that sensory bombardment yields adaptive behavior in patients with TBI. Continuous contact with sensory input can also produce habituation.

Occupational therapists should test the use of prescriptive environments that include sensory experiences, individualized for each patient to promote adaptive responses.

Brain cell transplants are one example of the technological revolution in neuroscience. Adrenal cell transplants have been conducted in patients with Parkinson disease at medical centers in Sweden, Mexico, China, and the United States. The brain has a degree of immunological privilege, so that when substances are placed within it, they grow relatively free of interference from the usual immunologic response. The advantages of brain cell transplants are that they

1. Can serve as endogenous sources of neurotransmitters in diseases where there is a transmitter deficit.
2. Induce an increase in plasticity and reorganization.
3. Cause a release of injury-induced trophic factors.
4. Promote new connections.

It is unclear whether brain cell transplants will facilitate long-term improvement in functional behavior. More work needs to be done with experimental models before behavioral outcomes are fully understood. In addition, although the brain does have some immunological privilege, cross-strain transplants do produce immunogenic activity leading to potential graft rejection. This finding raises the ethical, moral, and spiritual issue of how surgeons are to obtain viable transplant material for human beings. Genetic engineering offers us potential solutions to these problems. Occupational therapists may be routinely treating patients with brain cell transplants within the next two decades.

The major focus of my postdoctoral research was to determine if we could successfully transplant brain cells into a specific region of the brains of postischemic rats using a model of ischemia developed by Pulsinelli and Brierley (1979). Because ischemia produces a hostile cytotoxic environment, the scientific community believed that transplantation would not be successful. We hypothesized that if we delayed transplantation until the cytotoxicity stabilized, the transplanted cells would survive (Farber et al., 1988). Before we could transplant the brain cells, we had to demonstrate our ability to reproduce the model and determine baseline behavior. Figure 37.3 shows the performance of a normal rat and an ischemic rat in an open field maze, a test used to measure hippocampal function. The control and experimental animals were placed in a standardized open field maze box, and the following behaviors were quantified: (a) total number of squares entered; (b) location of squares (central or peripheral); and (c) number of rearing, grooming, defecation, and urination episodes. Rats were tested at 1 and 2 weeks postischemia. Marked, statistically significant differences were noted between the postischemic rats and the control rats (Farber et al., 1986). The control animals explored the maze freely (both the center and peripheral squares), urinated and defecated infrequently, and reared and groomed frequently. The postischemic animals stayed in the periphery of the maze; perseverated, urinated, and defecated often (an indication of emotionality); and groomed infrequently. Postischemic rats also demonstrated tactile defensiveness.

At 2 weeks postischemia, the control and postischemic rats received labeled hippocampal cell transplants taken from fetal rats of the same strain. It was necessary to use a

label on the transplanted cells to allow us to differentiate the transplant from the host. Figure 37.4 shows transplanted brain cells growing successfully in the brain of a postischemic rat. Nine out of 10 transplanted animals demonstrated successful transplants containing pyramidal and multipolar labeled cells, thus suggesting that transplants into focal regions of ischemically damaged brains are feasible.

In consideration of the future rehabilitation of patients with brain injury, the words of Lenn (1987) are particularly inspiring:

It is difficult to set reasonable expectations for the brain damaged child without making self-fulfilling prophesies of limited potential. Since we know many examples of this type of error on the part of our predecessors, we can assume that greater potential than currently observed is possible. So our attitude must be critical open-mindedness and enough realism to know current limitations, combined with enough humility to accept that progress will be made. (p. 182)

Neurobiology Curriculum Philosophy

I believe that students who are taught conceptual neurobiology with direct application to occupational therapy retain more knowledge and are likely to continue self-study, compared with students who are taught neurobiology as an

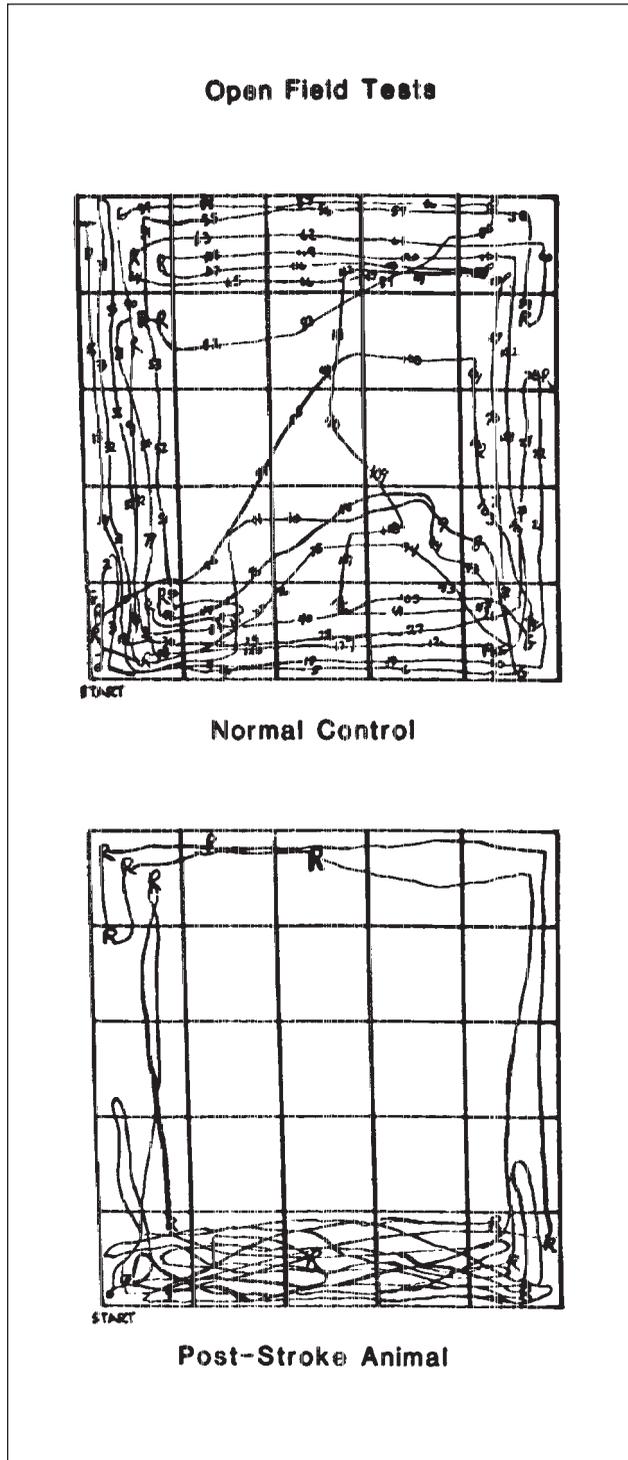


Figure 37.3. Comparison of the open field maze performances of a control rat and a postischemic, nontransplanted rat.

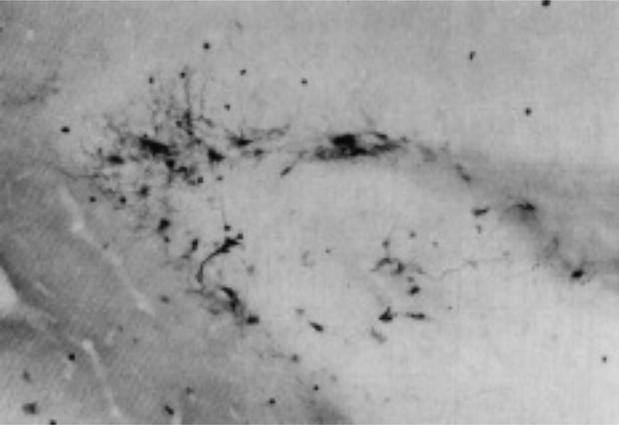


Figure 37.4. Labeled, transplanted fetal hippocampal cells in the hippocampus (dentate gyrus) of a post-ischemic rat (2 weeks after the transplant).

exercise in memorization of mindless minutiae. If we are to be effective in stimulating students, we must tune into the learning styles that are frequently used and employ a variety of methods to explain neurobiological concepts. In addition, it is essential that we develop a learning hierarchy of neuroscientific skills to be achieved by entry, master's, and doctoral level therapists so that we can better integrate neuroscience with occupational therapy theory and practice. It is vital that occupational therapists continue to explore the ever-evolving neuro-

science literature. As technological advancements allow scientists to uncover new information, the modification of current concepts may become necessary. Occupational therapists should seek neuroscience mentors if help is needed in translating confusing methodology and data into meaningful information.

Summary

There was a time in the early 1900s when leaders in neuroscience had a collective intuitive understanding of brain mechanisms without appropriate tools to explore and elaborate concepts. We are now in a technological revolution in brain sciences, and it is up to the creative minds of occupational therapists to incorporate these new methodologies and discoveries into therapeutic advances. In 1902, Joseph Conrad said, "The mind of man is capable of anything because everything is in it, all of the past as well as all of the future" (p. 843).

Acknowledgments

I would like to express my appreciation to the American Occupational Therapy Association for this award. Thanks are also due to my family, friends, and colleagues, whose nurturance and encouragement have facilitated my personal and professional growth.

References

- Andreasen, N. C. (1988). Brain imaging: Applications in psychiatry. *Science*, *239*, 1381–1388.
- Blalock, J. E., (1988). Immunologically-mediated pituitary adrenal activation. *Advances in Experimental Medical Biology*, *245*, 217–223.
- Blalock, J. E., Bost, K. L., & Smith, E. M. (1985). Neuroendocrine peptide hormones and their receptors in the immune system. *Journal of Neuroimmunology*, *10*, 31–40.
- Borysenko, J. Z. (1982). Behavioral-physiological factors in the development and management of cancer. *General Hospital Psychiatry*, *4*, 69–72.

- Bullock, K. (1987). The innervation of immune system tissues and organs. In C. W. Cotman, R. E. Brinton, A. Galaburda, & B. McEwen (Eds.), *The neuro-immune-endocrine connection* (pp. 33–47). New York: Raven Press.
- Calabrese, J. R., Kling, M. A., & Gold, P. W. (1987). Alterations in immunocompetence during stress, bereavement, and depression: Focus on neuroendocrine regulation. *American Journal of Psychiatry*, *144*, 1123–1134.
- Cohen, J. J. (1988). The immune system: An overview. In E. Middleton, Jr., C. E. Reed, E. F. Ellis, N. F. Adkinson, Jr., & J. W. Yunginger (Eds.), *Allergy principles and practice* (pp. 3–12). St. Louis: C. V. Mosby.
- Conrad, J. (1968). Heart of darkness. In J. Bartlett (Ed.), *Familiar quotations* (14th ed.) (p. 843). Boston: Little, Brown. (Original work published 1902)
- Cotman, C. W. (1983). Effect of conditioning lesion on survival of transplants into rat hippocampus: Evidence for lesion induced growth factor. *Brain Research*, *211*, 321–326.
- Cotman, C. W. (1985). *Synaptic plasticity*. New York: Guilford Press.
- Cotman, C. W., & Anderson, K. J. (1988). Synaptic plasticity and functional stabilization in the hippocampal formation: Possible role in Alzheimer's disease. In S. G. Waxman (Ed.), *Advances in neurology: Vol. 47. Functional recovery in neurological disease* (pp. 313–335). New York: Raven Press.
- Cotman, C. W., & Nieto-Sampedro, M. (1984). Cell biology of synaptic plasticity. *Science*, *225*, 1287–1294.
- Cousins, N. (1983). *Human options*. New York: Berkley Books.
- Crosson, B., & Hughes, C. W. (1987). Role of the thalamus in language: Is it related to schizophrenic thought disorders? *Schizophrenia Bulletin*, *13*, 605–621.
- Falkai, P., & Bogerts, B. (1986). Cell loss in the hippocampus of schizophrenics. *European Archives of Psychiatry and Neurological Science*, *236*, 154–161.
- Farber, S. D. (1982). *Neurorehabilitation: A multisensory approach*. Philadelphia: W. B. Saunders.
- Farber, S. D., Murphy, S. H., Wells, D. G., Vietje, B. P., Wells, J., & Low, W. C. (1986). Experimental cerebral ischemia, tissue damage, and neuronal transplantation. *Society of Neuroscience Abstracts*, *112*, 1287.
- Farber, S. D., Onifer, S. M., Kaseda, Y., Murphy, S. H., Wells, D. G., Vietje, B. P., Wells, J., & Low, W. C. (1988). Neural transplantation of horseradish peroxidase-labeled hippocampal cell suspensions in an experimental model of cerebral ischemia. *Progress in Brain Research*, *78*, 103–107.
- Farrar, W. L., Hill, J. M., Harel-Bellan, A., & Vinocour, M. (1987). The immune logical brain. *Immunological Reviews*, *100*, 361–378.
- Goetz, K. L., & van Kammen, D. P. (1986). Computerized axial tomography scans and subtypes of schizophrenia. *Journal of Nervous and Mental Disease*, *174*, 31–41.
- Golden, C. J. (1981). Hemispheric asymmetries in schizophrenia. *Biological Psychiatry*, *16*, 561–582.
- Green, P., & Kotenko, V. (1980). Superior speech comprehension in schizophrenics under monaural versus binaural listening conditions. *Journal of Abnormal Psychiatry*, *89*, 339–408.
- Hart, T., Chaimas, N., Moore, R. Y., & Stein, D. G. (1978). Effects of nerve growth factor on behavioral recovery following caudate nucleus lesions in rats. *Brain Research Bulletin*, *3*, 245–250.
- Henderson, A. (1988). Occupational therapy knowledge: From practice to theory. 1988 Eleanor Clarke Slagle Lecture. *American Journal of Occupational Therapy*, *42*, 567–576.
- Hornykiewicz, O. (1986). Brain noradrenaline and schizophrenia. *Progress in Brain Research*, *65*, 29–39.

- Johnstone, E. C., Crow, T. J., Frith, C. D., Husband, J., & Kreel, L. (1976). Cerebral ventricular size and cognitive impairment in chronic schizophrenia. *Lancet*, *ii*, 924–926.
- Joynt, R. J., & Benton, A. L. (1964). The memoir of Marc Dox on aphasia. *Neurology*, *14*, 851–854.
- Kelche, C., Dalrymple-Alford, J., & Will, B. (1987). Effects of post-operative environment on recovery of function after fimbria-fornix transection in the rat. *Physiology and Behavior*, *40*, 731–736.
- Kelley, K. W., Brief, S., Westly, H. J., Novakofski, J., Bechtel, P. J., Simon, J., & Walker, E. R. (1987). Hormonal regulation of the age-associated decline in immune function. *Annals of the New York Academy of Science*, *496*, 91–97.
- Kiecolt-Glaser, J. K., Glaser, R., & Williger, D. (1985). Psychosocial enhancement of immunocompetence in a geriatric population. *Health Psychology*, *4*, 25–29.
- King, L. J. (1974). A sensory-integrative approach to schizophrenia. *American Journal of Occupational Therapy*, *28*, 529–536.
- Kraepelin, E. (Ed.). (1919). *Dementia praecox and paraphrenia*. Edinburgh: Livingstone.
- Laszlo, J. (Ed.). (1988). *Understanding cancer*. New York: Harper & Row.
- Lenn, N. J. (1987). Neuroplasticity and the developing brain: Implications for therapy. *Pediatric Neuroscience*, *13*, 176–183.
- Lichtigfeld, F., Sandyk, R., & Gillman, M. (1988). New vistas in chronic schizophrenia. *International Journal of Neuroscience*, *38*, 355–367.
- Lishman, W. A. (1983). The apparatus of mind: Brain structure and function in mental disorders. *Psychosomatics*, *24*, 699–703, 709–711, 714–720.
- Lohr, J. B., & Jeste, D. V. (1988). Locus ceruleus morphometry in aging and in schizophrenia. *Acta Psychiatrica Scandinavica*, *77*, 689–697.
- Mackinnon, L. T. (1989). Exercise and natural killer cells. What is the relationship? *Sports Medicine*, *7*, 141–149.
- Morihisha, J. M., Duffy, F. H., & Wyatt, R. J. (1983). Brain electrical activity mapping (BEAM) in schizophrenic patients. *Archives of General Psychiatry*, *40*, 719–728.
- North, C. S. (1989). *Welcome silence*. New York: Avon Books.
- Ornitz, E. (1970). Vestibular dysfunction in schizophrenia and childhood autism. *Comprehensive Psychiatry*, *11*, 159–173.
- Patterson, T. (1987). Studies toward the subcortical pathogenesis of schizophrenia. *Schizophrenia Bulletin*, *13*, 555–576.
- Pearsall, P. (1987). *Superimmunity*. New York: Fawcett Gold Medal.
- Pierpaoli, W. (1985). Immunoregulatory and morphostatic function of bone marrow-derived factors. In R. Guillemin, M. Cohn, & T. Melnechuk (Eds.), *Neural modulation of immunity* (pp. 205–237). New York: Raven Press.
- Pierpaoli, W., & Maestroni, G.J.M. (1988). Neuroimmunomodulation: Some recent views and findings. *International Journal of Neuroscience*, *39*, 165–175.
- Pinchot, R. B. (Ed.). (1984). *The brain: Mystery of matter and mind*. New York: Torstar Books.
- Pulsinelli, W. A., & Brierley, J. B. (1979). A new model of bilateral ischemia in the unanesthetized rat. *Stroke*, *10*, 267–272.
- Rabin, B. S., Ganguli, R., Cunnick, J., & Lysle, D. T. (1988). The central nervous system-immune system relationship. *Clinics in Laboratory Medicine*, *8*, 253–268.
- Ritvo, E. R. (1969). Decreased postrotatory nystagmus in early infantile autism. *Neurology*, *19*, 653–658.

- Roberts, G. W., & Crow, T. J. (1987). The neuropathology of schizophrenia—A progress report. *British Medical Bulletin*, *43*, 599–615.
- Schleifer, S. J., Keller, S. E., Meyerson, A. T., Raskin, M. J., David, K. L., & Stein, M. (1984). Lymphocyte function in major depressive disorder. *Archives of General Psychiatry*, *41*, 484–486.
- Seidman, L. J. (1983). Schizophrenia and brain dysfunction: An integration of recent neurodiagnostic findings. *Psychological Bulletin*, *94*, 195–238.
- Sforzo, G. A. (1988). Opioids and exercise: An update. *Sports Medicine*, *7*, 109–124.
- Shelton, R. C., Karson, C. N., Doran, A. R., Pickar, D., Bigelow, L. B., & Weinberger, D. R. (1988). Cerebral structural pathology in schizophrenia: Evidence for a selective prefrontal cortical deficit. *American Journal of Psychiatry*, *145*, 154–163.
- Shelton, R. C., & Weinberger, D. R. (1986). X-ray computerized tomography in schizophrenia: A review and synthesis. In H. A. Nasrallah & D. R. Weinberger (Eds.), *Handbook of schizophrenia, vol. 1: The neurology of schizophrenia* (pp. 207–250). Amsterdam: Elsevier.
- Simonton, C. C., Matthews-Simonton, S., & Creighton, J. L. (Eds.). (1978). *Getting well again*. New York: Bantam Books.
- Skaper, S., Barbin, G., Longo, F. M., & Varon, S. (1982). Brain injury causes a time-dependent increase in neuronotrophic activity at the lesion site. *Science*, *217*, 860–861.
- Solomon, G. F. (1987). Psychoneuroimmunologic approaches to AIDS. *Annals of the New York Academy of Science*, *496*, 628–636.
- Solomon, G. F., Fiatarone, M. A., Benton, D., Morley, J. E., Bloom, E., & Makinodan, T. (1988). Psychoimmunologic and endorphin function in the aged. *Annals of the New York Academy of Science*, *521*, 43–57.
- Solomon, G. F., Temoshok, L., O'Leary, A., & Zich, J. (1987). An intensive psychoimmunologic study of long-surviving persons with AIDS. *Annals of the New York Academy of Science*, *496*, 647–655.
- Stein, D. G., Finger, S., & Hart, T. (1983). Brain damage and recovery: Problems and perspectives. *Behavioral and Neural Biology*, *37*, 185–222.
- Stein, F., & Nikolic, S. (1989). Teaching stress management techniques to a schizophrenic patient. *American Journal of Occupational Therapy*, *43*, 162–169.
- Stein, M. (1986). A reconsideration of specificity in psychosomatic medicine: From olfaction to the lymphocyte. *Psychosomatic Medicine*, *48*, 3–22.
- Stevens, J. R., & Casanova, M. F. (1988). Is there a neuropathology of schizophrenia? *Biological Psychiatry*, *24*, 123–128.
- Trauner, D. A. (1986). Barbiturate therapy in acute brain injury. *Journal of Pediatrics*, *109*, 742–746.
- Will, B. E., Rosenzweig, M. R., Bennett, E. L., Herbert, M., & Morimoto, H. (1977). Relatively brief environment enrichment aids recovery of learning capacity and alters brain measures after post-weaning brain lesions in rats. *Journal of Comparative and Physiological Psychology*, *91*, 33–50.