

Late human brain plasticity: vestibular substitution with a tongue *BrainPort* human-machine interface

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RESUME. Plasticité cérébrale tardive : substitution vestibulaire au moyen d'une interface homme-machine *BrainPort* sur la langue. Le cerveau est susceptible d'une réorganisation majeure, même plusieurs années après une lésion, à condition que le patient reçoive une rééducation appropriée. Le cerveau, à la plasticité très élevée, répond mieux lorsque le patient est motivé par la thérapie et reconnaît ses bénéfices. L'objectif principal de cette étude est d'évaluer la faisabilité d'un système de substitution vestibulaire électro-tactile (ETVSS) et son efficacité pour la récupération du contrôle de la posture chez des patients présentant une perte vestibulaire bilatérale, que ces patients soient assis ou debout. Les patients ont été entraînés au port de la prothèse (*BrainPort*) pendant 3 à 5 jours. Ils ont ensuite perçus facilement à la fois la position et le déplacement d'un stimulus « cible » de petite taille à partir du dispositif électro-tactile posé à la surface de la langue, et ils ont interprété ces informations pour corriger et ajuster leur posture de façon à ce que le stimulus cible soit centré. Deux sessions journalières de vingt minutes permettent une significative amélioration fonctionnelle valable toute la journée.

Mots clés : plasticité cérébrale, substitution vestibulaire électro-tactile (ETVSS), réhabilitation neurocérébrale tardive, interface homme-machine, substitution visuo-tactile, transmission en volume, neurotransmission par diffusion nonsynaptique.

ABSTRACT. The brain is capable of major reorganization even many years after an injury, with appropriate rehabilitation. The highly plastic brain responds best when the therapy is motivating and has a benefit that is recognized by the patient. The major objective of this study was to estimate feasibility and efficacy of an electro-tactile vestibular substitution system (ETVSS) in aiding recovery of posture control in patients with bilateral vestibular loss (BVL) during sitting and standing. Subjects used the BrainPort balance device for a period from 3 to 5 days. Subjects readily perceived both position and motion of a small 'target' stimulus on the tongue display, and interpreted this information to make corrective postural adjustments, causing the target stimulus to become centred. With two twenty minute sessions a day significant functional improvement lasts the whole day.

Key words: brain plasticity, electrotactile vestibular substitution (ETVSS), BrainPort, late brain rehabilitation, human-machine interface, tactile visual substitution (TVSS), volume transmission, nonsynaptic diffusion neurotransmission.

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INTRODUCTION

The brain is capable of major reorganization of function at all ages, and for many years following brain damage. It is also capable of adapting to substitute sensory information following sensory loss (blindness; tactile loss in Leprosy; damaged vestibular system due to ototoxicity, or general balance deficit as result of stroke or brain trauma), providing a suitable human-machine interface is used (reviewed in Bach-y-Rita, 1995; in press). One such interface is the tongue BrainPort interface (Bach-y-Rita, et al 1998; Tyler, et al, 2003).

Sensory substitution allows studies of the mechanisms of late brain plasticity, in addition to offering the possibility of practical solutions for persons with major sensory loss. It also offers the opportunity to study brain imaging correlates of the perceptual learning with the substitute system, such as PET scan studies demonstrating that the visual cortex of congenitally blind persons reveals activity after a few hours of vision substitution training; (Ptito, et al, 2005).

In this report tactile vision substitution (TVSS) will be briefly reviewed, followed by a more extensive discussion of electrotactile vestibular substitution (ETVSS) which will include a personal report by a subject. Some mechanisms related to the therapeutic effects will be presented, followed by a brief presentation of another area of therapeutic applications of late brain plasticity.

SENSORY SUBSTITUTION

The sensory substitution studies were initiated in the early 60's as models of brain plasticity. 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 (e.g., tactile) that have remained intact, offered unique opportunities to evaluate mechanisms of brain plasticity.

a) Vision substitution

A person who has suffered the total loss of a sensory modality has, indirectly, suffered a brain lesion. In blind persons, the input from over two million fibers from the optic nerves is absent. Without a modality such as sight, behavior and neural function must be reorganized. However, blind persons have not necessarily lost the capacity to see, because we do not see with the eyes, but with the brain (Bach-y-Rita, 1972).

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 electrotactile stimulation) that can be mediated by the skin or tongue receptors. The visual information reaches the per-

ceptual levels for analysis and interpretation via somatosensory pathways and structures.

The rest of the process of vision substitution depends 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). Blind persons experience the image in space, instead of on the skin or tongue. They learn to make perceptual judgments using visual means of analysis, such as perspective, parallax, looming and zooming, and depth judgments (c.f., Bach-y-Rita, 1972; 2005; Bach-y-Rita, et al, 1969).

Although TVSS interfaces have only had between 100- and 1032-point arrays, the low resolution has been sufficient to perform complex perception and "eye"-hand coordination tasks. These have included facial recognition, accurate judgment of speed and direction of a rolling ball with over 95% accuracy in batting a ball as it rolls over a table edge, and complex inspection-assembly tasks. The latter were performed on an electronics company assembly line with a 100-point vibrotactile array clipped to the work-bench against which the blind worker pressed the skin of his abdomen, and through which information from a TV camera substituting for the ocular piece of a dissection microscope was delivered to the human-machine interface (HMI) (cf., Bach-y-Rita, 1995).

b) Vestibular substitution

Rehabilitation of subjects with bilateral vestibular loss (BVL) is extremely difficult and not possible in many cases. Intensive physical rehabilitation and compensation methods can help BVL subjects regain some ability to keep balance and posture control. However, numerous symptoms - like nystagmus, oscillopsia, inability to stand or walk on soft ground, uneven surface, stand or walk in low luminance conditions, sleep deprivation, and cognitive functional deficit are outside of current therapeutic capability.

The major objective of our study was to estimate feasibility and efficacy of an electro-tactile vestibular substitution system (ETVSS) in aiding recovery of posture control in BVL subjects during sitting and standing.

Briefly, the system includes the following: A miniature 2-axis accelerometer (Analog Devices ADXL202) was mounted on a low-mass plastic hard hat (figure 1). Anterior-posterior and medial-lateral angular displacement data (derived by double integration of the acceleration data) were fed to a previously developed tongue display unit (TDU) that generates a patterned stimulus on a 100 or 144-point electrotactile array (10x10 or 12 x 12 matrix of 1.8 mm diameter gold-plated electrodes on 2.3 mm centres) held against the superior, anterior surface of the tongue. Subjects readily perceived both position and motion of a small 'target' stimulus on the tongue display, and interpreted this information to make corrective postural adjustments, causing the target stimulus to become centred.

Thirty nine research subjects used the BrainPort balance device for a period from 3 to 5 days. The subjects included 19 males and 20 females ranging in age from 25 to 78 years, with an average age of 55 years. Etiologies of the balance disorders included, but were not limited, to peripheral vestibular disorders, central vestibular disorders, cerebellar disorders and mixed etiology.

We found two groups of ETVSS effects on BVL subjects: immediate and residual. After a short (15-40 minutes) training procedure all subjects were

capable of maintaining vertical posture with closed eyes, and after additional training (30-160 minutes) some were capable of standing with closed eyes on a soft base or in a sharpened Romberg stance.

Residual effects were observed in all subjects after complete disconnection from ETVSS. The response can be subdivided into three groups. *Short-term after-effects* were observed in sitting subjects after 1-5 minutes of ETVSS exposure and lasted from 30 sec to 3 minutes, respectively.

Long-term after-effects were observed in trained subjects (after an average 5 training sessions) after 20 minutes standing with eyes closed and ETVSS use, with stability lasting from 4 to 12 hours, as measured by standard posturographic techniques and spectral analysis. Additionally, during that period subjects also experienced dramatic improvement in balance control during walking on uneven or soft surfaces, or even riding a bicycle.

Persisting effects were demonstrated in one subject after 40 training sessions and continued for 8 weeks after the last ETVSS session. Evaluation of the results and previous studies suggests that a small amount of surviving vestibular sensory tissue can be reorganized; previous studies suggest that as little as 2 percent of surviving neural tissue in a system can serve as the basis for functional reorganization (Bach-y-Rita, 2004).

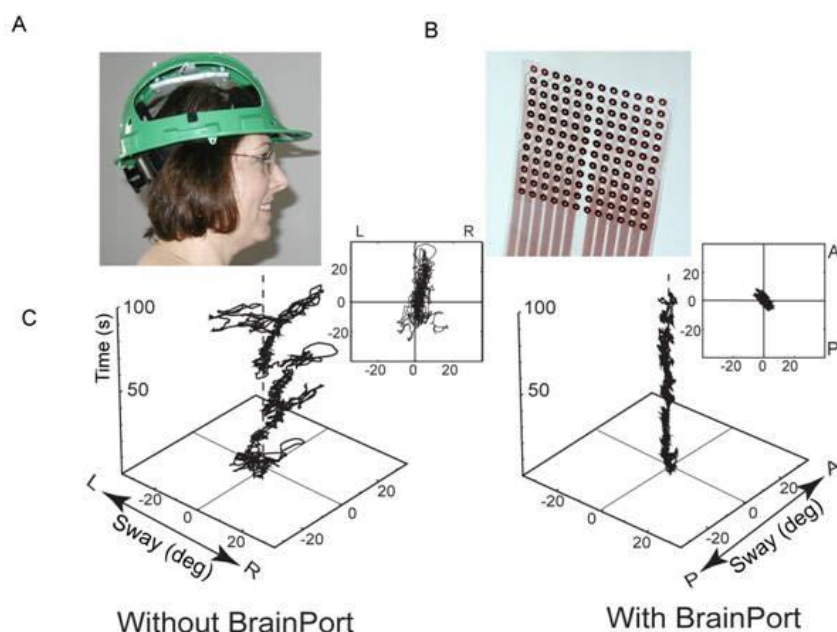


Figure 1. A – Helmet with built-in 2D MEMs accelerometer, registering the head displacement in the horizontal plane; B – Electrotactile tongue interface 144 - electrode array; C - 'Spaghetti' plots of the head horizontal displacement profiles. 3-Dimensional graphs show head position as a function of time (vertical axis). They demonstrate performance of a BVL subject without (left) and with tactile vestibular substitution (right). Insets: 2-D projection onto horizontal plane.

These studies offer behavioral and physiological data-based (Figure 1) insights into the mechanisms of reorganization and demonstrate persisting function after a period of use (Tyler, et al, 2003).

Below is the personal account of a subject:

“My name is Luann, I'm 51 and have been a wobbler since 1999 when I was given gentamycin while in the hospital. I thought I would be a wobbler forever.

Recently I participated in a one week research study at Wicab, Inc. in Middleton, WI, (www.wicab.com). The study is for people with vestibular systems damaged by gentamycin. It was a very rewarding and successful experience for me. I was thrilled to find out that I can feel “normal” again and do many things I had not been able to do for four years.

At the study a cap (helmet) was placed on my head with wires going to a TDU (Tongue Display Unit). The TDU with 144 electrodes was placed on my tongue for 20 minutes sending signals to the brain. The process is completely painless and no medication or drugs involved.

After the first 20 min. session I was able to walk a straight line, walk and turn my head to the side, I didn't need my cane for balance. I could bend down and pick up something without falling over. I could walk backwards and even spin around in a circle. Steps were so easy now.

Usually an uneven surface would throw off my balance – but now I could walk on gravel and then onto grass without feeling like my legs were rubber. I was so amazed at the difference I felt. My body didn't feel stiff and rigid any more. The buffet line at a restaurant became easy to manage. Large crowds of people were not frightening as I use to feel that I was spinning whenever in crowds.

My oscillopsia improved as the week and sessions continued. It was easier to read the newspaper. Colors seemed more vivid. My side vision improved. My mind seemed clearer and more able to carry on an intelligent conversation. My mind no longer felt foggy.

I know this may sound like something out of science fiction – but it really worked. I had two 20 min. sessions with the TDU each day. Each time the effects of the TDU lasted longer. The “normal” feeling gradually starts to fade.

Another improvement from this device was I found I was sleeping much better through the night and not waking up at 3:00 AM thinking it must be morning. I felt I had more energy and wanted to do as much as possible. My fingers even had more dexterity and I was to hook my own necklace.

The only bad part is that the wonderful “normal” feeling doesn't last very long. At the end of my week at Wicab the effects lasted about 24 hours. By Monday I was pretty much back to my same wobbly self.”

LATE STROKE AND HEAD INJURY REHABILITATION

We have designed rehabilitation programs that can be provided a year or more after the damage. The goals are to obtain functional improvement and evidence for brain plasticity, and to develop scientifically validated highly motivating rehabilitation procedures (Bach-y-Rita, 1995). Late programs have been developed for stroke and brain lesioned persons. We consider persons

receiving rehabilitation one year or more after the damage to the brain to be receiving late rehabilitation.

Among the rehabilitation approaches we have developed is a computer assisted motivating rehabilitation (CAMR) device; instead of exercise, the subject is engaged in a game (e.g., ping-pong) and with practice, instead of concentrating on the specific movements, he/she is concentrating on the game, with the movements (e.g., with a standard Herring track arm movement device) becoming sub-conscious. Subjects, even those who initially consider that they can not accomplish the task, show interest and improvement, and functional recovery appears to be extended beyond the specific movements that are trained (Bach-y-Rita, et al, 2003).

MECHANISMS OF LATE BRAIN PLASTICITY

Unmasking, closing of an abnormal open loop system, volume transmission, stimulation-produced mechanisms such as those related to long-term potentiation, and nonsynaptic diffusion neurotransmission (also called volume transmission, or VT) are among the probable mechanisms of late brain plasticity.

a) Unmasking (Wall, 1980) may play a role in the reorganization. Wall's experiments revealed pathways that exist in the normal state, but do not appear to function until "unmasked" by injury or temporary conduction block. PET scan studies in congenitally blind persons reveal that activity in the visual cortex becomes prominent with a few hours of training with the tongue BrainPort interface (Ptito, et al, 2005). These more tenuous pathways may be the type of masked pathways that are unmasked following neural lesion, if there is an appropriate rehabilitation or substitution program, and if there is the functional demand and the motivation to obtain the increased function.

b) Closing of an abnormal open loop system. In normal persons, sensory data from vestibular, visual, tactile and proprioceptive systems are integrated as linearly additive inputs that drive multiple sensory motor loops to provide effective coordinated body movement, posture and alignment. The instability resulting from vestibular dysfunction can be related to noise in a functionally open-loop control system; indeed the recordings obtained from the output of the head mounted accelerometer before, during and after training with the BrainPort support this interpretation (Tyler, et al, 2003).

c) Volume transmission. Synaptic transmission may not be quantitatively the principal means of neurotransmission in the brain: Herkenham (1987) considers that receptor-transmitter release site mismatches (in comparison to synapses, at which they are in close opposition) are the rule rather than the exception. The exclusivity of the synapse as a means of transmitting information had been questioned, when results obtained from intra- and extracellular microelectrode studies of polysensory brain stem neurons could not be fit into the prevailing connectionist theory of brain function (Bach-y-Rita, 1964). This has been called "nonsynaptic diffusion" or "volume transmission" (VT). The subject has been reviewed extensively including in Bach-y-Rita (1995; 2003).

VT plays a role in brain space and energetic efficacy, in drug actions, and in recovery from brain damage. VT may be the primary information transmission mechanism in certain normal mass, sustained functions, such as sleep, vigilance, hunger, brain tone and mood, and the mechanisms of certain drugs (Bach-y-Rita, 1994), as well as certain responses to sensory stimuli, and sev-

eral abnormal functions, such as mood disorders, spinal shock, spasticity, and shoulder-hand and autonomic dysreflexia syndromes, and drug addiction (Bach-y-Rita, 1995; 2003).

Volume transmission (VT) 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 (and possible intrasynaptic receptors reached by diffusion into the synaptic cleft). In contrast to the one-to-one, point-to-point “private” intercellular synaptic communication in the brain, VT is a slow, one-to-many, widespread intercellular communication (Zoli, et al 1999). Combinations of both synaptic and diffusion neurotransmission may be the general rule. VT may play a role in the evolution of species (Bach-y-Rita and Aiello, 2001). In brain damage, some neurotransmitter systems are up-regulated, while others are down-regulated (Westerberg, et al, 1989); thus offering a substrate for VT to have an effect in brain reorganization. Drug therapy and rehabilitation may induce functional recovery by influencing the affected neurotransmitter systems.

d) Long-term potentiation (LTP) is the strengthening (or potentiation) of the connection between two nerve cells which lasts for an extended period of time (minutes to hours in vitro and hours to days and months in vivo). LTP can be induced experimentally by applying a sequence of short, high-frequency stimulations to nerve cell synapses. The phenomenon was discovered in the mammalian hippocampus by Terje Lomo and collaborators (Andersen, Blackstad and Lomo, 1966) and is commonly regarded as the cellular basis of memory.

Multiple effects of our vestibular substitution training (balance, motor control, sleep and cognitive function recovery) can be explained, at least partially, as results of stimulation-produced potentiation. Indeed, the BrainPort stimulates the anterior third of the tongue surface with sequence of short, high frequency (50 and 200 Hz) trains of electrical impulses during 20 minutes.

Simultaneous stimulation of two groups of nerve fibers (and activation of corresponding nuclei in brainstem) - lingual nerve (projecting main sensory part of trigeminal nuclei) and chorda tympani (projecting to nucleus of the solitary tract), may produce LTP-like potentiation in multiple circuitries of brain stem (or even higher brain structures) and facilitate recovery of multiple brain functions.

CONCLUDING COMMENTS

The studies discussed here support the conceptual change occurring in the neurosciences during the last few years. The recognition that the brain is highly plastic at all ages will lead to a therapeutic emphasis on late recovery of function based on highly motivating functionally oriented programs. Furthermore, the brain deals with sensory images transformed in a neural code, and can adapt to information from artificial sensory receptors also transferred to a neural code and sent to the brain via an intact sensory pathway. Thus, with the increasing availability of miniature inexpensive technology, practical sensory substitution devices, such as for vestibular damaged, blind and deaf persons, will be commonly available.

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