### PART 3

# *Alternative Treatment Approaches to Neurofeedback*

## Hemoencephalography: Photon-based blood flow neurofeedback

Hershel Toomim<sup>1</sup>, Ph.D. and Jeffrey Carmen<sup>2</sup>, Ph.D.

<sup>1</sup>Biocomp Research Institute, Los Angeles, California, USA <sup>2</sup>Clinical psychology practice, Manlius, New York, USA

This chapter provides information about the voluntary control of cerebral blood flow as a form of neurofeedback. The formal name of the process is hemoencephalography, but we have shortened the term to HEG for ease of pronunciation. A list of FAQs (frequently asked questions) can be found at the end of this chapter. For those who are unfamiliar with the concepts involved with HEG, reading the FAQs first may make the rest of the chapter easier to understand.

Natasha had been blind for three years as a result of toxic encephalopathy. Her SPECT study showed severe hypoperfusion in the right medioposterior temporal lobe. This is exactly where face and object recognition begins. Her visual processing functions were destroyed by exposure to toxic hydrocarbon emissions from freshly laid asphalt paving in the atrium next to her art studio. Although her brain continued to receive visual input, she was no longer able to make sense out of this data. She had become functionally blind. Differential diagnosis ruled out a conversion disorder. She was certified legally blind by the Braille Institute.

Hemoencephalography (HEG) and Hyperbaric Oxygen (HBO) helped her recover her sight after three years. She now proudly drives her own car. She has 20/20 vision—better than before the toxic exposure.

#### I. HEG AS A FORM OF NEUROFEEDBACK

The training of body functions to achieve restoration to health is now broadly accessible through complex instrumentation which is capable of capturing a variety of body responses. The term *biofeedback* refers to the process of "feeding back" physiological signals non-invasively from externally reached areas of the body. The feedback has the intent of teaching control over these signals. It has a long and respected history of assisting people in the management of troublesome physiological and emotional conditions. The term *neurofeedback* is a distinctive subset

of biofeedback. It makes use of physiological signals that originate within the brain, as opposed to signals that originate from other sites such as cardiac or skeletal muscle activity. Neurofeedback includes both electroencephalography (EEG) and hemoencephalography (HEG) feedback.

Hemoencephalography (nirHEG) is the system developed by Hershel Toomim. The term, introduced by Marjory and Hershel Toomim at the AAPB annual meeting in 1995 (Toomin, 1995), implements near infrared spectroscopy (NIRS) to voluntarily control cerebral blood flow changes through increasing blood oxygen levels. The process involves the use of light in red and near infrared wavelengths (blood color) instead of magnetic fields as in functional magnetic resonance imaging (fMRI).

Passive infrared hemoencephalography (pirHEG) is the system developed by Jeffrey Carmen. This system increases voluntary cerebral blood flow changes through exerting changes in brain thermal activity. The process involves the use of light in far infrared wavelengths.

#### A. Details of nirHEG development

Near infrared spectroscopy (NIRS) emerged from the work of F. F. Jobsis in 1977 (Proctor *et al.*, 1982). Jobsis invented non-invasive infrared monitoring of the oxygen content of brain tissue and blood flow. Britton Chance, Department of Biochemistry and Biophysics at the University of Pennsylvania School of Medicine, with his students, developed significant progress in the measurement of intercellular oxidation through his systematic efforts (Chance, 1962; Chance *et al.*, 1988).

Hershel Toomim, while concurrently investigating a new field of training brain waves using an electroencephalograph, sought to understand the physical principle of how brain wave training succeeded. Toomim's study was to investigate if there was a lasting blood flow change in the brain area being trained, in line with studies by Ingvar and Anders (1976). Alas, the history of development of a line of research is frequently replete with events that block its progress. Toomim's experiment used what was at the time the gold standard of brain blood flow measurement: single photon emission computed tomography (SPECT). In this test a bolus of radioactive material is injected into a vein. As the material circulates in the blood stream some of it lodges in brain tissues where it can be detected with a radiation scanner.

The experiment was planned as follows. The experiment was to train an individual to achieve a lasting change in brain waves that could be detected by SPECT blood flow activity. The experiment required SPECT studies before and after brain wave training. Arrangements were made with Dr. Russ Hibler of the Union Memorial Hospital in Baltimore, Maryland to do the SPECT studies with two Ph.D. psychology students (Julie Weiner of N.Y. University and Jean Scammon of the University of Maryland) to conduct the experiment. As politics would have it, a new doctor was appointed to be in charge of the Nuclear Medicine Service at Union Memorial Hospital who withdrew his support. In the

meantime a Britton Chance study (Chance *et al.*, 1988), measuring brain blood oxygenation with near infrared spectroscopy (NIRS), provided an alternative method for conducting the experiment.

The spectroscope idea presented by Britton Chance's paper was a simple model for Toomim to build. Even without a stimulus, simply through self regulatory control, it was possible to easily control the readings. Testing began with volunteers who had various brain disorders such as ADHD, toxic encephalopathy, stroke, aging memory loss, depression, and even schizophrenia. Every test result turned to gold. All these people improved. One person who regained his memory wrote a testimonial saying "He has a gold mind." HEG was born! This instrument provided the makings of a new way to exercise the brain.

Toomim describes the use of the instrument experience thus: nirHEG shines a light on your brain. "A light on my brain? How can you do that?" Have you ever shone a flashlight on your palm and noticed that the dark side glows? Light travels through your tissue. Your skull is like that. It's not dark in there! It glows like a lampshade lighted from the outside. Light that gets in can also get out. Light coming out is the color of your brain.

Your brain changes color and warms when you use any part of it. Metabolism makes it warmer and bright red when you are using it, cooler and purple when you aren't. If you have seen the blood being drawn from your arm for a blood test you have seen the dark purple blood collect in the evacuated vial. On the other hand, when you cut yourself you see bright red blood. Blood turns red when it collects oxygen from your lungs or the air.



FIGURE 7.1 Present nirHEG sensor. Training area is marked by the white disc. Cerebral blood flow dynamics from the nir perspective.

Blood arrives in your lungs as used blood, a deep purple color. It absorbs oxygen and leaves your lungs bright red to begin its journey to your brain. It may come as a surprise that your brain is the most voracious user of fresh red blood in your body. Your brain weighs about three pounds, about one fiftieth of your body weight, yet at rest it uses about one fifth of all the fresh blood leaving your heart. It uses about 10 times as much blood per pound as the rest of your body.

When you use your brain it uses more blood. To keep your brain alive it has to be very careful in the way it uses blood. It keeps the blood supply to a minimum when it is at rest, and calls for more blood only in the nuclei being used at any time. When you use a nucleus it turns red. This feature has led to the important advance in the brain science we are seeing today a powerful scientific tool, the functional magnetic resonance imager (fMRI). With this instrument we can see the red areas being used at any time. We can see what parts of your brain are red when you talk, sing, or even think. Great instrument—too bad it costs so much. These are voluntary functions, right? So you can voluntarily change the color of your brain!

Now what is hemoencephalography? It is the poor man's fMRI. Hemoencephalography (HEG), literally brain blood graphics, is a form of neurofeedback whereby voluntary increases in cerebral blood flow form the basis of cerebral exercise.

Cerebral exercise has been shown to increase synaptogenesis (more synapses) and angiogenesis (more capillaries and arterioles) in rats (Diamond *et al.*, 1977). Further work with humans has reinforced this concept (Taub *et al.*, 1993; Maguire *et al.*, 2000). We now know that physical exercise improves brain function via angiogenesis, and mental exercise improves brain function by both synaptogenesis and angiogenesis. Your brain actually grows when you exercise it, just like a muscle does. It gets larger. And, like a muscle, your brain gets tired when you exercise it. Also, like a muscle, it wastes away when you don't use it. As Marion Diamond said "Use it or lose it." (Diamond, 1964). This suggests it is continually shrugging off old cells and building new ones. When the rate of loss equals the rate of cell gain, your brain is stable.

You might ask where it finds the room to grow. The brain has fluid filled spaces called *ventricles*. These spaces are filled with cerebral spinal fluid (CSF) that is continually being secreted and absorbed to maintain a constant pressure in your brain and spinal cord. New tissue displaces CSF. The growth is very small; Einstein's brain was hardly larger than the normal variation in brain sizes.

We harness HEG in the service of brain exercise. nirHEG shines a light through the skull onto the brain. Reflected light is the color of the brain. pirHEG monitors the radiation of excess thermal energy. Brain color and temperature is our clue to brain use. You can change the color and temperature at will. When you choose a brain action, like solving a problem, your brain requests more oxygen and glucose from the blood stream. As fresh oxygenated blood infuses the requesting tissue it becomes redder. As it uses the new blood-borne nutrients it warms. The increased blood flow then helps maintain thermal homeostasis in these cells. The NIR probe light, reflected from the redder tissue, informs a computer of the change in color, it warms as the new energy is used. We can harness the computer to control a display of sound and video as a lure toward more energy use. We find we can control the computer display. We get tired when we overdo it. We have a brain gymnasium!

The brain is built of many compartments, each for a basic function. Vision, for example, resides in the back of the brain. So it is with functions like speech, muscle control, face recognition, etc. Each has its own nucleus. Our brain gymnasium can work with most of these. We merely have to exercise the chosen nucleus.

A simple experiment shows the loss of efficiency due to training at a distance from the module of primary interest. Two nirHEG headbands were simultaneously activated. One was at the top of the head at Cz, and the other was just above where the eyebrows meet at Fpz. Sound feedback, the only feedback, derived from the top site, Cz, was supplied to the subject for the first 5 minutes. A high level of action at the Cz headband was measured. The sound was then switched for control by Fpz, the frontal site, without the testee's knowledge. Choice of the headband controlling the sound required the operator only to press a different computer key. The testee unknowingly, by following the feedback, activated the headband that was the source of the sound. He began with the sound from the Cz headband then, after 5 minutes, sound was switched to the Fpz headband. Activation position on the head, by brain activation, followed the sound feedback as well.

As you can see in Fig. 7.2 there was a subsequent switch in the elicited activity from the top of head site to the frontal site. During the first 5 minutes the frontal



FIGURE 7.2 The ratio of Fpz at the end of the graph to that at the end of 5 minutes is approximately 3 to 1. Treating at the prefrontal cortex for prefrontal disorders is three times more effective than training at Cz for this disorder.



FIGURE 7.3 Number of references using brain imaging for locating specified brain disorders. Note the predominance of the prefrontal cortex.

activity at Fpz increased to a value approximately one third as large as the action at the top site, Cz. After the switch this activity at Fpz rapidly increased to about the level achieved earlier at the top site, Cz. Action at the sound source, now at Fpz, is shown in the lower panel to be about three times higher than when the controlling source was at Cz.

Selection of brain nuclei to train is an art/science in itself. At first thought it seems as though the training positions should be dictated by Quantitative Electroencephalography (QEEG), and that behavioral deficits in standard deviations from normal would be a good guide. It turns out to be not so simple.

Behavioral deficits, when mapped onto brain nuclei, need emphasis not given by standard deviations. Emphasis needs to be placed on the map in deviation values that represent the behavioral importance of that position to the behavioral deficit being investigated.

The frontal lobes, especially the prefrontal region, represent the most recent evolutionary changes in the human brain. Because of this, there have been fewer iterations making "software bugs" more likely than parts of the brain that have had more evolutionary years to become refined.

As shown in Fig. 7.3 the prefrontal cortex is the most likely source of aberrant behavior. Behavior becomes a useful guide to best locate treatable areas. Efficiency of training is dependent on choice of selected brain areas. Brain areas remote from the primary origin of disorder reduce training efficiency; training in these areas requires more sessions.

However, Fig. 7.4 nevertheless illustrates that a remote effect exists. In this SPECT study, a measure of abnormal blood flow, one can see the posterior cingulate



After HEG

FIGURE 7.4 Hypoperfused (blue) area shrinks after 23 sessions of HEG training at Fp1 and Fp2. Illustrated here is the remote effect. In this SPECT study, a measure of abnormal blood flow, one can see the posterior cingulate gyrus becomes more normal even though the training was at the prefrontal cortex (see also color plate).

gyrus becomes more normal (the yellow area) even though the training was at the prefrontal cortex.

Given that behavioral deficits are the presenting symptoms, behavioral tests were applied before and after each 10 sessions as a guiding record of progress. Selected tests were MicroCog, Beck Depression Inventory, Beck Anxiety Inventory, TOVA, SCL90, and Elaine Aron's Sensitivity Test.

MicroCog, a computer administered and scored test, was selected because its subtests are readily mapped to well-known behavioral traits and point to involved brain nuclei. The advantage is that poor response on a behavioral subtest points to the brain position involved that needs improvement (Fig. 7.5).

To partially satisfy the need for a method of finding an appropriate brain training location, and also because of dissatisfaction with a single reference for training positions, Toomim developed a questionnaire in order to establish important behavioral/cognitive areas for training. He used the categories as named in the MicroCog Test, including: Mental Control, Reasoning and Calculation, Memory, Spatial Processing, Response Time, Processing Speed, Processing Accuracy, and Cognitive Proficiency to categorize behavioral/cognitive activities. Responses to the questionnaire established the behaviorally important areas reported by the patient, and helped to measure improvement in behavioral categories in relation to a scale set to 100 for changes in hemoencephalography. Details of the questionnaire can be found on the web site www.Biocompresearch.org.

The TOVA (test of variables of attention) is also useful as a measurement of behavioral/cognitive change. It was originally designed to optimize medication dosage for attention deficit disorder. The test constructs a race between two brain pathways to reach the motor strip, activation areas C3 and C4. One route,



FIGURE 7.5 Effectiveness of nirHEG brain exercise is shown in improved cognitive characteristics. MicroCog relates cognitive changes in points per session on a 100 point scale for various trained behavioral functions.

the impulsive one, has primitive evolutionary advantages in activating life-saving action with a minimum of thought. Another cognitive pathway, a later, slower development, takes time for thought. A fast brain can afford that time. If an early, timely non-response decision reaches the muscle activation area in the brain, a correct non-response can be made. Otherwise, in error, it seems the thumb on the button has a mind of its own, and an incorrect button press occurs. The number of incorrect button presses becomes the basis for a score where 100 is the score for the average number of errors made by a population of normal subjects distributed by age and education level.

#### B. Details of pirHEG development

In 1997, while Hershel Toomim was developing the concept of near infrared spectroscopy as a way to monitor cerebral blood flow, Jeffrey Carmen had been exploring the use of infrared detection without direct contact with the skin as a way to monitor body thermal behavior. Initially he had applied this concept to the task of training fingers and hands to increase blood flow. Training for increased blood flow using contact thermometry had already been well established in the biofeedback field as a training procedure for relaxation in general, and migraine treatment in particular. Training without the need for skin contact was a new concept.

The infrared detector used had a round field of view approximately 32 mm in diameter. It responded to infrared wavelengths in the 7–14 micron range, responding to signal changes with a very fast settling time of 80 milliseconds.

The results of this experimentation with infrared thermal monitoring yielded outcomes that were at least equivalent to contact thermometry and, in some cases, appeared to be more effective. There were three advantages for using a non-contact infrared system for monitoring human body thermal behavior. Firstly, the infrared sensor had a larger area of skin to which it responded. Secondly, since it was non-contact in nature it did not influence the thermal behavior of the surface being measured. Thirdly, the response time was very fast, taking about 80 milliseconds to reach 67% of the ultimate detected level.

Having validated the use of non-contact infrared technology as at least equivalent in efficacy to contact thermal training, the technology was applied to a disorder that was known at the time as reflex sympathetic dystrophy (RSD). The term has subsequently been renamed as Complex Regional Pain Disorder (CRPD) to reflect more current understanding of the mechanism. This is a condition involving extreme pain of unknown etiology. Typically a relatively minor injury produces extreme pain in part or all of a limb. Typically also, there is a resting pain level that never drops to zero, and an episodic pain level that is almost intolerable, stimulated by minimal sensory stimuli to the affected area. The extreme pain resulting from even slight skin contact precludes the use of contact thermal training, although on a theoretical basis this type of training made sense as a physiologically-based behavioral treatment for RSD.

It was hypothesized that if a person with RSD were trained to increase blood flow to the symptomatic area, pain might be reduced, and possibly the disorder itself would become less severe. The use of non-contact infrared temperature training seemed like a natural fit. It worked quite well, more or less. The technique was very effective in training the RSD sufferer to increase blood flow to the affected area. The negative side to this observation was that the increase in blood flow was accompanied by an extreme increase in pain. In essence, the treatment backfired but also validated the use of non-contact infrared technology for training control over thermal activity.

A second focus for application of pirHEG was in migraine headache events. The generally accepted theory of migraine pathophysiology involved excessive dilation of extra-cranial and intra-cranial blood vessels (Diamond, 1994). If the migraine sufferer could learn to voluntarily constrict these excessively dilated blood vessels, control over migraine activity might be achieved. However, attempts to teach people to reduce cerebral blood flow proved to be a complete failure. Physiologically this type of control may be a very difficult thing to achieve. Although cerebral blood flow responds to brain demand by increasing supply to the demand areas, the mechanism to create a local reduction in demand for blood is much less clear. To reduce localized cerebral blood flow would require reduction of brain activity in that area. It is very difficult to will a particular brain module to work less intensively, since attention to that function generally causes an increase in activity. It is the physiological equivalent to "not thinking about a pink elephant."

Concurrently with the observation that training people to reduce cerebral blood flow was very difficult, the theories of migraine pathophysiology began to change (Goadsby, 2001). The newly evolving theories centered around excessive brain excitability and irritability. Blood vessel behavior was hypothesized to be a correlate rather than a cause of migraine pain. Also, at about this same time, Carmen became aware of Toomim's work using NIR technology to train increases in brain activity in the prefrontal cortex.

Toomim observed that when individuals learned to increase brain activity in the prefrontal cortex, using the NIR technology, global brain control improved. Carmen hypothesized that it might be possible to achieve a similar training effect using non-contact infrared technology, and that the improved brain function might in some way be helpful with migraine management. This hypothesis was consistent with the newer theories regarding migraine pathophysiology. The effects turned out to be even stronger than anticipated. Toomim had been correct on two points. Firstly, it became clear that it was very easy to learn to increase brain activity using blood flow as a dependent variable. Secondly, increases in brain activity in the region of the prefrontal cortex resulted in a brain that functioned under better self-regulation.

This somewhat convoluted but serendipitous series of events led to a convergence between the ideas being explored independently by the two authors. They met for the first time at the Society for Neuronal Regulation conference in 1999, at which time they began to share ideas and plan cooperative research.

Carmen continued to develop this process with a major emphasis on the treatment of migraine headaches. In 2004 Carmen reported on the treatment of 100 migraine patients, using the passive infrared process. The reported effect for the more than 90% of migraine sufferers who continued for six sessions was a significant improvement in their migraines (Carmen, 2004).

Carmen reports the following as treatment guidelines: "I have established the following treatment guideline for session frequency and number of sessions. Once symptoms stabilize, I start to spread out the number of days between sessions. This process continues until or if the symptoms start to return. The effect of this process is that some people will end up needing to have practice sessions indefinitely, while others spread appointments out quickly, stabilize and never need another session."

## C. Cerebral blood flow dynamics from the PIR perspective

The electromagnetic spectrum represents a continuum. Although all the wavelength bands have some characteristics that they share with all the other bands, there are also characteristics unique to each band. For example, X-rays can penetrate living tissue and can be recorded when they exit. Microwaves do not pass



FIGURE 7.6 This is the current pirHEG sensor mounted on the forehead at Fpz, effectively covering a field of view 32 mm high by 46mm wide.

through living tissue, but produce a heating effect as they transfer energy to the tissue. Within the infrared range of wavelengths (wavelengths longer than visible red light), NIR is close in frequency to visible light, but carries very little information regarding thermal activity. The wavelengths used by PIR are longer, and respond to changes in thermal activity, especially in the range of human body temperature.

The signal acquisition in the PIR system represents a conversion of excess brain thermal activity into a temperature equivalent. It is a very sensitive system for measuring and feeding back changes in regional thermal output of the brain. Its main usefulness is in "exercising" brain function. The underlying physiological mechanism is cellular metabolism. The dependent variable that is being measured to reflect these metabolic changes is cerebral blood flow. It is the change in regional cerebral blood flow that accounts for most of the transfer of thermal energy from metabolizing cells to the external environment.

The mechanism of infrared radiation and detection of this metabolic thermal waste product has been intensively studied in the rat brain by Shevelev (1992), and the human brain (Shevelev, 1998). He found a high degree of correlation between localization of thermal activity and localization of conditioned neural responses. He determined the relative contribution of increased thermal output to be predominantly a function of local cerebral blood flow increases with a smaller but significant contribution coming directly from local metabolic activity.



FIGURE 7.7 The wavelengths used in the NIR system are shorter than those used in the PIR system. The primary difference between short wavelength infrared and long wavelength infrared is that the longer wavelengths are sensitive to heat in the range of human body temperature whereas short wavelength infrared is insensitive to heat in that range. Both systems are based on photon detection, making them immune to electrical signal artifacts. By contrast, EEG neurofeedback is based on electron detection (see color plate).

There are parallels between the infrared detection system used with pirHEG and those infrared detection systems that already exist in nature. The PIR infrared sensor functions in a very similar manner to the infrared detection system of the pit viper. The pit viper monitors environmental thermal changes through the use of an infrared sensing organ. With this detection system, the pit viper monitors changes in the thermal environment produced by the motion of prey animals. In a similar manner, the PIR detector monitors changes in the environment. However the environment of interest is inside the skull, and the changes are the result of brain activity variations rather than physical motion.

For training purposes, the PIR headset detects changes in infrared radiation from the forehead. This radiation rises and falls with changes in regional cerebral blood flow, which in turn rises and falls in response to changes in regional cellular metabolism. The training signal is converted into analog and digital information that the individual can easily interpret. However it is not very useful as diagnostic data. The useful diagnostic data gets lost in the process of averaging across a large field of view for the purpose of feedback. Useful diagnostic data can be obtained from an infrared camera that presents pictures of the patterns of prefrontal cortical blood flow as the excess heat exits the forehead.

In terms of the specific signal components, some of the IR signal originating from brain tissue passes directly through the skull and surface tissues, and radiates directly into the environment in much the same way the beam from a flashlight would pass through a piece of translucent plastic. Secondly, some of the signal is absorbed by the skull and surface tissue as heat, which then gets reradiated as infrared. The pirHEG system measures a complex composite of these two signals.



FIGURE 7.8 The wavelengths used in the PIR system are between 7 and 14 microns. The Pit Viper uses this portion of the electromagnetic spectrum for hunting. Image reproduced with permission from Exergen Corporation (Pompei and Pompei, 1996).

Since it measures only wavelengths longer than visible light, the visible intensity of light in the room has no effect on the signal.

Carmen's original work with the PIR system involved focal sensor placements that were consistent with the symptoms of the patient. He abandoned this focal approach in favor of a single Fpz placement for all interventions. Others using the PIR system have continued to use a variety of placements. Both approaches produce positive effects. The probable reason for the positive effects of the Fpz placement is that it picks up a large portion of the prefrontal cortex, and has the effect of gently increasing smooth arousal regulation. Toomim has followed a different path. He began his work mostly targeting brain areas directly under the forehead, but in recent years has begun to target a wide variety of brain locations.

#### D. Infrared thermography

#### Using the Infrared Camera to Monitor Localized Changes in Brain Function

A very useful technique for monitoring cerebral blood flow in the prefrontal cortex is the use of infrared thermography. By definition, long wave infrared signals have no perceptible color when viewed by the human eye and, in fact, are not detectable by the human eye. However, some specially designed cameras are sensitive to those wavelengths. The use of such a camera can help monitor brain activity in those parts of the skull that are not covered by hair. The pattern changes viewed by this type of camera are meaningful as a pre-/post-session measure, and also as a change measure over multiple sessions. For people who are not bald, the area that is most easily monitored is the forehead. Fortunately the forehead is in the very front of the frontal lobes, which is a region of special interest.

This first image (Fig. 7.9) is the first stage of a precision infrared image capture. The camera captures wavelengths between 7 and 14 microns, and registers them on a grayscale with a  $320 \times 240$  pixel resolution. The two image sequence is presented as an example of the type of precision the infrared camera is capable of providing.



FIGURE 7.9 Calibration gives all images a common thermal reference (see color plate).



FIGURE 7.10 The final step in the sequence is the introduction of *false color*. This is called *false color* because wavelengths in this frequency have no color. The computer injects the color to make it easier for human interpretation of the image. This is an image of a "normal forehead." (see color plate)

Although the use of an infrared camera is not an essential part of the pir HEG system, its use can provide real time monitoring of cerebral blood flow changes. Both Hershel and Carmen have been using infrared imaging technology to monitor brain activity changes.

#### Using the Infrared Camera to Record Pre-/Post-Treatment Effects

One of the unanticipated benefits of developing the two separate HEG systems independently has been the evolution of different diagnostic and treatment styles. While Toomim emphasized cognitive testing and SPECT imaging to monitor treatment effects, Carmen developed a method of imaging brain activity in the prefrontal cortex by using an infrared camera. This is performed before and after each session. One of the fascinating aspects of this imaging is that it is very easy for a person to attribute meaning to the image. After a few sessions, people tend to be able to report what the image will look like prior to capturing the image. Typically, productive sessions produce a reduction of thermal variability in the image. Typically also, the baseline image taken before each session shows similar reductions in variation over time, paralleling symptom improvement.

Typically, for individuals who are left lateralized for language, dark areas on the forehead represent areas of relatively low brain activity. Dark areas in the center of the forehead are seen in individuals with attentional and emotional control difficulties. The dark region over the left eye is often seen in individuals with depression, however in this instance it is indicative of his language function difficulties rather than depression. Images must be captured without the person talking; otherwise the language side of the forehead produces too much thermal energy to



FIGURE 7.11 This is an example of a pre-session image captured with infrared camera. This image is of a 16-year-old male with severe concentration problems and severe word finding problems (see color plate).



FIGURE 7.12 Post-session image. Previously dark areas on the forehead are lighter. Previously light areas on the forehead are less intense. There is less variability across the forehead. In this postsession image, the pinna of the left ear has a large increase in thermal output. Sometimes it is seen on the non-language side instead. Research on temperature changes of the pinna has not confirmed its meaning, although the general consensus is that it is probably related to language activity (Schiffer, 1998) (see color plate).

capture subtle patterns. Talking during image capture can represent artifact since it hides the baseline image, but because of that effect infrared imaging can also be a useful tool for helping to determine language lateralization.

Of equal importance to the reduction of thermal variability is the change in symptoms, even in such a short period of time. After a 25-minute pirHEG session, this young man's word-finding problems cleared up completely, and attentional patterns normalized. It is important to realize that the improvement initially does not last more than a day or two. That was the case here. In some situations, the symptoms eventually subside and don't reappear. However in other situations such as this one, the symptoms remain under control for a limited length of time. He can manage excellent symptom control for three to four weeks, after which the control fades.

With continued practice there are permanent improvements in brain function causing behavior patterns to permanently change. However, under intense stress people tend to revert to older stable behavior patterns. In other situations, the older stable behavior patterns are so strong that even without intense stress these patterns tend to re-emerge. This last response pattern describes the young man in these images. In his case he obtained his own HEG system, and practices with it when he feels the need.

#### II. A NEW PARADIGM

HEG represents a new paradigm. The two described techniques use light to access brain changes. They differ in the colors of light they use. Both depend on recording

changes in characteristics of blood when changed during the course of brain metabolism. Carmen's PIR instrument measures the thermal waste product of cellular metabolism that is emitted through the forehead. This system uses long wavelength infrared light in the range of 7–14 microns (wavelengths sensitive to body temperature). Toomim's NIR instrument uses relatively short wavelengths, 680 and 850 nanometers (wavelengths sensitive to color). Blood warms and changes color as it is used as a result of oxygen and glucose metabolism. The generation of heat is also the result of oxygen and glucose metabolism.

The process of passive infrared hemoencephalography (pirHEG) seems similar in response characteristics and effects to the near infrared hemoencephalography (nirHEG) system. Reports from clinicians who have used both suggest similarities; especially similar responses to cognitive focus. As cognitive focus increases so does the signal. Experience with both systems suggests that the cognitive and affective state that produces a signal increase in the PIR system will also produce a signal increase in the NIR system.

One of the differences between the two systems is the size of the area of brain activity being monitored. Toomim's work has evolved in the direction of specificity of site monitoring, with a sensor that can target specific areas. Carmen's work has evolved in the direction of generalized monitoring, creating a sensor that has a very large field of view. Consequently, some of the differences in function between the two systems can be attributed to sensor specificity.

HEG has been used successfully in the treatment of attention deficit hyperactivity disorder of the inattentive and also hyperactive type, autistic spectrum disorders, bipolar disorder, traumatic brain injury, age-related memory loss, stroke, migraine headaches, epilepsy, Tourette's disorder, obsessive compulsive disorder, depression, schizophrenia, and toxic encephalopathy. We should point out that we are not typically talking about curing these disorders. We are talking about an intervention that reduces their severity, albeit sometimes dramatically so.

All these disorders (and many others) share a common element. Along with other symptoms, they represent a response by the brain to relatively minor stimuli that is excessive in terms of both rate and magnitude. This suggests that increasing the level of control the brain exerts over its own activities may be useful across a wide variety of disorders or dysfunctions.

We have learned that brain exercise via HEG has beneficial results. We have also learned that an approach that is too aggressive has the potential to produce side effects. The number of sessions, selection of brain nuclei, duration of sessions, and client sensitivity must all be considered in any treatment plan. Side effects will be discussed separately in this chapter. Typically they represent over-training or exhaustion of the area being targeted.

To avoid confusion in describing the concept of hemoencephalography, we decided to give suitable names to these two instruments. Toomim's system uses near infrared light and thus became known as *nirHEG*. Carmen's system required no light source and was passive, so in this regard it became known as passive, pirHEG.

pirHEG differs a bit from nirHEG in the nature of the cognitive and affective approach to increasing the signal output. For a person to increase the output of the PIR signal requires a simultaneously high level of "mental effort" (Pribram and McGuinness, 1975), combined with a relaxed, non-frustrated emotional state. Of particular interest is the effect of frustration. Even a very small level of frustration blocks the signal from increasing or may even produce a signal decrease. However, relaxation in the absence of mental effort has the same effect. The process requires a simultaneous combination of mental effort and a relaxed affective state. nirHEG is similar but is a little more tolerant of emotional discomfort. This may be due to the difference in technology or the difference in the volume of brain tissue monitored. At this point it is unclear which difference is responsible.

#### A. Human frontal lobes and behavioral pathology

The frontal lobes are the most recent evolutionary development of the human brain. The frontal lobes probably began to take their present form around 50,000 years ago (Jerison, 2007). In terms of evolutionary development, human frontal lobes have not had much time to be refined. Using a software analogy, the frontal lobes are still in "beta" format.

One of the major functions of the prefrontal region of the frontal lobes is smooth regulation of other brain modules so that they all work together. Damage or dysfunction of this region allows other modules to operate in an unregulated manner. In reviewing the DSM IV (American Psychiatric Association, 1994), it can be seen that many if not most of the diagnostic categories represent excesses of rate and magnitude in response to stimuli that are not very significant.

The latest hypotheses accounting for the aberrant action noted by the QEEG is that the prefrontal cortex determines the linkages between modules. Failure of this executive control system to adequately control the applicable modules results in improper operation of these modules. Unregulated brain modules operate in a manner inconsistent with a smoothly functioning organism.

For daily activities that are not emergency response activities, the brain works best when excitation and inhibition are smoothly regulated. This has often been named the "executive" system (Goldberg, 2001). It permits and favors careful thinking and analysis of life's challenges. This regulation is initiated in and regulated by the prefrontal portion of the frontal lobes. When the prefrontal cortex is functioning in a sub-optimal manner, the relationship between excitation and inhibition is compromised, resulting in other brain modules operating in an independent, unregulated manner.

A literature search for prefrontal cortex executive yielded 137,000 responses. A typical response: Tomita and Hyoe (1999) "The prefrontal cortex in intimately involved in emotion, memory, judgment, and error detection." Also it is noted

that: "Interactions between the thalamus and the cortex mediate shifts in our states of consciousness, the sleep-wake cycle, quiet rest, or attention. Imbalances in the communication between thalamus and cortex is at the core of a host of psychiatric and neurological conditions. Yet, most of our ideas about thalamo-cortrical communication are based on sensory systems, but little is known about high-order association areas of the cortex that govern our thoughts, emotions, and actions" (Zikopoulos and Baras, 2007).

The frontal lobes, especially the prefrontal lobes, manage the balance between activation and inhibition for the rest of the brain (Chow and Cummings, 2007). As HEG science and clinical efficacy advance more and more, selection of training areas must follow the advancing understanding of brain functional connections. A recent advance has taken the thalamus and basal ganglia into consideration. The thalamus is controlled via the basal ganglia. We all know how we can focus attention at will on whatever we want. There must be some brain nucleus that makes focus possible. Now, evidence is available that the basal ganglia are involved in focus. It connects prefrontal areas to the thalamus. The thalamus is an information distributing nucleus. Except for the sense of smell all sensory organs send their information to the thalamus. From the thalamus information is distributed to function specialized nuclei.

We are all familiar with the highly variable intensity we perceive from our senses. The perceived intensity is controlled by the thalamus. We are also well aware that we can change the perception intensity at will by merely focusing on what we want to investigate. Two primary prefrontal areas have been found to activate separate individual basal ganglia focusing connections to the thalamus. One frontal position intensifies our responses while the other quiets these responses. These prefrontal areas are Brodmann's area 9, AFz, for quieting instructions to the thalamus, via the basal ganglia and the subthalamic nucleus, and the orbitofrontal areas between the eyebrows, Brodmann's areas 11 and 12, AFpz, then to the basal ganglia and thence to the subthalamic nucleus of the thalamus.

The thalamus, on receiving appropriate stimulation, then distributes intensitycontrolled activation to function-specific nuclei in the cortex. With these two functions we have an accelerator between the eyebrows to intensity activity, and a brake at the middle hairline to quiet cerebral activity. These two areas serve in a balancing act to maintain an appropriate equilibrium between excitement and passivity. From the standpoint of neurotherapy we can arrange an appropriate balance by using nirHEG to appropriately adjust the tipping point between these levels (Viamontes and Beitman, 2007).

If the prefrontal cortex is functioning in a sub-optimal manner, improving its function will improve self-regulation. Even if the prefrontal cortex is functioning adequately, increasing the level of inhibition may also compensate for malfunctioning brain modules far removed from the front of the brain as illustrated in Fig. 7.2 (Toomim and Carmen, 1999).

#### III. BASIC HEG CONCEPTS

A summary of the basic concepts which can be gleaned from this chapter is as follows:

- 1. The brain is very plastic and has been shown to change as required to enhance its ability to deal with a challenge.
- 2. Brain exercise is a basic brain repair and growth promoting technique. Education level increases age of AD onset. Physical exercise increases brain angiogenesis. Brain exercise increases synaptogenesis and angiogenesis. Memory increases correlate with synaptic number increase. Brain nuclei volume has been shown to increase with brain use.
- 3. Brain activity can be measured non-invasively by cerebral tissue oxygenation and by brain blood temperature. fMRI measures the magnetic moment of deoxygenated hemoglobin and is an accepted scientific standard of brain activity. Blood temperature has been shown to correlate highly with brain metabolism. The Fick method of measuring energy use of the brain, the gold standard, depends on oxygen depletion in exiting venous blood vs. newly entering arterial oxygenated blood.
- 4. Brain activity is controlled voluntarily. Every voluntary body action or thought is consciously controlled. Body action/thought can be initiated by intent. Blood flow increases in affected brain nuclei to supply the energy that fuels the brain for life support, actions and thought.
- 5. Brain tissue oxygenation is easily measured by an external light operated spectrophotometer. Brain blood temperature, affected by brain metabolism, can also be used to train brain improvement. It is measurable with an infrared radiation sensitive thermometer.
- 6. With guidance from the blood flow or temperature mediated measurements, brain blood flow can be increased at will to levels beyond those reached in normal living. This is easily demonstrated with use of oxygen or temperature measuring instruments. We hypothesize that this higher than normal activity in the prefrontal cortex allows the brain to manage other brain modules that may otherwise malfunction.
- 7. Oxygen increase measurements with an external infrared spectrometer, voluntarily raised to maximum, routinely exceed 10% and have been shown to increase 100%.
- 8. Published studies have shown clinical improvements in brain function resulting from repeated brain exercise guided by temperature or oxygenation measurements.

#### A. Cautions, precautions, side effects

Although both authors are very enthusiastic about the use of this new technology, any system capable of having a powerful effect on the human brain has also, by definition, the ability to cause problems. Both forms of HEG have similar side effect profiles. Although the exact mechanism of these side effects remains unknown, most are consistent with the symptoms that would be expected from fatigue of the prefrontal cortex.

Headache: This is an interesting phenomenon because although it is described as a "headache," people often report that there is no real pain. The sensation is that of frontal throbbing rather than actual pain. It is likely that this represents a perception of a sensation with which the person is unfamiliar, and is due to increased cerebral blood flow to the prefrontal cortex. The sensation usually dissipates within one minute of stopping the session. This may not be due to frontal fatigue as much as the presence of an unfamiliar sensation.

Fatigue of the prefrontal cortex: If someone is trained for too long or too intensively, especially during the first session, that person may experience a general loss of self-regulation for the balance of that day. The symptoms are usually an exaggeration of the person's typical symptoms. Support for the hypothesis of frontal fatigue comes from the fact that the following day, after a night's sleep, the symptoms are dramatically reduced.

Difficulty initiating and maintaining sleep: It is unclear if this represents excessive arousal or failure of inhibition. Typically the person leaves with a high level of mental alertness but has difficulty sleeping that evening. This is especially true if the first session takes place late in the day. The effect is dimished after the first few sessions. The solution is to conduct the first few sessions in the morning if at all possible.

#### B. Overall training guidelines for both HEG systems

*Applications*: Both forms of HEG have been applied to a wide variety of conditions and disorders. It is becoming apparent to both of us that people who have focal brain modules that are malfunctioning, and people with arousal and inhibition difficulties, are likely to benefit from a trial with HEG technology.

Sensor location: Training locations should be carefully selected, based on current scientific knowledge of brain function. This is likely to change as knowledge of brain mechanisms becomes more precise. Both PIR and NIR systems can be used to target localized brain functions. The NIR system design is more efficient at targeting small areas while the PIR system is more efficient at targeting large areas. Hershel has primarily emphasized targeted placements while Jeff has primarily emphasized a frontal central training location.

*Intensity and duration*: The intensity and duration of training during each session should be guided by sensitivity and gentleness. Aggressive training is more likely to produce temporary side effects with no increase in training effectiveness.

Session frequency: Acceptable gains, possibly even maximum gains can be obtained with a frequency of once per week. HEG effectiveness is based on brain growth. Sessions that are too close to each other may not allow sufficient time to recover from brain exercise. The exact recovery and growth time varies with each individual, but sessions that are more frequent than twice a week are probably not a good idea.

Because some readers may be more familiar with EEG technology and dynamics than HEG, we decided to end this chapter with FAQs (Frequently Asked Questions). The answers will be provided by each of us, which will serve to demonstrate similarities and differences in personal perspectives as well as instrumentation.

#### IV. FREQUENTLY ASKED QUESTIONS

Q: I have heard that PIR measures brain temperature. Is that true?

Jeff: No, at least not in the strictest sense. Having the display look like temperature was in retrospect a mistake, but it is too late to undo it. What is being measured is a thermal waste product from increased levels of cellular metabolism. This process of getting rid of extra heat is what keeps brain cells from overheating. The bare human forehead makes a nice exiting location for excess heat, as well as a convenient location for PIR and NIR sensors.

Q: If PIR measures thermal waste, what does NIR measure?

Hershel: nirHEG measures the color of brain blood flow. Higher demand placed on a brain requires energy to maintain life. The brain lives on glucose (sugar) and oxygen. Increased demand speeds the flow of capillary blood. Fresh blood enters the capillaries and brings oxygenated blood to the neural network. Fresh oxygen colors the brain red. In nirHEG we strive to make the brain as red as possible. With this effort we voluntarily speed blood flow and thereby exercise the targeted brain module. This is a natural activity. We do it all the time. We breathe life into our brains to solve problems, experience love, even to move.

Q: Can a person really be trained to directly control cerebral blood flow?

Hershel: No. This is a common misunderstanding of HEG. Both forms of HEG monitor changes of blood flow. However it is cellular activity, not blood flow, that is being trained. Using other means of inducing increases in cerebral blood flow does not alter focal symptoms.

Jeff: We agree on this. It is even possible that a person cannot be trained to directly control either cerebral blood flow or brain waves. Both blood flow and brain waves represent dependent variables. They are responses to brain cellular demand. However they are reliable in their response, and make convenient data to measure. In both cases, what is being trained is brain cellular activity rather than the dependent variables being monitored.

#### Q: Why does the brain demand localized increases in blood flow?

Hershel: Blood supply is determined by the load put upon localized areas. Often, in distant brain modules, poor operation can be traced to poor prefrontal control (see Fig. 7.7). Locating the most efficient training position is a science in itself largely dependent on existing prefrontal cortex nerve trunks and brain physiology.

Jeff: It is well known that the increase in blood supply is a response to increased cellular requirements for oxygen and glucose. What is less well known is that an equally important function is thermoregulation. A brain that overheats is at risk of self-destruction. Increased blood flow is one way to help maintain thermal stability. Humans have a forehead that is free from body hair, making the forehead a useful location from which excess brain heat can be transferred from within the skull to the external environment.

Q: Where on the head are the HEG sensors placed?

Hershel: NIR training is very targeted, based on symptoms and localized brain mechanisms. The forehead has widely varying effective areas. Each has a clearly defined function. There are areas for increasing and others for decreasing activity, areas for right brain emotional and others for left brain logical enhancements. The choice of training areas is determined by the needs of the client.

Jeff: This is an area in which Hershel and I have moved in opposite directions. Initially, I tried to apply PIR technology over a wide variety of skull placements based on neuropsychological assessment. This made intuitive sense. However, the strongest effects I found were always from frontal placements. For reasons partially related to differences in language lateralization, I have standardized on sensor placement at Fpz. It is possible to run into trouble by training the wrong side of the brain if the person has language lateralization on the right side of the brain rather than the left. Depression is one serious example in which training on the "wrong" side of the brain may worsen symptoms. Maintaining the sensor at Fpz avoids that problem. Another possible reason for my observations regarding differential placement effectiveness is the difference between PIR and NIR technology. PIR lends itself to monitoring larger more generalized changes whereas NIR lends itself to very focal measurement.

Q: What do you mean by generalized versus focal sensor placement?

Hershel: nirHEG lends itself beautifully to targeted placements. Because of the relatively small volume of brain tissue activity monitored, it can selectively monitor brain activity in a specific area while ignoring brain activity in adjacent areas. This can be very valuable in treatment of stroke where there is a penumbra of viable tissue surrounding the scar tissue damaged by the stroke.

Brain modules normally talk to each other. In autism, viable brain modules are often isolated from other brain modules by inadequate nerve connections. Activating viable brain modules wherever they exist, that often have never been used, exercises the connecting nerves and aids in development of supporting brain areas. Jeff: pirHEG has a relatively large field of view. The original sensor monitored a circular area with a diameter of about 32 mm. The new sensor developed in 2007 monitors the same vertical response but expands the horizontal response to a 46 mm wide oval. It may be that the large volume of brain activity monitored lends itself more to a single central placement.

Q: So, if these two systems are so different, which one is better to use in a clinical setting?

Hershel and Jeff: This is an area in which we both completely agree. We feel there is a place for each type of technology, and that ideally a clinician should have access to both. Now, if you are new to HEG, reading these FAQs may help make the details of this chapter make more sense.

#### REFERENCES

- Albert, T., Painted, C., Wienbruch, C., Rockstroh, B. and Taub, E. (1995). Increased cortical representation of the fingers of the left hand in string players. *Science*, 270, 305–307.
- Amen, D. G. (1994). New Directions in the Theory, Diagnosis, and Treatment of Mental Disorders: The Use of SPECT Imaging in Everyday Clinical Practice. In *The Neuropsychology of Mental Disorders* (L. F. Koziol and C. E. Stout, eds), pp. 286–311. Springfield, IL: Charles C. Thomas.
- American Psychiatric Association (1994). Diagnostic and Statistical Manual IV. Washington, DC.
- Bednarczyk, E., Remier, B., Weikert, C., Nelson, A. and Reed, R. (1998). Global blood flow, blood volume, and oxygen metabolism in patients with migraine headache. *Neurology*, **50(6)**, 1736–1740.
- Berger, H. (1929). Das Electroenkephalogramm des Menchen. Archive fur Psychiatrie und Nervenkrankheiten, 87(40), 160–179.
- Buchsbaum, M. S., Kessler, R., King, A., Johnson, J. and Capeletti, (1984). Simultaneous cerebral glucography with positron emission tomography and topographic electroencephalograph: Brain ischemia: quantitative EEG and imaging techniques. *Progress in Brain Research*, 62, 263–370.
- Carmen, J. A. (2002). Passive Infrared Hemoencephalography: Four years and 100 migraines later. Paper presented at Society for Neuronal Regulation annual conference, September, Scottsdale Arizona.
- Carmen, J. A. (2004). Infrared Hemoencephalography: Four Years and 100 Migraines. Journal of Neurotherapy, 8(3), 23–51.
- Chance, B., Cohen, P., Jobsis, F. and Schoener, B. (1962). Intracellular oxidation and reduction in vivo. *Science*, 137, 499–508.
- Chance, B., Leigh, J. S., Miyake, H., et al. (1988). Comparison of Time-Resolved and -Unresolved Measurements of Deoxyhemoglobin in Brain. Proc. Natl Acad. Sci., July, 85(14), 4971–4975.
- Chow, T. W. and Cummings, J. L. (2007). Frontal-Subcortical Circuits, 25–43, in Miller, B. L. and Cummings, J. L. (eds.) The Human Frontal Lobes, second edition. The Guilford Press, New York.
- Diamond, M. C., Kretch, D. and Rosenzweig, M. R. (1964). The effects of an enriched environment on the histology of the rat cerebral cortex. J. Comp. Neurol., 123, 111–120.
- Diamond, S. (1994). Head Pain: diagnosis and management. Clinical Symposia, 46(3), 2-34.
- Goadsby, P. (2001). Pathophysiology of headache. In Wolff's Headache and other Head Pain (S. Silberstein, R. Lipton and D. Dalessio, eds), 7th edition, pp. 57–72. New York: Oxford University Press, Inc.
- Goldberg, E. (2001). The executive brain. New York: Oxford University Press, Inc.
- Gratton, G., Maier, J. S., Fabiani, M., Mantulin, and Gratton, E. (1994). Feasibility of intracranial nearinfrared optical scanning. *Psychophysiology*, 31, 211–215.
- Gratton, G., Corballis, P. M., Cho, E., Fabiani, M. and Hood, D. C. (1995a). Shades of gray matter: Noninvasive optical images of human brain responses during visual stimulation. *Psychophysiology*, 32, 505–509.

- Gratton, G., Fabiani, M. and Corballis, P. M. (1995). Can we measure correlates of neuronal activity with non-invasive optical methods? Optical Imaging of Brain Function and Metabolism: Physiological Basis and Comparison to other Functional Neuroimaging Methods. In Advances in Experimental Medicine and Biology (A.Villinger and U. Dirnagel, eds). New York: N.Y. Plenum Press.
- Gratton, G., Fabiani, M., Friedman, D., et al. (1995). Rapid changes of optical parameters in the human brain during a tapping task. J. Cog. Neuro Sci., 7(4), 446–458.
- Grey, and Walter, W. (1964). Contingent negative variation: An electrical sign of sensorimotor association and expectancy in the human brain. *Nature*, 203, 380–384.
- Hoshi, Y. and Tamura, M. (1993). Detection of dynamic changes in cerebral oxygenation coupled to neuronal function during mental work in man. *Neuroscience Letters*, **150**, 5–8.
- Hoshi, Y. and Tamura, M. (1994). Multichannel near-infrared optical imaging of brain activity. Neuro Science Protocols, 94-070-04-02-15.
- Ingvar, B. S. and Anders, A. (1976). Correlation between dominant EEG frequency, cerebral oxygen uptake and blood flow. *Enceph. Clin. Neurophysiol.*, 41, 268–276.
- Janzen, T., Graap, K., Stephanson, S., Marshall, W. and Fitzsimmons, G. (1995). Differences in baseline measures for ADD and normally achieving preadolescent males. *Biofeedback and Self Regulation*, 20(1).
- Jerison, H. J. (2007). Evolution of the Frontal Lobes. In (B. L. Miller and J. L. Cummings, eds). The Human frontal lobes 2nd ed. pp. 107–118, New York: Guilford Press.
- Kiyaikin, E. A. (2002). Brain temperature fluctuation: a reflection of functional neural activation. European Journal of Neuroscience, 16(1), 164–168.
- Kurth, C. D., Steven, J. M., Benaron, D. and Chance, B. (1993). Near infra-red monitoring of the cerebral circulation. J. Clin. Monitoring, 9(3), July, 163–170.
- Lassen, N. A. (1959). Cerebral blood flow and oxygen consumption in man. *Physiological Reviews*, 39(2), 183–238.
- Lipton, R. B., Stewart, W. F., Diamond, S., Diamond, M. and Reed, M. L. (2001). Prevalence and burden of migraine in the United States: Results from American Migraine Study II. *Headache*, 41(7), 646–657.
- Maguire, E. A., Gadian, D. G., Johnsrude, I. S., Good, C. D., Ashbrunner, J. and Frakowiack, R. S. (2000). Navigation-related structural change in the hippocampi of taxi drivers. *Proc. Natl Acad. Sci. U.S.A.*, 97, 4398–4403.
- Mann, C. A., Lubar, J., Zimmerman, A. W., Miller, C. A. and Muenchen, R. A. (1992). Quantitative analysis of EEG in boys with attention deficit disorder: Controlled study with clinical implications. *Pediatric Neurology*, 8(1), 30–36.
- Meyer, J. S., Sakamoto, K., Akiyama, M., Yoshida, K. and Yoshitake, S. (1967). Monitoring cerebral blood flow, metabolism and EEG. *Electroenceph. Clin. Neuro.*, 23, 97–508.
- Moskowitz, M. (1998). Migraine and stroke a review of cerebral blood flow. *Cephalalgia*, **18(22)**, 22–25.
- Pinker, S. (1997). How the mind works. New York: W.W. Norton & Company, Inc.
- Pompei, F. and Pompei, M. (1996). Physicians Reference Handbook on Temperature; Vital Sign Assessment with Infrared Thermometry. Watertown: Exergen Corporation.
- Pribram, K. and McGuinness, D. (1975). Arousal, activation, and effort in control of attention. *Psychological Review*, 82(2), 116–149.
- Proctor, H. J., Sylvia, A. L. and Jobsis, F. F. (1982). Failure of brain cytochrome alpha, alpha3 redox after hypoxic hypotension as determined by in vivo reflectance spectrophotometry. *Stroke*, 13(1), Jan–Feb, 89–92.
- Raichle, M. E. (1987). Circulatory and metabolic correlates of brain function in normal humans. In Handbook of Physiology The Nervous System. (V. B. Mountcastle, F. Plum and S. R. Geiger, eds) Vol. 5. Bethesda Maryland: American Physiology Society.
- Roland, P. E. (1993). Brain Activation. John A. Wiley & Sons. , Ch 18. 469-503
- Roy, S. and Sherrington, C. J. (1890). On the regulation of the blood supply of the brain. J. Physiol., 11, 85–108.
- Sacks, O. (1992). Migraine. England: University of California Press.

- Shevelev, I. A. (1992). Temperature topography of the brain cortex: Thermoencephaloscopy. Brain Topography, 6(2), 77–85.
- Shevelev, I. A. (1998). Functional imaging of the brain by infrared radiation (thermoencephaloscopy). Progress in Neurobiology, 56(3), 269–305.
- Schiffer, F. (1998). Of Two Minds. New York: The Free Press.
- Swerdlow, B. and Dieter, J. (1991). The value of medical thermography for the diagnosis of chronic headache. *Headache Quarterly*, 2(2), 96–104.
- Taub, E., Miller, N. E., Novack, T. A., Cook, E. W., Fleming, W. C. and Nepomuceno, C. S. (1993). Technique to improve chronic motor deficit after stroke. *Archives of Physical Medicine*, 74, 347–354.
- Tinius T. ed. (2004). New developments in blood flow hemoencephalography. Binghamton, New York: Haworth Medical Press.
- Tokarev, V. and Fleishman, A. (1998). Technical and engineering implementation of REG (Rheoencephalography) biofeedback training at the West Siberian Metallurgical Plant. *Russian Academy of Medical Science*, 20, 432–435.
- Tomita, M. and Hyoe, M. (1999). Top down signal from prefrontal cortex in executive control of memory retrieval. *Nature*, 461, 10/14/99, 699–703.
- Toomim, H. (1995). Brain blood flow and neurofeedback. Presented at annual meeting of the AAPB. Available from *Biocomp Research Institute*.
- Toomim, H. (2002). Neurofeedback with hemoencephalography. Explore for the Professional, 11(2), 19–21.
- Toomim, H. and Carmen, J. A. (1999). Hemoencephalography (HEG). Biofeedback Society of California News letter, 27(4), 10–14.
- Toomim, H., Carmen, J.A., and Collura, T. F. (2007). Intelligent activation of stem cells. Paper presented at annual conference of *International Society for Neuronal Regulation*.
- Toomim, H., Marsh, R., Kowalski, G. P., et al. (2004). Intentional Increase of Cerebral Blood Oxygenation Using Hemoencephalography (HEG): An Efficient Brain Exercise Therapy. Journal of Neurotherapy, 8(3), 5–21.
- Toomim, H. and Marsh, R. (1999). Biofeedback of Human Central Nervous System Activity Using. Radiation Detection. Washington D.C.: US Patent and Trademark Office. US Patent number 5,995,857.
- van Prang, H., Christie, B. R., Terrence, J., Sejnowski, T. J. and Gage, F. H. (1999). Running enhances neurogenesis, learning, and long term potentiation in mice. PNAS, 96(23), 13427–13439.
- Viamontes, G. I. and Beitman, B. D. (2007). Neural Substrates of Psychotherapeutic Change: Beyond Default Mode. Psychiatric Annals, . , 00:0 Month 200x 238–245. In Press.
- Yamashita, Y., Maki, A. and Ito, Y. (1995). Noninvasive near-infrared topography of human brain activity. J. Optical Society, 212 650 5530;#7/16 8–7
- Zametkin, A. J., Nordahl, T. E., Gross, et al. (1990). Cerebral glucose metabolism in adults with hyperactivity of childhood onset. The New England Journal of Medicine, 323(20), 1361–1366.
- Zikopoulos, B. and Baras, H. (2007). Parallel driving and modulatory pathways link the prefrontal cortex and thalamus. *Public Library of Science*, 2(9), e848.dol10 1371/journal.pone 0000848.