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# Late post-acute neurologic rehabilitation: neuroscience, engineering and clinical programs

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**ABSTRACT**

*This article highlights about scientific neurological rehabilitation based in research.These establish the rehabilitation medicine with the scientific aground more the less than empiric rehabilitation. my principal efforts in rehabilitation have been to study: (1) mechanisms of brain plasticity related to reorganization of the brain and recovery of function; (2) late postacute rehabilitation; (3) sensory substitution; and (4) rehabilitation engineering. A principal goal has been to aid in the development of a strong scientific base in rehabilitation.*

**KEYWORDS:** *Brain, neuronal plasticity, rehabilitation.*

**RESUMEN**

Este artículo resalta la investigación en rehabilitación neurológica sustentada en el método científico y permite hacer de la rehabilitación una entidad mejor comprendida y menos empírica. Los esfuerzos principales en la rehabilitación han sido estudiar: (1) los mecanismos de plasticidad del cerebro relacionaron a la reorganización del cerebro y recuperación de función; (2) la rehabilitación del postacute tarde; (3) la substitución sensoria; y (4) la ingeniería de la rehabilitación. Una meta principal ha sido ayudar en el desarrollo de una base científica fuerte en la rehabilitación.

**PALABRAS CLAVE:** Cerebro, plasticidad neuronal, rehabilitación.

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The occasion of the Coulter Lecture is an appropriate time to review the highlights of my career in rehabilitation research. My life-long interest in neuroscience led to a mid-career change, from a professorship in basic science to a resident in physical medicine and rehabilitation. My father had made a dramatic recovery from a major stroke with a home program developed by my brother. After my father's death from a stroke 7 years later while mountain hiking at 9000 feet (he was still working full-time), the autopsy revealed that recovery had taken place despite very extensive brain damage.[1,2] The clear demonstration of restoration of function by means of rehabilitation was an irresistible stimulus for a career change.

My goal has been to aid in the development of a strong scientific base in rehabilitation. Previous areas of research have included brain plasticity and sensory substitution, neuropharmacology,[3] visual cortex[4] and brainstem[5] neurophysiology, and oculomotion.[6,7]

My principal efforts in rehabilitation have been to study: (1) mechanisms of brain plasticity related to reorganization of the brain and recovery of function; (2) late postacute rehabilitation; (3) sensory substitution; and (4) rehabilitation engineering.

## BRAIN PLASTICITY

The brain has an enormous capacity to respond to functional need. Brain plasticity–related changes in function are accompanied by measurable brain changes such as the greatly increased cortical representation of a fingertip area in monkeys after training in haptic exploration.[8] Brain plasticity also is the basis for recovery from brain damage, either direct (eg, stroke, head injury) or indirect (eg, blindness, in which the brain must reorganize after the loss of a major sensory input); this is also accompanied by demonstrable brain changes such as in the sensorimotor cortex in Braille readers.[9]

For 150 years after Broca's seminal description of cerebral localization, the neurosciences were totally dominated by concepts of connectionism and strict point-to-point localization.[10,11] The idea of a malleable brain was overwhelmed during this time, which had a very negative effect on the field of rehabilitation. Because brain plasticity was not a part of the conceptual substance of the basic or clinical neurosciences, how could clinicians expect reorganization? My first publication with "plasticity" in the title was rejected by a number of journals before being published in the *Acta Neurological Scandinavia*.[12] It has been exciting to observe the important role brain plasticity has now gained and the clinical brain reorganization programs based on brain plasticity that are now common.

However, even during these "dark ages" for brain plasticity and rehabilitation, there were voices of reason. These include: Bethe, Goldstein, Lashley (a student of Franz), Foerster, and others.[11,13] One of the most important of these voices was Franz, whose contribution, Colotla and Bach-y-Rita[14] recently reviewed. Franz described many of the plasticity concepts and laboratory and clinical applications that have reappeared in recent years, such as loss of function from disuse, centrally initiated movements, brain plasticity (eg, by partial recovery from serial brain lesions), late stroke rehabilitation including the role of motivation, the field of neuropsychology, unmasking, and limb-restraint–related recovery. We concluded in our review of Franz's work that his "important findings, and even more important concepts, have foreshadowed the development of brain plasticity as an important area of the neurosciences, and contributed to the development of theory-based functional, motivating rehabilitation methodologies that obtain significant functional recovery in brain damaged persons".[14](p147)

The scientific literature on specific mechanisms of brain plasticity[2,11,15-17] has been reviewed. Here I will discuss only one; nonsynaptic diffusion neurotransmission, which is usually called volume transmission.

## Volume transmission

Volume transmission includes the diffusion, through the extracellular fluid, of neurotransmitters released at points that may be remote from the target cells, with the resulting activation of extrasynaptic receptors. I have reviewed relevant studies;[10,17-19] this lecture includes portions from some of them. Other work on the subject includes that by Bach-y-Rita[11] and Fuxe et al.[20,21]

The role of synapses in neurocommunication in the brain was established more than a century ago.[11] Generally, little consideration is given to other modes of neurotransmission. In the 1950s, I participated in studies at the Killam Laboratory on the action of γ-aminobutyric acid analog on thalamic mechanisms. We injected the analog into cat ventricles because it does not cross the blood-brain barrier.[22,23] At the time, we did not consider diffusion neurotransmission as a mechanism of action. However, later intra- and extracellular microelectrode studies[5] in cat brainstem resulted in the suggestion that diffusion neurotransmission was the mechanism, and that it could play a role in the multiplexing of the polysensory cells.

Individual movements or functions, such as playing the piano or watching a tennis match, require great selectivity, rapid initiation, and rapid ending; for such functions, synaptic action is essential. However, for mass sustained functions (eg, sleep, mood, hunger), sustained, widespread activity (rather than speed and selectivity) is required, and synaptic mechanisms may be unnecessarily costly in energy and space.[24,25] Aiello and Bach-y-Rita[26] have calculated the cost of an action potential in the brain. Many functions may require combinations of both types of neurotransmission.

In a piano-playing example, in addition to the relevant synaptic mechanisms, the finger movements can be more precise in the presence of adequate preparation, including changes in brain tone (probably mediated by noradrenaline). Information transmission through the retina may not be entirely synaptically mediated: Dowling[27] noted there is evidence that horizontal cells make synapses back onto the photoreceptor terminals, but noted that they are not seen. In 1995, I suggested that they may not be seen "…because they may not exist; rather the mechanisms may be by diffusion in the extracellular fluid".[11](p60)

The visual perception of a tennis game may require neuronal receptivity to be set at a high level, probably involving several neurotransmitters, including nitric oxide and dopamine in the retina, serotonin and histamine in the lateral geniculate nucleus, and noradrenaline in the visual cortex. These effects appear to be primarily nonsynaptically mediated. Some of them have been called modulation; the modulation of synaptic activity by diffusion outside the synaptic gap is a volume transmission–mediated activity.

Among the range of functions in which volume transmission plays a role are many of those mediated by noradrenaline.[11] Volume transmission may be the primary information transmission mechanism in several abnormal functions, such as mood disorders, spinal shock, spasticity, shoulder-hand and autonomic dysreflexia syndromes, pain, and drug addiction.[18,28-30]

Work carried out in the Routtenberg Laboratory[31] in the late 1960s suggested that transmitters could readily move in the extracellular space (the fluid that surrounds neurons in the brain) and travel over distances by directional flow. Furthermore, a large number of receptor subtypes have been identified; these provide a mechanism for selective activation even if the volume transmission neurotransmitter is massively diffused over an area; high affinity receptors on cells distant from the transmitter release can bind the neurotransmitter and cause a neuron response, while closer neurons without those specific receptor subtypes will not respond.

Volume transmission may be more common in certain brain regions; nonsynaptic interneuronal communication is very common in the greater limbic system[32] and may play an important role in the organization and regulation of behavior by the core and paracore regions of the brain.[33] Volume transmission may also be an important mechanism in the highest levels of the human brain: physical anthropologists are puzzled because the human brain does not use more energy than the smaller brains of animals of comparable corporal weight; Bach-y-Rita and Aiello[34] have suggested that the parts of the human brain that show the greatest size increase over other animals (eg, prefrontal cortex) may

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be exactly those parts in which highly nonsynaptic-based functions have their neuronal representation. Music appreciation and intellectual functions, for example, may not require the high-frequency (and energetically costly) alternating cycles of activation-inactivation of synaptic transmission, and may be largely replaced by volume transmission.

## Recovery from brain damage

Receptor plasticity, both at synapses and on the cell membrane away from synapses (reached by volume transmission), may play a major role in the reorganization of function after brain damage. Volume transmission may also be the principal means of neurotransmission in the noradrenergic system, which is involved in so many activities related to recovery from brain damage. Both acetylcholine and norepinephrine can provide a state of excitability consistent with cognition, which is consistent with inhibition of the locus ceruleus activity during lack of vigilance. These findings may relate directly to the results of rehabilitation programs: when vigilance is high and the patient is actively involved, good results are more likely to be obtained. There may also be a relationship to functional rehabilitation programs that are based on the interests of the individual patient, and to the positive results obtained with some home programs. In these cases, the increased vigilance and participation may lead to greater locus ceruleus production of noradrenaline. This and other neurotransmitter changes may also be mechanisms by which psychosocial factors influence recovery.

Noradrenaline-mediated neurotransmission offers an example of the differences between synaptic and volume transmission. With volume transmission, the effect of nonjunctional noradrenaline is likely to be longer lasting than a similar quantity of noradrenaline released at synapses. Absent such a junction, inactivation of the noradrenaline is slowed; while the synapse has a full panoply of degradation enzymes and reuptake mechanisms, nonjunctional receptor sites have few if any of these inactivating devices.(35) Due to the slow activation and inactivation, there is a reduced need for nerve action potentials and for neurotransmitter production, transport, and heat generation. The brain is efficient in the use of energy; thus the widespread sustained activation of groups of neurons via diffusion of neuroactive substances through the extracellular fluid should be more energy efficient than synaptic activation of those same neurons.(11) Our modeling studies support this interpretation.(25)

The effects of brain damage are not uniform in the various neurotransmitter systems. In a rat model, Westerberg et al(36) studied the effects of transient cerebral ischemia in the rat hippocampal subfields on excitatory amino acid receptor ligand binding. They noted that their results demonstrated a lack of correlation between receptor changes in the early recovery period after ischemia and the development of neuronal necrosis in different hippocampal regions; they also noted long-lasting receptor changes in areas considered resistant to an ischemic insult. Some receptors are down-regulated while others appear to be up-regulated on the surviving cells. Volume transmission may contribute to the survival of partially denervated neurons and to brain reorganization after brain damage by selective up-and down-regulation of receptors. These issues have been discussed elsewhere,(3,11,18,37) with regard to brain injury and spinal cord injury (SCI).

De Keyser et al(38) demonstrated an up-regulation of D1 dopamine receptors in the neocortex of persons whose death was due to a recent unilateral infarct of the ventral midbrain, producing a unilateral relative dopamine depletion. In autopsies of patients at 9, 19, and 27 days poststroke, there was a 27 to 37% increase in receptors on the lesioned side. Because the massive brainstem lesion unilaterally destroyed ascending dopamine fibers, it is very likely that the receptor up-regulation was not related to dopamine synapses; rather it is likely that it represents extrasynaptic volume transmission-related receptors.

## Drug action on the brain

Vizi(39) noted that drugs have difficulty reaching the receptors intrasynaptically. Widely used drugs in clinical practice have been developed or applied on the concept of presynaptic modulation of neurochemical transmission. He pointed out that the sensitivity of nonsynaptic receptors is higher, and they are much more accessible to drugs. Vizi(39) suggested that diffusion neurotransmission may be the primary means of activation of receptors by externally applied or administered drugs. (40)

Drug therapy and rehabilitation may induce functional recovery by influencing the affected neurotransmitter systems. Volume transmission may also be the principal mode of action of psychoactive drugs.(41) Vizi's studies on the nonsynaptic modulation of transmitter release(42,43) led him to propose(42) that the essence of brain function (eg, learning, thinking) lies not in variations of neuronal circuitry (hardware) but rather in the chemical communication itself, which is partly wired (synaptic) and partly unwired (nonsynaptic) transmission.

## Extracellular space volume fraction

The extracellular space, which averages more than 20% of the mass of the brain,(44) plays a role in many functions, including volume transmission. In an assembly of brain cells, the distance between neurons can be reduced by 50% with neuron activity that causes them to swell.(45,46) This has an effect on the excitability and metabolism of the cells by changing the distance between the neurons, which produces, among other things, changes in ionic concentrations and dynamics.(47)

Changes in the size of the extracellular volume fraction may play a role in membrane excitability in pathologic brain states (eg, brain damage), and in the survival of partially denervated neurons during the postinjury period of receptor up-regulation that can lead to reorganization of brain function by unmasking and other mechanisms. Under pathologic conditions such as anoxia, the extracellular volume fraction is reduced,[48-50] and it is also reduced (by up to 50%) in hyperexcitability, by changes in the concentration of potassium, and by epileptiform discharges.[45,46]

Brain cell swelling due to anoxia and brain trauma, leading to a decreased extracellular volume fraction, may aid in the survival of partially denervated neurons during the postinjury period of receptor up- and down-regulation, which has been shown to follow brain damage in animal models[36] as well in humans.[38] Those cells may respond to previously subthreshold stimuli, either synaptically, or by volume transmission, which generally involves activation of membrane surface receptors. However, it is also possible that hyperexcitability due to a volume fraction decrease, either independently or in combination with excitotoxic activity, may increase secondary cell death after brain damage.[51]

### Computational neuroscience

To understand the role of a low-energy neurotransmission mechanism such as volume transmission, Aiello and Bach-y-Rita[26] calculated the cost of an action potential in the brain, thus allowing us to calculate the energy savings with volume transmission. Fully synaptically connected cell assemblies-of the type Hebb[52] envisioned to explain mental states, such as thought, expectancy, interest, and attention-might exceed metabolic resources: the volume of the nerve fibers necessary to fully connect the brain synaptically would create a brain so large that it would not fit in the skull.[53]

Hebb imagined cell assemblies as modules comprising enormous numbers of neurons, each connected directly to each other. The resulting connectivity of the brain on this scale is beyond comprehension, and strongly suggests that mechanisms such as volume transmission play an important role in the brain. It is quite likely that the brain does not waste energy or space. Synaptic transmission requires nerve fibers and alternating cycles of activation-inactivation (nerve spike), which allows the nerve spikes to occur in rapid sequence, providing fine functional control. When such fine control is not needed (eg, for mass sustained functions such as hunger), it appears to be excessively costly to use the synaptic mechanism. Thus, I suggested, based on these studies, a Law of the Conservation of Space and Energy in the Brain.[54]

Hebb[52] noted that integration is fundamentally a question of timing, which has its effect in the functioning of the cell assembly and the interrelation of assemblies. He considered them to be diffuse, anatomically irregular structures that function briefly as closed systems, and do so only by virtue of the time relations in the firing of constituent cells. He could not explain the up to half-second delays, which, he noted, is characteristic of thought. However, delays are a characteristic of the volume transmission model of cell assemblies; as noted elsewhere, the initial volume transmission studies revealed delays of up to 4 seconds, which were considered to be related to multiplexing of polysensory pontine cells that could have the effect of reducing the numbers of cells needed for sensory messages.[5]

Rather than purely synaptic or purely diffusive, it is likely that hybrid neuronal networks, exhibiting varying combinations of hard-wired (synaptic) and wireless (volume transmission) connectivities, would fit into the available volume in the brain, with a significant cut in space and energetic costs resulting from removing a significant number of "hard" links (and the nerve fibers needed to connect them) and replacing them with "soft", diffusive pathways. The burgeoning field of artificial neural nets is based on the concept of a fully synaptic connected brain. However, in view of the role volume transmission may play in the brain, I have explored the development of partially synaptically connected neural nets.[25]

## LATE POSTACUTE REHABILITATION

The need for functional rehabilitation programs that are of interest to the individual patient has been discussed previously.[2,11,16,55] Such programs are designed to obtain the active, alert, motivated, and consistent participation of the patient, thus making maximum use of the patient's resources. The patient's interest and dedication add a dimension that may be lost in more formal programs. In my father's case, extensive home rehabilitation program led to significant motor recovery over a 5-year period. After extensive brain damage, the functional rehabilitation apparently unmasked previously existing pathways that, prior to injury, had not had the same relationship to the recovered functions. The damage included the destruction of the pyramidal tract, verified at autopsy 7 years later, which contained only approximately 3% of normal appearing axons scattered throughout the scar tissue. His home program emphasized very high patient participation in the continuing rehabilitation process.

In recent years, several rehabilitation programs have been tested that were specifically designed to obtain late recovery from stroke. Among these is the program of Tangeman et al,[56] who studied 40 patients from 1 to 23 years poststroke. Comments from their patients indicated that the stress of the acute stroke phase prevented them from benefiting completely from their acute inpatient rehabilitation. A period at home provided the patients with the opportunity to experience directly how the stroke affected their daily lives, and they had renewed interest in improving their skills and level of independence. Tangeman noted the appropriateness of home therapy, but chose a clinic-based program for the study for practical reasons. Tangeman demonstrated significant gains in functional measures, and concluded that functional improvement after intensive rehabilitation therapy is possible for chronic stroke patients who are at least one year poststroke.[56](p__)

Concepts of brain plasticity form the basis for late postacute neurologic rehabilitation. Plasticity is a characteristic of our lifelong existence, and thus brain reorganization is possible even many years after brain damage occurs. I have been engaged in a major effort to counteract the nihilism frequently encountered in the rehabilitation environment regarding the potential for late recovery of function. My principal research models have been late recovery from stroke, late recovery from facial paralysis, and sensory substitution for persons with blindness and other sensory losses.

I[11,57 59] have helped to establish late rehabilitation programs in Santa Cruz (Cabrillo College), CA and Madison, WI, in which most of the rehabilitation takes place at home without the need for a skilled therapist. In those programs, the physiatrist and the therapists have been specially trained to work with patients over long periods of time, to design home programs, to set the long-term goals, and to address issues such as motivation and "plateau periods."

The normal learning process is no longer thought to plateau, in the sense of reaching a final stage. Rather, it apparently progresses step-like in stages of acquisition and consolidation.[2,55] With acquisition of each skill, the patient goes through a cognitive phase that requires much concentration, an associative phase in which the patient begins to develop an internal awareness of movement and begins to work on fine control, and an automatic phase during which movement can be performed with minimal conscious awareness. In postacute rehabilitation, this learning process can be lengthy. Sequential, small, goal attainment over several months is emphasized.

Home programs are also appropriate for some cases of early rehabilitation. I have helped to explore the feasibility of home stroke rehabilitation in Sweden,[60-63] based on a pilot study[64,65] and, later, a successful prospective randomized study.[66] Results from this program have demonstrated the advantages of developing rehabilitation devices for home rehabilitation, which we are continuing in our computer-assisted motivating rehabilitation (CAMR) programs.[67]

Innovative approaches to late rehabilitation include the delivery of services within an educational model.This is particularly pertinent for late rehabilitation, because the disabled person is not sick, but merely disabled.As discussed elsewhere,[67] for more than 20 years, a community college in California (Cabrillo College) has been offering a course for students who have had a stroke.This cost-effective program offers classes in independent living skills, mobility and fitness, speech and language development, and counseling in a small group setting; in this program students choose their own functional goals. Individuals with disabilities register for educational rehabilitation classes, paying only a modest amount, and students may attend classes 4 days a week, for 4½ hours daily.The emphasis of this late rehabilitation program is on functional skill development and community reintegration activities.

### Facial paralysis

Balliet et al[68] have developed a facial paralysis home rehabilitation program that started as a research project; it has been a clinical service for many years.[11,69,70] In patients with persistent facial nerve dysfunction after surgery for the removal of an acoustic neuroma, anastomosis at cranial nerves (CN) VI to XII is a surgical option that can restore innervation to the denervated facial muscles.Although persons with anastomoses at CN VII to XII do not have brain damage comparable to persons with stroke or traumatic brain injury, they do present an opportunity in which brain reorganization can be explored and documented.The subjects will have had total VII nerve sections, followed by the anastomosis of all or a portion of the ipsilateral XII nerve to the peripheral stump of the VII nerve.The new innervation to the ipsilateral facial muscles will be from the XII nerve, and thus from the XII nerve nucleus and its cortical representation and other inputs. Willer et al[71] have provided evidence that the redirection of the hypoglossal (CN XII) to facial muscles alters central connectivity in humans, and alters the excitability of hypoglossal motoneurons.[72] Specific rehabilitation to obtain selective voluntary and automatic facial movements may further alter the connectivity and excitability of the hypoglossal neurons.

In this program, we have demonstrated that, even many years after the neural damage, a large increase in function is possible in patients with various etiologies (the majority have had facial dysfunction secondary to tumor, generally an acoustic neuroma), including those who have had anastomoses of CN XII to VII. We are able to obtain movements such as eye closure and automatic bilateral (voluntary or emotional) smile, and to facilitate the ability to eat in public without synkinesic movements; this requires reorganization of the brain, such that the CN XII nucleus and nerve, which are genetically programmed to produce tongue movements, instead control facial muscles and movements.The changed role of the afferent information and the changes in efferent outflow and the integration into the control of facial movements (including those related to emotional expression) are evidence of reorganization in the adult brain (and, therefore, brain plasticity) in response to functional demand and appropriate rehabilitation.

Facial paralysis rehabilitation is an ideal model for developing objective, quantified outcome measures. A preliminary prototype image analysis system has been developed.[11]

## SENSORY SUBSTITUTION

In 1969, *Nature* published an article entitled "Vision substitution by tactile image projection".[73] The sensory substitution studies had been initiated a number of years ago as models of brain plasticity; persons with congenital sensory loss presented a Jacksonian model (Hughlings Jackson emphasized the opportunities for discovery offered by the experiments made on the brain by disease [excerpts in Clarke and O'Malley[74]]). Persons with blindness or other sensory losses since early infancy do not have one or more of the major afferent inputs, and thus have not developed the mechanisms for analyzing information through the lost system.

Thus, a thorough study of persons learning to use a sensory substitution system, with the information from an artificial receptor delivered to the brain through sensory systems (eg, tactile) that have remained intact, offered unique opportunities to evaluate mechanisms of brain plasticity.

It has taken more than 30 years for instrumentation technology and neuroscience concepts to evolve to the level necessary for the expected major applications to emerge from those studies, but it now appears that the stage is set for those to occur.

## Tactile vision substitution

A person who has suffered the total loss of a sensory modality has, indirectly, suffered a brain lesion. In blind persons, about 2 million fibers from the optic nerves are absent. Absent a modality such as sight, behavior and neural function must be reorganized. However, blind persons have not necessarily lost the capacity to see,[(13)] because we do not see with the eyes, but with the brain. In normal sight, the optical image does not get beyond the retina. From the retina to the central perceptual structures, the image, now transformed into nerve pulses, is carried over nerve fibers. It is in the central nervous system that pulse-coded information is interpreted, and the subjective visual experience results. It appears to be possible for the same subjective experience that is produced by a visual image on the retina to be produced by an optical image captured by an artificial eye (a television camera), when a way is found to deliver the image from the camera to a sensory system that can carry it to the brain. Optical images picked up by a television camera are transduced into a form of energy (vibratory or direct electric stimulation) that can be mediated by the skin receptors. The visual information reaches the perceptual levels for analysis and interpretation via somatosensory pathways and structures.

The rest of the process of vision substitution should then depend on experience and training, and the ability of the subject to have the same control over the image capture as with eyes; thus, camera movement must be under the control of one of the subject's motor systems (hand, head movement, or any other). Indeed, we[(13)] have shown that this is possible once the blind person has learned the mechanics. This includes camera control: zooming, aperture and focus, and the correct interpretation of the effects of camera movement, such as occurs when the camera is moved from left to right and the image seems to move from right to left. After sufficient training with the tactile vision substitution system (TVSS), our subjects reported experiencing the image in space, rather than on the skin. They learn to make perceptual judgments using visual means of analysis, such as perspective, parallax, looming and zooming, and depth judgments. Furthermore, many phenomena associated with vision have to be learned; for example, when viewing a person seated behind a desk, the partial image of the person must be correctly interpreted as a complete person with the image of the desk interposed, rather than perceiving just half a person. The subjective experience is comparable, if not qualitatively identical to, vision, including subjective spatial localization in the 3-dimensional world. Even the visual illusions that have been tested (eg, waterfall effect) are the same as vision.

My studies with the TVSS have been extensively described;[(13,75-79)] the system is designed to deliver visual information to the brain via arrays of stimulators in contact with the skin of one of several parts of the body (abdomen, back, thigh).

Once the subject has learned with 1 motor system (eg, hand held-camera, thus using the corresponding kinesthetic system), the camera can be switched to another system (eg, mounted on the head), with no loss of perceptual capacity. And when the man-machine interface, the electro-or vibrotactile array, is moved from 1 area of skin to another (eg, from the back to the abdomen or to the forehead), there is no loss of correct spatial localization, even when the array is switched from back to front, because the trained blind subject is not perceiving the image on the skin, but is locating it correctly in space. Similarly, a blind person using a long cane does not perceive the resulting stimulation as being in the hand, but correctly locates it on the ground being swept with the cane, and a person writing with a pen does not perceive the contact as being on the fingers, but rather locates it subjectively on the paper.

Elsewhere we[(78,80-82)] have examined perceptual implications of our sensory substitution studies. Our principal work has been with persons who are congenitally blind. There are psychologic issues that must be addressed before a system can be practical. Thus, exploring the face of a loved one can be very disappointing, because the emotional messages that the long experience with vision have provided have not been perceived with our TVSS (similar problems are confronted by congenitally blind persons who acquire sight through surgical correction of the cause, such as congenital cataracts, that had prevented vision).

In the Bach-y-Rita and Hughes, we noted that "An understanding of the functional equivalence between visual and vibrotactile processing would have both basic scientific and practical implications, the former because it would bear on whether information for the various perceptual systems ought to be considered modality specific or amodal, and the latter because the data would suggest the possibilities and constraints for vision substitution and other prosthetic developments.… Although the early system was termed a tactile vision substitution system, we have been reluctant to suggest that blind users of the device are actually seeing".[(81)p(179)] Others[(83,84)] have not been so reluctant, claiming that because blind subjects are being given similar information to that which causes the sighted to see and are capable of giving similar responses, one is left with little alternative but to admit that they are seeing (and not merely "seeing").

### Vestibular substitution

Persons who have bilateral vestibular damage, such as from the ototoxicity of gentamicin, experience functional difficulties that include postural wobbling (both sitting and standing), unsteady gait, and oscillopsia. We developed a vestibular substitution system using a head-mounted accelerometer and an electrotactile brain-machine interface through the tongue (TVSS). The use of the TVSS produces a strong stabilization effect on head-body coordination in subjects with bilateral vestibular damage.[85] Under these conditions, we identified 3 characteristic and unique head motion features (drift, sway, long-period perturbations) that consistently appear in the head-postural behavior of subjects with bilateral vestibular damage, but are greatly reduced or eliminated with the TVSS (Tyler ME, et al, unpublished manuscript; 2002).

Subjects with bilateral vestibular damage using the TVSS reported feeling "normal" and "stable" or having reduced perceptual "noise" while using the TVSS and for short periods after removing the TVSS. The web page *http://www.buonfresco.com/Madison/mftmw.html* includes video clips demonstrating these results.

### Tactile loss

With others, I have collaborated on 2 projects to explore tactile sensory substitution for tactile loss. In the first, persons who had peripheral sensory loss from leprosy used a special glove with a single pressure transducer per fingertip, which (with movement of the finger over a surface) relayed the pattern on the fingertips to an area of skin on the forehead where sensation was intact. Within minutes, subjects were able to distinguish rough from smooth surfaces, and soft and hard objects, and were able to discern the structure (eg, curved, irregular) of the surface as if coming from the fingers. In fact, a small crack in the table surface could be detected. After 1 day of use, 1 subject expressed delight at feeling the finger contact when he touched his wife, something that he had been unable to experience for 20 years.[11,86] Thus, even though the actual human-machine interface was on the forehead, the patient with leprosy perceived the sensation on the fingertip, as his motor control over the placement of the substitute tactile sensors directed the localization in space to the surface where the stimulation originated. Under US National Aeronautics and Space Administration sponsorship, we[87] have extended this work to develop gloves for astronauts. Sensors were placed in the fingertips of gloves in order to compensate for the loss of tactile sensation that causes the decrease in manual performance.

The technology was been extended to sensory loss from diabetic neuropathy. An insole-pressure pad receptor system was developed for diabetic persons with insensate feet.[88,89] The pressure data acquisition system consisted of a pair of insoles instrumented with 14 pressure sensors, a portable microprocessor-based data acquisition system, and a microcomputer. The user wore the electrotactile array on the back of the thigh, and readily learned to recognize and use the pressure distribution information to reestablish functional postural control sufficient to stand and walk slow.

To date, our studies have been aimed at substituting for a single sensory function. However, persons with SCI suffer the loss of a number of sensory systems. We are considering the development of multiple sensory loss replacement, with multiplexed substitute sensory information. For example, using pressure points while sitting in a wheelchair, bladder filling could be signaled as background information, at a low frequency (eg, once per 30s) through a tongue interface, while the subject is using the interface for other sensory information such as touch from a robotic hand. I predict that the subject will learn subconsciously to incorporate the background data from the pressure and other sensors, taking appropriate corrective actions, which is what neurologically intact persons do.

### Human-in-the-loop

Because sensory substitution via the tongue–brain-machine interface has worked for various sensory modalities, it is likely that almost any electronically generated data stream can be coupled into the human nervous system through the brain-machine interface, and can then be experienced by the user as a direct sense perception. Applications could include the monitoring of data streams generated by industrial, commercial, and military processes (Bach-y-Rita and Kercel, in press). In a field such as industrial control, incorporating humans-in-the-loop should greatly increase speed and efficiency, and reduce fatigue. Instead of reading meters and readouts, interpreting results, and pondering what they mean about the process, the operator would experience the process by direct perception. For example, the ability to determine directly and inexpensively whether or the product meets specifications is an enormous problem for the steel industry (and for virtually all other manufacturers). A thickness gauge in a tube-piercing mill produces a thickness profile consisting of approximately 3000 numbers per tube. Interpreting the numbers to tell whether the tube is within specification is difficult and tedious. Incorporating humans-in-the-loop, the operator would experience the tube passing through the gauge in much the same way as one experiences the feeling of sliding the finger over a surface. The experience might feel smooth, or it might feel rough, or somewhere in between. The well-trained operator could distinguish directly from experiencing the perception whether the tube is smooth enough to meet standards.

Direct perception could lead to automating workers into the process, instead of the more conventional strategy of automating them out. It should also complement the present effort to engineer the human out-of-the-loop (for fully autonomous activities) and lead to greater use of systems with the human engineered in the loop (Bach-y-Rita and Kercel, in press).

## REHABILITATION ENGINEERING

Two early research projects can be considered forerunners of what now appears to be a developing area: computer-assisted motivating rehabilitation (CAMR).

In the mid 1970s, when newly introduced electronic pong games could be connected to a home television and played by 2 persons controlling individual joy-sticks, we adapted a pong game for the functional training of upper extremities of persons with a hemiparetic limb.[90] Three different hand pieces were machined to coincide with the varying grips of the stroke patients for use with a modified exercise track. A patient had to reach forward to 90° of shoulder flexion with full elbow extension to reach balls at the top of the screen. With practice, and during the emotionally involving game, the patient ceases to think of arm movements and begins to think in terms of accomplishing the goal. We noted that

The game concept helps to maintain a high level of interest, enhances motivation, and adds enjoyment to the hard work of rehabilitation.... During a pong game, the patient has an immediate goal for every movement of the arm. The patient also receives immediate visual feedback as to the accuracy of the movement.... Patients quickly find themselves absorbed in playing the game. Some patients prefer playing against the built-in computer, or against their unaffected arm. Others enjoy the socialization which develops during a game with an aide or another patient.[90]p(188)

This may have been the first clinical application of what today would be called nonimmersive virtual reality.

To produce coordinated eye movements sufficient to permit one to learn to read, in children with cerebral palsy, Gauthier et al[91] developed a functional pendulum. They had noted that the children resisted the usual therapy with a pendulum, getting bored and disinterested. They used a large projection screen, sat the child in front of it, with his head immobilized, and projected children's movies (Snow White, Mickey Mouse) from the opposite side of the screen, but in a small dimension (similar to a small television image). As the child observed the film, the image projected against a galvanometer-controlled mirror (and back-projected to the screen while the child's head was held in a fixed position) moved slowly from side to side in pendular movements. Subjects had intense 2-hour training sessions 3 times a week. As the children gained more oculomotor control, the pendular movements became larger, and faster, and other types of movements (irregular, interrupted) were introduced. Thus, various types of eye movements could be trained. With this functional training program, sessions could last 2 hours without boredom or fatigue. Marked improvement in oculomotor control was obtained.

More than 20 years after the publication of the Cogan study,[90] the second version of the CAMR was designed and built by the students of an engineering design class in Mexico.[92] In addition to controlling the game, the system can record the movements of patients' hemiparetic limb and these objective data are intended to help track patients' rehabilitation progress. Using this system, subjects practiced with the "palanca" (as version 2 has been called), controlling a computer video game, daily for 25 to 40 minutes for a total of 13 days. All subjects attended the entire 13 days, except 2, who missed 2 sessions each. All subjects participated enthusiastically in the video game activity. However, 1 subject with severe cognitive deficits due to frontal lobe damage, with poor attention to task as well as a severe left hemianopsia, required constant positive feedback and encouragement, as well as a quiet environment to participate in the activity. Patients showed a high level of concentration. One hemiparetic aged man initially refused to use the system because he did not think his arm could perform the task; but, after a short session in which he performed well, he took it home. He later demonstrated, with surprise, his ability to extend his wrist, which he had been unable to do for 22 years.[67]

In the past, we explored the use of a Nintendo Power Glove (no longer produced) for persons with hemiparetic hand dysfunction to control a video game, and the use of a Nintendo Power Pad for pregait training. In the latter, a man with hemiparesis sustained himself on the parallel bars while he stepped (with the paretic lower extremity) on a sequence of Power Pad contacts on the floor to control a video race car game. This suggests that there are many forms of "games" and other activities that interest. In the future, comparable devices are expected to be commonplace in CAMR programs, some of which will include finger movements, lower-extremity training, and other motor training.

## OBSERVATIONS

Rehabilitation medicine has a wonderful mandate: to the restoration of function. The reality of the financing of medical services has created increasing problems in fulfilling that mandate. I think we must be much more innovative; it is necessary to develop a strong scientific infrastructure and to validate treatments with objective quantitative data, but it is also necessary to develop very cost-effective rehabilitation, such as CAMR. We emphasize motivation; the patient is the best therapist, and responds best when the environment, the attitudes of the personnel,[91,92] and the rehabilitation programs are based on these conditions. Persons with disabilities should be able to follow motivating rehabilitation with minimal supervision, in home, institutional, and educational programs, taking advantage of modern technology such as videogames and the Internet. It should be routine for persons at home to interact in therapeutic programs with both the therapist and with other persons in other homes. Advances in sensory substitution should lead to sensate prostheses, sensory losses such as macular degeneration and diabetic insensate feet, the incorporation into the brain of multiple streams of sensory data from below the level of an SCI, as well as sensory augmentation such as for sensate robots for persons with SCI and for surgery.

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