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Expert Assessment of Neuroimaging and Brain-Computer Interface

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Defence R&D Canada
CONTRACTOR REPORT
DRDC CR 2005-005
October 2005

Canada

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Prepared by the Institute for Biodiagnostics, National Research Council Canada for Defence Research and Development Canada and Director Defence Analysis

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Executive Summary

The field of neurofunctional imaging has evolved over the past two decades. What started out as a means to confirm information derived from brain damage subjects has emerged as a tool for many applications. Of particular interest to the Defence sector is the field of forensic neuroimaging. The overall goal of forensic imaging is to unravel the biological basis of violence and psychopathy but neuroimaging techniques are also being investigated as tools for lie detection and may someday provide personality assessment.

The neuroimaging techniques discussed in this context include Positron Emission Tomography (PET), Electroencephalography (EEG), Magnetic Resonance Imaging (MRI), Magnetoencephalography (MEG), Transcranial Magnetic Stimulation (TMS), Optical Tomography (OT), Molecular Imaging (MI) as well as nonmedical imaging techniques. Their current status, limitations and future developments are addressed in detail.

Seven key applications of neuroimaging that may be of interest to the Defence sector have been identified: Hand-held anatomical imaging device, hand-held functional imaging device, brain-machine interfaces for instrumentation control, two-way brain computer interfaces, interrogation / lie detection, determining one's intent to do harm and remote imaging / detection. The neuroimaging technologies most likely to aid in the development of these applications are magnetic resonance imaging (MRI), electroencephalography (EEG) and optical imaging.

The current limitations of applying neurofunctional imaging to problems specific to the defense sector are not those of technological developments in the imaging methods themselves. The techniques are continuously being improved and refined for medical applications and this trend is likely to continue for the next twenty years. These improvements will quickly translate to any application of neurofunctional imaging. The true limit to applying neurofunctional imaging to problems like lie detection, brain-computer interfaces, etc, is our lack of understanding of how the physical and physiological measurements that we can make on the brain relate to those aspects of the mind that we want to detect. Cognition and the brain processes that relate to it are not well understood. This lack of understanding can lead to misinterpretations of neurofunctional imaging results. Thus, for neurofunctional imaging to be used in these cases, more work needs to be performed both on the methods used to cause brain activation (paradigms) as well as processing methods for the resulting data that provide clear interpretations of the results. This will require a deeper understanding of the mind than is currently available but would provide the biggest technological leap in the field and would greatly accelerate the timelines of all neurofunctional imaging applications for defence sector interests.

Uses of Neuroimaging

Neuroimaging has predominantly been used in the medical field to diagnose disease or determine the response to treatment. More recently several neuroimaging techniques such as positron emission tomography (PET), magnetic resonance imaging (MRI) and electroencephalography (EEG) have been used to monitor or measure brain function. Neuroimaging consists of two major branches of use: anatomical and functional imaging. The type of information being sought by anatomical imaging tends to be abnormalities of structure such as might occur in certain disease states. Recently, neuroimaging has found a role in studying development by following the production of neural fibre tracks. In addition, predisposition to certain disease states can be inferred from the size of various brain structures. Brain structural studies have been performed to explore gender differences and number of days a person has been depressed. While much can be inferred from the brain structure, the structure does not tell one about how the brain can and will function. For example, if a person has a small hippocampus (brain structure which is a source of memory) due to past depressive episodes, it does not tell us whether the person is currently depressed. The lack of ability to infer function from structure has sparked the development of the neurofunctional imaging field.

In a broad sense, functional imaging encompasses a wide variety of functional measurements (physiological and metabolic) such as perfusion, blood flow, metabolism, drug receptor distribution, to name just a few. However, the most prominent association people have with the term neurofunctional imaging is neural activity, or how the brain thinks. The relationship between the brain (physical) and mind (thoughts) has been argued for centuries. It is certainly true that damage to the brain can impede thought processes so there is a definite connection between the two but how much the structure of the brain determines one's thoughts is still an area of great debate and gets at the heart of the nature versus nurture arguments concerning behavior. However, if there is one truth the decade of the brain (90's) produced in the scientific community, it is that we still know little about how the brain functions to produce thoughts and emotions or even how it stores memories. On a positive note, all the intense study of the brain did yield an important fact that stared in the face of dogma; the brain can and does change and grow continuously throughout one's life. We are not doomed to the structure or function of our youthful brain. It can grow new tissue and learn new functions and keeping it active is one of the best ways to guard against dementia as one ages. However, this capacity to change (plasticity) makes it difficult to determine or intervene in the thought process since neuronal firing patterns may be highly influenced by the conditions in which the task is being performed.

The future uses of neurofunctional imaging are really unpredictable and rely not only on technological developments but also on the development of a better understanding of how the brain works and the relationship between the brain and thoughts. However, it is easy to identify some possible areas that are likely to be heavily investigated. The most obvious is the collection of knowledge through brain activity mapping. For the last two decades, neuroimaging has provided unprecedented power in observing the brain while it thinks, confirming in some cases the knowledge of brain function derived from people who had localized brain damage while yielding surprising results in others. An infant field, but one of great interest, is forensic neuroimaging. This is leading to the development of different means of lie detection and intelligence gathering. The holy grail of this area of applications is the ability to measure

criminal intent. As the knowledge gained about how the brain functions using neuroimaging grows, one can see the development of personality assessment that is not based on questionnaires but rather neural activity in response to various stimuli. These personality assessments might be used to screen law enforcement or military personnel for specific jobs. They could eventually be used for job interviews and school admission. A fourth field of interest that is beginning to benefit from neurofunctional imaging is that of brain-computer interfaces. The most obvious applications are for use in controlling prostheses or remote machines with direct neural feedback from the device, but the idea of implanting thoughts into one's brain as a result of such work also comes to mind.

Current Imaging Technologies

Currently, neuroimaging methods are used for variety of medical and research applications. Broad categorical applications include anatomical/morphological assessment, molecular / metabolic assessment and functional assessments. Functional neuroimaging techniques that are used to study cognition can be classified into two broad categories. Electrophysiological measures: These basically take advantage of the electromagnetic properties of neural[1] activity. Hemodynamic measures basically take advantage of indirect measures of blood oxygen, flow, and volume (as well as glucose) that change as a function of changes in metabolic demand during neural activity. Originally, imaging techniques were developed to primarily address one of these. However, as the technologies have progressed, the importance of integrating some of these categories has emerged.

Positron Emission Tomography (PET)

The PET scanner detects the decay of positrons using the fact that two gamma rays are emitted simultaneously during the decay of certain unstable nuclei. These gamma rays travel outward from the site of decay on paths that are 180 degrees to each other. Thus simultaneous detection of the two gamma rays provides a line along which the chemical (tracer) containing the nuclei that decayed must have resided. This information is used to reconstruct PET images. Since positron emitters are not naturally found in the body, PET utilizes an exogenous tracer, traditionally F18- fluorodeoxyglucose and O15-labelled water, to localize areas of increase metabolism or blood flow, respectively. Traditionally, these two tracers have been used to perform functional neuroimaging. 18F has a relatively long half-life and does not allow many repetitive measurements because the background signal eventually gets too high to easily distinguish the activated site. O15 has a short half-life, which allows repetative measures. Both methods require that the brain be put into a "state" and then imaged. Transient brain states cannot yet be measured using PET. The resolution of state-of-the-art PET imaging is below 1 cm which has improved in recent years due to better detector synchronization and reconstruction algorithm improvements. One recent advance is the combination of PET/CT into one scanner, which allows the CT image to guide PET anatomically. Combined MRI/PET scanners are being developed (Simon Cherry, ref) for small animal work and are likely in 5-10 years be available in human size. This will provide an advance in neurofunctional imaging. The temporal time course of the physiological responses of PET is on the order of minutes for 18F PET and 15O

[1] It is useful to distinguish between 'neural' and 'neuronal' activity. The former is more general and refers to the summation of activity from multiple neurons (e.g., volume conducted electromagnetic activity from open field configuration pyramidal cells). The latter is more specific and refers to the recording of events at the cellular level, which are generally not the focus of non-invasive functional neuroimaging.

where blood flow response is 4-6 seconds. However, PET cannot measure transient states of the brain because the counts from the decaying tracers are too low and must be averaged over minutes. In addition, group averages are used in PET scanning for brain activation studies. Thus single individuals and single event detection is not yet available. SPECT (single photon emission computed tomography) scanners have also been improving with combined CT/SPECT approaches and new tracers providing the largest boost in sensitivity and resolution. This form of detection may be important in molecular imaging approaches.

Electroencephalography (EEG)

EEG obtains its signals from electrodes attached to the scalp. It picks up electrical signals generated indirectly from neural activity. These signals are not created from single neurons but rather from local neural circuitry. The localization of these signals arises from modeling the circuits as dipoles and back calculating their location due to multiple electrodes. Its spatial resolution is on the order of centimeters while the time of response to a stimulus is on the order of 100s of milliseconds. Currently EEG reconstructions are based on a crude model of brain anatomy and with no knowledge of the placement of electrodes with respect to that anatomy. Combining EEG with MRI and providing an MR observable signal on the electrode would allow the spatial reconstruction model to be based on subject-specific electrode placement and subject-specific anatomy. Therefore, multimodal imaging has a role to play in providing better localization for EEG signals.

Magnetic resonance imaging (MRI)

The uses of magnetic resonance imaging (MRI) in the clinical arena have exploded in the past three decades. The primary signal arises from the protons (hydrogen) on the water molecule (and lipid/fat). The signal is created by providing energy to the tissue at frequencies that cause transitions between the energy levels of the nuclear spin of the proton. The exact frequency of this energy is dependent on the strength of the magnetic field in which the sample sits. In addition, the amount of signal that can be obtained is ultimately dependent on the strength of the magnetic field. MR images are obtained by varying the strength of the magnetic field in a spatially dependent manner and recording the distribution of the signal over the resulting frequencies. In addition, the nuclear spin is sensitive to its environment and thus this can affect the strength of the signal obtained as well. This sensitivity provides the exquisite anatomical detail of soft tissue provided by MR images. Some physiological phenomena also affect the MR signal. For example, blood flow through a changing magnetic field will change the phase of the MR signal and thus the speed of blood flow can be obtained. The diffusion and direction of diffusion of water can also be measured which allows fiber tracking in the brain. Using contrast agents (typically chelated gadolinium or superparamagnetic iron nanoparticles), tissue perfusion by blood and differential tissue uptake of the agents can be measured. Important for monitoring brain activity is the sensitivity of the MR signal to the oxygenation state of the blood. Thus, changes in blood flow and blood oxygenation state in response to neural activity can be detected in a spatially dependent manner. The spatial resolution can be sub-millimeter with temporal resolutions on the order of seconds. Transient measurements of brain activation are possible with MR. The ability to measure solitary neural events is not yet possible but improvements in sensitivity have been mad steadily over the past 10 years.

Magnetoencephalography (MEG)

MEG detects using SQUIDs (superconducting quantum interference device) the magnetic field component of electrical signals associated with neural activity. Because of the low strength of these signals and the high level of interference in the atmosphere, MEG has traditionally been performed inside rooms designed to shield against all electrical signals and magnetic field fluctuations. Better methods of detecting this interference and correction for them in real-time have allowed MEG equipment to be more assessable. Because of its reliance on the same signal that produces EEG, MEG has similar spatial resolution and temporal resolution to that of EEG. The major difference is that a magnetic dipole is detected instead of an electric dipole. The detection of that magnetic dipole does not require the MEG detectors to be in physical contact with the subject being studied. However, because of the high level of interference signals, the detectors must be in close proximity to the subject.

Transcranial Magnetic Stimulation (TMS)

TMS is similar to MEG in that magnetic fields are used. However, instead of detecting a magnetic field, TMS utilizes a fluctuating magnetic field to stimulate the brain. This has been used to map the brain function by determining where TMS interrupts that function. For example, a person may be asked to name all the animals they can think of that live in North America and the TMS signal directed to different regions of the brain. Where that signal is pointed at when the subject is impeded from performing that task would provide information about where some stage in the cognitive function occurs. The spatial accuracy of this method has yet to be determined. As TMS and its ability to interrupt function becomes better understood, it might be possible to utilize it for feedback of signals to the subject using a brain-computer interface. This could be accomplished without any probes connected directly to the subject. However, the probes must be in close proximity to the area of the brain that is to be affected in order to spatially direct the effort.

Optical tomography

Optical imaging is beginning to play a role in medical applications. While it has low spatial resolution due to scattering of the light, it has high sensitivity especially for molecular imaging agents. Optical imaging has been used for functional brain mapping in block design protocols where changes in oxyhemoglobin as a result of local hemodynamic response has been the first method used to explore brain function. However, a fast response signal with a temporal resolution similar to EEG has been found, however, the signal is 30 times weaker than the hemodynamic response signal. It is believed that this signal is a result of changes in the scattering properties of the brain tissue in areas of activation due to biochemical changes associated with neural activation. This signal appears to be better localized than surface EEG measurements. Investigation of this signal and its apparent use in brain-computer interfaces is currently in its infancy but clearly is an area of future investigation. The sensitivity problems associated with optical imaging through the skull have been steadily reduced over the last few years. The fast response signal has been shown to correlate with the evoked EEG signal as well. Basically, it offers an important alternative to EEG with the promise of being better localized.

One difficulty of optical tomography is the need for a signal to be injected into the head (usually laser light) and changes to it through scattering or absorption obtained in a spatially dependent way. Thus, one not only requires signal acquisition hardware but also some device to generate

the signal such as diodes of appropriate frequencies. However, this technology has exciting possibilities and has been steadily improving over the past 15 years.

Molecular Imaging

Molecular imaging is a growing research discipline aimed at developing and testing novel tools, reagents and methods to image specific molecular pathways in vivo - particularly those that are key targets in disease process. Molecular imaging uses the imaging technologies described above to detect specifically designed chemical probes that are targeted to genes, proteins or receptors in the body. Delivery of such agents to the brain is difficult because of the special properties of the blood/brain barrier, which attempts to keep out most foreign substances. The most advanced area of molecular imaging is the design of specific agents for PET to detect tumors. For new molecular imaging agents to play a role in neurofunctional imaging, more knowledge about the brain at the biochemical level needs to be developed.

Non-medical imaging techniques

Magnetic resonance and other techniques have made the transition from medical applications to other fields such as geology. For example, MRI has been used to map oil contamination in underground water and to determine the porosity of shale along oil wells (Prammer, 2004). Other magnetic resonance methods are utilized for inline chemical process monitoring and food industry. X-rays and MRI are also used in the food industry. Traditional imaging devices such as radar and electro-impedance measurements are currently used in geological measurements and other fields in need of nondestructive imaging methods. Some of these techniques are currently being explored for medical applications.

Present Status of Neurofunctional Imaging Technology

Table 1 provides a summary of the techniques being presently being used to map brain function. The physiology on which the signal is obtained is provided. The physiological response often sets the minimum time resolution. The spatial resolution is dependent on the amount of signal that can be obtained as well as the methods used to encode the spatial information. One important fact to understand about neurofunctional imaging is that all the methods currently require knowledge of the timing of a neural event in order to determine the location of that function of the brain. Neural activity and its subsequent physiological responses are produced by stimuli given on a timed schedule. This is called a paradigm. The type of stimulus provided determines the function to be assessed while the timing allows the researcher to correlate changes in the neurofunctional imaging signal with the pattern of stimuli. Typically, statistical analysis is used in order to ascertain where the changes in signal correlate and thus the resulting maps of the brain function are statistical inferences.

Table 1 State of Neurofunctional Imaging

Modality	Physiology	Spatial Resolution	Temporal Resolution
15O-water PET	Blood Flow	1 cm	minutes
18FDG PET	Glucose Metabolism	1 cm	Minutes
fMRI	Hemodynamic Response	0.5 mm	4-6 seconds
fMRI	Blood Flow	0.1 mm	1 second
EEG	Neural activity	1 cm	100's ms
MEG	Neural activity	1 cm	100's ms
Optical Tomography	Hemodynamic Response	1 cm	4-6 seconds
Optical Tomography	Neural activity	2 cm	100's ms
TEM	Neural activity by interrupting its function	Centimeters	milliseconds

Current Limitations of Neurofunctional Imaging

There are several limitations that hinder widespread use of neurofunctional imaging in applications. These are discussed below.

The instrumentation is expensive and ungainly. For PET, MRI and MEG, the instrumentation is large and requires a large amount of electronics. While the electronics are miniaturizing taking large equipment rooms down to a cabinet, the magnetic fields, shielding and/or detectors are still quite large and expensive. Optical and EEG equipment are more compact and wireless technology is likely to improve both. However, the computational power needed for reconstructions are considerable and for real-time applications of any complexity, not yet available in portable devices.

Neurofunctional imaging requires compliance of the subject to perform the task. If the task is not performed or not performed on the expected timeline, then it is currently possible to detect brain function only on trivial tasks. This can be overcome by developing paradigms/tasks that do not require effort by the subject but these tend not to probe cognition / thinking. Another approach is to monitor closely what the subject is doing, relying on other physiological measurements such as heart rate, skin conductance, or to require some feedback that is dependent on the task. Then the data can be analyzed based on actual performance.

Data analysis is currently performed on groups of subjects not individuals. To date, most neurofunctional imaging studies have concentrated on finding regions of the brain that are activated in response to a task by most people within a group, thereby, looking for consensus regions of activations. The field is only beginning to look at individual differences. In addition, the field does not yet know under what conditions individuals activate the same regions. The initial state of the brain is not known in enough details to determine if variations in activations occur because of different starting conditions even on the same individual.

False positive and false negative rates are unknown. The neurofunctional imaging field does not yet know how often the currently obtained responses should are or should not be there. Much more research needs to be performed. Currently when the research sees what he expects, they assume the experiment has gone along correctly and when they don't see what is expected then either the subject is not performing the task or there was something technically wrong with the data acquisition. Analysis of "failed" experiments and better monitors of task performance will aid in determining the rates of false positives and false negatives.

All neurofunctional imaging measurements are indirect measures of neuron firings. It remains to be seen if direct monitoring of neurons is required for many of the applications. It may be that looking at individual neurons is too fine of a scale to investigate reproducible brain function. There is some evidence that neuron firings differ with differing initial conditions.

Simple tasks / paradigms are being used to investigate brain function. The paradigms used to produce brain responses are by necessity simplistic and very easy for the subject to perform at this early point in the field. As the field progresses towards an understanding of how the brain functions under these simplistic tasks, better paradigms will be developed.

Our understanding of brain/mind interactions is very limited. Perhaps the biggest limitation of neurofunctional imaging is our lack of knowledge about how the brain/mind works. It is obvious that by some means biochemical reactions produce thought. But why specific thoughts in response to specific stimuli is not understood at all. How these thoughts are influenced by past and present experiences and environmental factors are definitely not understood. Thus, much more work in the area of brain/mind interaction and development of the mind needs to be performed.

Future Developments of Neurofunctional Imaging

Table 2 provides a list of physical and biological improvements that will advance neurofunctional imaging. Any advances in the instrumentation and biological knowledge will quickly improve the speed at which applications of these technologies can be developed.

Table 2 – Future Directions of Neurofunctional Imaging

Modality	Physical Improvements	Biological Improvements
PET	New detector tech (increase temporal resolution Multi-Modality (increase spatial resolution	Specific Biomarkers for new tracers Increase Understanding of Brain/Mind
EEG	Wireless / Noninvasive electrodes Multi-modality (increase spatial resolution) Signal Processing (single event detection)	Increase Understanding of Brain/Mind
MRI	Faster scanning (increase spatial/temporal resolution) Signal Processing (single event detection) Hand-held device	Specific Biomarkers for new tracers Increase Understanding of Brain/Mind
Optical Tomography	MicroLasers (hand-held detector) Multi-modality (increase spatial resolution) Improved detectors (increase S/N) Signal processing (Single event detection)	Specific Biomarkers for new tracers Increase Understanding of Brain/Mind
MEG	Improved detectors (increase temporal resolution) Multi-modality (increase spatial resolution) Better interference noise suppression (increase temporal resolution)	Increase Understanding of Brain/Mind
Molecular Imaging	Chemistry for multi-modality tracers Chemistry for biocompatibility	Indentification of specific biomarkers Increase Understanding of Brain/Mind
New Modalities	Electrical Impedance imaging, Terahertz imaging, Others ….	Identification of biological/physiological response associated with the imaging modalities

Technical Description of the BCI Methods

BCI is an interesting and highly interdisciplinary research topic at the interface between medicine, psychology, neurology, engineering, man-machine interaction, mathematics and computer science. Most BCIs modeled for use by humans are based on extracranial electroencephalography (EEG) recordings. However, in an effort to overcome the problem of the low signal-to-noise ratio of the EEG, some authors have recently investigated the use of more invasive BCIs based on intra-cranial EEG recordings or electrocorticography (ECoG) (Kennedy et al., 2000; Levine et al., 1999, 2000; Graimann et al., 2004; Lal et al. 2004b).

The analysis of EEG or ECoG from individual events ("single-trial") is a challenge for signal processing. The difficulty stems from the need to extract complex spatial and temporal patterns from noisy multidimensional time series obtained from EEG. However, in contrast to a few attempts at detecting and classifying patterns of fMRI activity over a single time interval (e.g. Cox and Savoy, 2003; Weiskopf et al., 2004; Mitchell et al., 2004), there has been over the past 20 years productive and growing interest on EEG-based BCIs in the machine learning community. Indeed, in addition to the advent of powerful, low-cost computer equipment, the interest and success of BCIs are primarily driven by the progress of single-trial analysis (also called "online" analysis) of EEG.

Present Status of BCI Technology

Examples of systems that utilize single-trial analysis

Present-day BCIs determine the intent of the user (e.g. patients with severe neuromuscular disorders, such as amyotrophic lateral sclerosis, brainstem stroke, and spinal cord injury) from a variety of different electrophysiological signals: EEG rhythms, slow cortical potential shifts (e.g. the pre-movement Bereitschaftspotential) and evoked potentials (e.g. P300 potential). The two first signals are independent of the external environment, whereas evoked potentials need external stimulation from a specific modality (visual or/and auditory). Below is a list of several BCI systems that are based on these different kinds of signals.

1. The Thought Translation Devise (TTD)

Birbaumer et al (1999, 2000, 2003) have developed a BCI, called the Thought Translation Device (TTD), which allows paralyzed patients to write text on the screen of a computer. A well-trained user requires about 30 seconds to write one character. During the training step of this system, the subjects learn to produce and regulate their Slow Cortical Potentials (SCP) at a central location at will, and this information is fed back to the users. During the spelling phase, patients choose between two banks of letters. Once selected, a bank splits in two, continuing a process of elimination until the final chosen letter.

2. The Graz BCI system

Pfurtscheller et al (1997) built a BCI system based on event-related (de)synchronization (ERD/ERS), typically of the mu and central beta rhythm, which are electrical oscillations originating from the motor areas of the brain in some specific frequency ranges. The basis of using rhythmic EEG components as neural input signals for a BCI is that preparation or planning of a specific movement results in a change of these rhythms. This system is used for on-line classification of imaginations or preparations of, for example, left/right index finger, feet, and tongue movement. A quadriplegic (i.e. paralyzed in all limbs resulting from injury to the spinal cord) controls his hand orthosis using the Graz BCI system.

3. Interface for cursor control

Wolpaw and colleagues (Wolpaw et al., 1991; Wolpaw and McFarland, 1994) have proposed a BCI system for paralyzed individuals. Subjects learn to use two channels of bipolar EEG activity to control 2-dimensional movement of a cursor on a computer screen. They learn to control 8-12 Hz EEG amplitudes at two different locations simultaneously and thereby control cursor movement in two dimensions.

4. P300-based speller system

This BCI system utilizes the fact that rare events in an oddball paradigm elicit a P300 component. The 26 letters of the alphabet, together with several other symbols and commands, are displayed on a computer screen in a matrix of 6 by 6 cells. The user focuses attention on the cell containing the letter to be communicated while the rows and the columns of the matrix are intensified. The system detects the chosen character on-line and in real time (Farwell and Donchin, 1988; Donchin et al., 2000).

Table 3 Groups/Companies Doing BCI with EEG or Implanted Electrodes

Name	Institute	Country	Website or Email
Niels Birbaumer	Institute of Medical Psychology and Behavioral Neurobiology, Eberhard-Karls-University of Tübingen.	Germany	niels.birbaumer@uni-tuebingen.de
Benjamin Blankertz	Intelligent Data Analysis (IDA) group at Fraunhofer FIRST, Berlin.	Germany	benjamin.blankertz@first.fhg.de
Emanuel Donchin	Department of Psychology, University of Illinois, Champaigne-Urbanna	U.S.A	edonchin@uiuc.edu
Scott Makeig	Swartz Center for Computational Neuroscience, Institute for Neural Computation, San Diego	U.S.A	smakeig@ucsd.edu
Jose del R. Millan	Institut Dalle Molle d'Intelligence Artificielle Perceptive (IDIAP) Research Institute, Martigny	Switzerland	jose.millan@idiap.ch
Gert Pfurtscheller	Laboratory of Brain-Computer Interfaces (BCI-Lab), Institute for Computer Graphics and Vision, Graz University of Technology.	Austria	pfurtscheller@tugraz.at
Alois Schlögl	Department for Medical Informatics, Institute of Biomedical Engineering, Graz University of Technology.	Austria	alois.schloegl@tugraz.at
Jonathan Wolpaw	Laboratory of Nervous System Disorders, Wadsworth Center, New York State Department of Health, Albany.	U.S.A	wolpaw@wadsworth.org
Gary Birch	Neil Squire Foundation Burnaby, BC	Canada	www.neilsquire.ca

Future Developments of BCI Technology

Single trial analysis: Why is it important?

1. Variability of the EEG signal

The problem is in the high inter-trial variability of the EEG signal, where the potential interesting characteristics (e.g. components, slow shifts of the cortical potential etc.) are largely hidden in the background activity and only become evident by averaging over a large number of trials. However, signal averaging assumes that the detected signal in each single trial has stable characteristics, such as constant waveform morphology, amplitude, and latency across single trials. Unfortunately, average ERP may present only a gross picture of the neural processes elicited by the event of interest. For example, if the latency of an ERP component varies from trial to trial (latency jitter), the amplitude of the component in the average will be reduced and its shape distorted (Brazier, 1964).

In addition, a few studies have investigated the issue of ERP component interrelationship across single trials. One example is the examination of the latency variability of the N1, P2, N2, and P300 components in an auditory oddball task by Michalewski, Prasher and Starr (1986). They used a single-trial detection technique to estimate the latency of each component on every trial, and found that the latencies of the N1 and P2 components were correlated, as were the latencies of the N2 and P300. This approach is necessary if one wishes to take full advantage of the

temporal information available in the ERP to construct models of information processing in the brain.

2. Real time systems
Successful BCIs require that: 1) the user encodes intents (or commands) in the electrophysiological signals (EEG/ERP); and 2) the BCI recognizes and derives the commands from these signals. Current BCIs have maximum information transfer rates up to 10-25 bits/min (Wolpaw et al., 2002).

A large number of cognitive tasks have features that can be observed by EEG, but only by averaging the results of many repetitions of the same task. In order to be applicable to BCI systems, one must be able to detect cognitive activity from a single performance of a task, without the benefit of averaging. Future progress will therefore depend on efficient algorithms for quickly conveying messages and commands to the external world, i.e. translating intents that are encoded in the signal, preferably in single trials, into device commands.

Challenging problems or open questions for practical BCI systems

1. Session-to-session transfer (Lal et al. 2004b)
Imagine that a classifier that was trained on one day has to classify data recorded during following days (if possible, without retraining): the participant (healthy subject or patient) is probably in a different mental state (e.g. motivation, vigilance, fatigue…) so that his/her brain will show different electrical activities. The recording system might also have undergone slight changes concerning electrode positions and impedances. In this kind of situation, it is still an open question whether the classifying function can be transferred from session to session.

2. Small training sets (Dornhege et al., 2004).
When developing a BCI, a set of training data is available, and the system is designed by exploiting this "a priori" information i.e. labeled single-trial data are used to "teach the classifier". To this end, the user usually performs a tedious and delicate calibration measurement before starting with BCI feedback applications. One important objective in BCI research is to reduce the time needed for this initial measurement. This issue poses the challenge of training the classifier with only a little amount of training data.

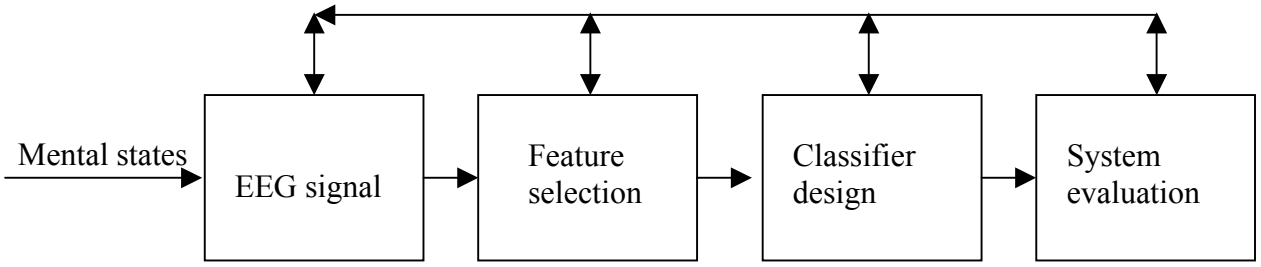
3. Subject-to-subject transfer
One potential approach to the previous problem is to use information from other subjects' measurements to reduce the amount of training data needed for a new subject. However, as has already been pointed out previously, this subject-to-subject transfer is challenging because there is high inter-trial variability.

4. Classification of continuous EEG without trial structure (Dornhege et al., 2004)
Algorithms on BCI data are typically performed on intervals of EEG trials, i.e., windowed EEG signals for fixed length (or epoch in the ERP terminology), where each trial corresponds to a specific mental state. But in BCI applications with continuous feedback one is faced with the problem that the classifier has to be applied continuously to the incoming EEG without having

cues of when the subject is switching her/his intentions. This kind of data set poses the challenge of applying a classifier to continuous EEG for which no cue information is given.

How? Machine learning techniques

A BCI has to perform two tasks, the parameter estimation task (or feature selection stage), which attempts to describe the properties of the EEG signal and the classification task, which separates the different EEG patterns based on the estimated parameters. In practice, a larger than necessary number of candidate features is generated and then the "best" of them is adopted. Extracting these features reduces the amount of data that is fed to the classifying method and thus reduces the processing time of the BCI system. The figure below shows the main stages followed for the design of a single-trial EEG classification system.



The feedback arrows illustrate the fact that these stages are not independent. On the contrary, they are interrelated and depending on the results, one may go back to redesign earlier stages in order to improve the overall performance. Furthermore, there are some methods that combine stages, for example, the feature selection and the classifier design stage, in a common optimization task. Note also that a stage of signal preprocessing is often included to remove the artifacts that creep into the signal for various reasons, like eye blinking or muscular activity. Numerous classification methods have been used to identify optimum demarcating boundaries for the various classes of signals in the feature space:

Adaptive autoregressive model (AAR) (Schlögl, Flotzinger and Pfurtscheller, 1997)
Artificial Neural Networks (ANN) (Kalcher et al., 1996; Pfurtscheller et al., 1997; Pregenzer et al., 1996; Costa and Cabral, 2000; Haselsteiner and Pfurtscheller, 2000).
Bayesian decision rule by utilizing the average signal and its variance as a generative model for each event class (Kohlmorgen and Blankertz, 2004).
Fisher's linear discriminant (LD) (Guger et al., 2000, 2001).
Hidden Markov models (HMMs) (Obermaier et al., 2001).
Support Vector Machines (SVMs) (Lal et al. 2004a, Lal et al. 2004b).
Wavelet analysis (Quiroga and Garcia, 2003).
Combination of different techniques each specifically tailored for different physiological phenomena (Dornhege et al., 2004)

Thus, given the large number of these techniques, it seems necessary to encourage attempts that aim to compare methods for EEG signal classification on the same data sets (e.g. Garrett et al., 2003, Sajda et al., 2003). It is also usually agreed that simplicity is generally best and therefore, the use of linear methods is recommended wherever possible, particularly in cases where there is limited knowledge of the data sets. However, non-linear methods in some applications can

provide better results, particularly with complex and/or very large data sets (Müller, Anderson and Birch, 2003).

Present Status of Neuroimaging of Deception and Determining Intent

Can we use NeuroImaging Techniques to detect Deception?
Understanding the neurocircuitry of deception could have a profound impact on society. The traditional tool to measure deception, the polygraph, has elicited much controversy, and the National Academy of Sciences concluded that there is little scientific evidence that polygraph measures can reliably identify a liar (NRC, 2003). Polygraph measures rely on the assumption that a person who is guilty and fearful will have increased activity in the autonomic nervous system (Wade et al., 2003). However, most researchers regard polygraph tests as invalid because no physiological patterns of autonomic arousal are specific to lying. Currently, researchers are using Blood Oxygen Level Dependent (BOLD) functional Magnetic Resonance Imaging (fMRI) and Event Related Potentials (ERP) to more directly characterize the neurocircuitry of deception. This report summarizes the research utilizing these neuroimaging techniques and addresses limitations and future directions of this work.

Several investigators (Farwell and Donchin, 1991; Rosenfeld et al., 1991; Johnson and Rosenfeld, 1992) observed an interesting ERP trace called the P300 because it starts about 300 milliseconds after an event and generally occurs when a stimulus holds specific significance for a subject. The P300 electrical brain wave response is widely known and accepted in the scientific community. There have been hundreds of studies conducted and articles published on it over the past thirty years. The P300 has been used to detect guilty knowledge (Farewell and Donchin, 1991), deception (Rosenfeld et al., 1991, Johnson and Rosenfeld 1992), concealed learning (Allen et al., 1992) and feigned recognition memory (Tardif et al., 2000). Farwell and Donchin (1991) using the Guilty Knowledge Test (GKT) showed that the P300 could be used to reveal hidden knowledge of a mock crime. The GKT is a method of polygraph interrogation that facilitates psychophysiological detection of prior knowledge of crime details that would be known only to a suspect involved in the crime (Lykken, 1991). Rosenfeld et al., (1991), and Johnson and Rosenfeld, (1992) extended these findings by studying the P300, not in a mock crime, but asking student subjects about undesirable acts (with reasonable probabilities, such as cheating on a test, using false identification….) they may have actually committed. Guilty students were identified with a close to 90% accuracy. However, Rosenfeld and colleagues (2004) also published an interesting paper on countermeasures of detection of concealed information. Generating covert responses to irrelevant stimuli was successful; test-beaters could not be caught.

More recently, a Canadian group conducted an interesting study. Girodo et al., (2002) looked at the P300 in response to altering one's personal identity. Since the P300 is affected by the psychological or personal relevance of the stimulus, the authors examined whether the P300 amplitude previously linked to true-identity stimuli might be suppressed by adopting a new identity and also if the P300 response is modulated if subjects role-played their new identity in real life. As expected, the P300 was larger in response to words describing the subjects' true identity and a later P550 was also larger in this regard. When subjects took on a new identity the

P300 became larger in response to this new identity and the P550 remained large for both the true and new identity. When subjects role-played their new identities for 3 days, the P550 for the true identity became smaller but remained large for the new identity. The authors suggest that one's own true identity only begins to lose relevance over time, and that role playing the new identity increases the P550. However, the authors caution that their student subjects may not have placed any particular significance on their new identity roles and that professionals such as actors or undercover agents, who deny their true identity as part of their careers, may show completely different electrophysiological traces.

All together, there isn't a large volume of literature examining the ERP signature in response to deception. Although the P300 response has been described in several studies, differences in the accuracy in determining a lie or the concealment of information have been reported (Farwell and Donchin, 1991; Rosenfeld et al., 1991, Johnson and Rosenfeld, 1992).

FMRI has also been used to study deception. Though few in number, and using very different experimental protocols, studies published in the peer-reviewed literature exhibit certain consistencies. The first fMRI study on deception (Spence et al., 2001) demonstrated that lying was associated with longer behavioural response times (approximately 200ms longer during lying) and greater activity in bilateral ventrolateral cortices, medial prefrontal (anterior cingulate) and premotor cortices and left inferior parietal and lateral premotor cortices. One year later two further studies were published (Langleben et al, 2002; Lee et al., 2002). Langleben and colleagues (2002) tested 18 volunteers on a 4 Tesla MRI using the Guilty Knowledge Test (GKT). As mentioned above the GKT is a method of polygraph interrogation that facilitates psychophysiological detection of prior knowledge of crime details that would be known only to a suspect involved in the crime (Lykken, 1991). Denying the possession of a target playing card (ie. the "lie or prior knowledge of the crime") was associated with greater activation of the anterior cingulate gyrus and left parietal cortex. Lee et al., (2002) were interested in determining whether astute liars or malingerers (persons who intentionally falsify or fraudulently simulate or exaggerate a physical or psychological disease, or other defects) may provide unique patterns of brain activation and thus provide a specific brain signature of deception. The group found, that compared to truthful responding, malingering was associated with increased activation in bilateral dorsolateral prefrontal, inferior parietal, middle temporal, and posterior cingulate cortices. In 2003 Ganis et al. criticized that lie detection methods have rested on the assumption that there is only one type of lie. His group compared lies that were spontaneous and isolated (SI) to lies that were well memorized and part of a coherent scenario (MS). Similar to prior studies, both types of lie were associated with greater activation in bilateral prefrontal cortices. Increased activity was also seen in bilateral hippocampal gyri. SI and MS were distinguished by greater anterior cingulate and visual cortex activation in the former and greater right frontal activation in the latter. Therefore the authors caution that different lies are associated with different brain activation patterns and that inappropriate pooling of data may increase the variability in the data and thus obscure the ability to identify brain activation patterns that are specific to different types of deception.

Rather than studying direct deception by the subject, Grèzes et al., (2004) were interested in identifying the neural networks that mediate people's perception that they are being deceived. When the actions of others reflected deceptive intentions, subjects showed increased activity in

the amygdala and anterior cingulate cortex. Recently, Kozel et al., (2004a) hypothesized that specific brain regions would activate during deception, and that these areas would correlate with changes in electrodermal activity (one of the polygraph measures). Although he found that electrodermal activity correlated with blood flow changes in the orbitofrontal cortex and anterior cingulate gyrus, he reported that individual results were inconsistent and lack good predictive power. He therefore replicated his study (Kozel et al., 2004b) using a stronger magnetic field (3T compared to 1.5T), but also made some paradigm modifications to investigate brain activation patterns during deception at an individual level. Even though individual results were more consistent, he concluded that his results did not support the use of fMRI to detect deception in an individual. The most recent fMRI publication (Phan et al., 2005) points out that many fMRI studies on deception use tasks that recruit neural networks that are also engaged in the recall of autobiographical memories and therefore activation patterns may be due to recalling these types of memories rather than the generation of lies. The authors used a task that minimized the involvement of autobiographical memory recall and also added a stress component by telling subjects that their performance would be measured and followed. Similar to previous studies the authors found increased activation in temporal and frontal regions the latter including the ventrolateral prefrontal and the dorsal medial prefrontal cortices.

Overall, the most consistent finding in all of the aforementioned studies is the involvement of prefrontal regions during deception. However, it must be kept in mind that deception is a complex cognitive activity including the awareness of one's own and others' thoughts, generation of novel responses (lies and different types of lies), inhibition of pre-potent responses (truth telling), task switching and updating and the motivation for keeping lies covert (Phan et al., 2005). How each one of these components is reflected in neural circuitry remains to be determined.

Can we use Neuroimaging Imaging Techniques to determine Intent?

"March 8th, 2080. Jack, Laura and Jim are at the International Terminal of the Winnipeg Airport. They throw their baggage onto the security-scanning belt and Laura proceeds through the Security Brain Wave Scanner. A red light flashes and a little buzzer sounds. Excuse me, Miss, I have to escort you to the interrogation chambers exclaims the security technologist. Laura shows her GSA government identity card, insisting she works for the Government Security Agency. Red Alert today, Miss, I am sorry, please make yourself comfortable for the 15 minute EEG interview procedure." Can we use brain imaging techniques to predict violent or terrorist behaviour before it surfaces? Some research has focused on individuals whose violent behaviour is the manifestation of a psychiatric condition (DSM IV, American Psychiatric Association, 2000). In addition, forensic neuroimaging research efforts are underway to investigate the relation between brain function, emotion and personality in murderers, violent and psychopathic individuals. Beyond the attempt to characterize a brain signature for psychopaths and murders, there is an interest to determine whether such neural signatures could be used to monitor individuals who are at risk of carrying out a criminal/terrorist act.

The overall goal of Forensic NeuroImaging is to unravel the biological basis of violence and psychopathy. There are several papers demonstrating that criminal offenders, murderers and aggressive psychiatric patients show hypoperfusion and reduced glucose uptake in the prefrontal cortex (Soloff et al., 2003; Raine et al., 1994). Even though a causal link between lowered

prefrontal metabolism and violence is difficult to establish, because both may be the result of other environmental, developmental or genetic influences (Canli et al., 2002); neuroimaging studies have taken a closer look at prefrontal activity in relation to moral reasoning. Moral reasoning engages parts of the brain that are not involved in other forms of reasoning and studies have found reduced activity in some of the same brain regions among convicted murderers. Research demonstrating that prefrontal regions are concerned with the processing of moral or social knowledge comes from neuroimaging studies in healthy, normal, non-violent volunteers. In one study comparing impersonal, non-moral dilemmas to personal moral dilemmas, the latter produced significant increases of activation in the medial frontal, posterior cingulate and angular gyri (Greene et al., 2001). In another study (Moll et al., 2002) moral, relative to non-moral negative pictures produced significant activation in prefrontal regions including the medial prefrontal gyrus and orbitofrontal cortex. The caveat of applying such knowledge to measuring someone's immoral intent (ie, hijack a plane, for example) is that this intent may not be immoral to the person intending to commit such an act. This will be further discussed under the future directions and limitations of this research.

Very interesting research has been conducted using event related potentials (ERPs) to identify whether or not specific information about a crime scene is stored in an individual's brain. Farwell, introduced earlier in the section on ERPs and lie detection, has created Brain Fingerprinting Laboratories, a United States company using ERPs for criminal proceedings and counter-terrorism applications. On his website he advertises that brain fingerprinting can 1.aid in determining who has participated in terrorist acts, directly or indirectly; 2. aid in identifying trained terrorists with the potential to commit future terrorist acts, even if they are in a "sleeper" cell and have not been active for years; 3. help to identify people who have knowledge or training in banking, finance or communications and who are associated with terrorist teams and acts and finally 4. help to determine if an individual is in a leadership role within a terrorist organization. He explains that the fundamental difference between a terrorist and an innocent suspect is that the terrorist has detailed knowledge of terrorist activities stored in his/her brain and an innocent person does not. His work has received much public attention and is supported by several research papers. In one of his recent papers Farwell and Smith (2000) state that ERP MERMER® (memory and encoding related multifaceted electroencephalographic response) testing has a 100% accuracy without false negatives, false positives or indeterminate cases. The MERMER comprises a P300 response, occurring 300 to 800 ms after the stimulus, and additional patterns occurring more than 800 ms after the stimulus, providing even more accurate results. Even when subjects make efforts to conceal their knowledge MERMER testing was 99.9% accurate in five cases and 90% accurate in one case.

Limitations and Future Developments in Neuroimaging of Deception and Determining Intent

Both ERP and fMRI research have made exciting discoveries in regards to understanding the neural circuitry of deception. However, it would be nearsighted not to point out some of the limitations this type of research has encountered. These limitations should guide future developments in neuroimaging efforts of deception and determining intent.
It should be kept in mind that the experiments reviewed in this report generally involve compliant subjects telling trivial lies. Real life "high stake" situations may introduce new

challenges that will have to be addressed. In terms of paradigm design, polygraph and ERP research have used two types of "interrogative examinations": the control question technique and the guilty knowledge test. Each type of examination has advantages and disadvantages. Ultimately, the control question technique suffers from quite a large number of false positive outcomes; the innocent can be incorrectly classified as guilty. The reverse is true for the guilty knowledge test. The guilty knowledge test is characterized by a high number of false negative outcomes; the guilty are incorrectly classified as innocent. Hence one of the future directions of this research has to be the optimization of the interrogation method. ERP has excellent temporal but limited spatial resolution. The latter can be addressed with fMRI. FMRI can directly examine the functional neuroanatomy of the organ that produces lies, the brain. Although there are consistencies in terms of the involvement of prefrontal brain regions during deception, the majority of fMRI studies have used group analyses to assess whether a person is telling the truth or lying. The only exception is work done by Kozel et al., (2004), who concludes that within individuals fMRI is not able to detect consistent activation patterns due to lying. However, he also stresses that this does not in any way mean that activation patterns specific to lying are not achievable in the individual, but that further work needs to be done to determine whether this goal can be achieved. The only way fMRI can become a powerful tool for the use of lie detection is if a lie can be detected on an individual basis. To do this deception paradigms and analyses methods need to be refined.

FMRI neuroimaging techniques are still a very long way from being able to read a person's mind or infer intent. The possibility of being able to do so is a topic of much discussion and speculation. There are the issues of individual differences as well as experiences, morals and values leading up to the intent. Moreover, inferring mental events from brain images is limited to experimental conditions with well-defined trials, precisely known timing, a limited number of events and cooperating subjects (Dehaene et al., 1998). Taking such measurements into the "real world with real people" will introduce a whole new set of scientific questions that will have to be addressed. Even in cases where science (forensic neuroimaging) has a well-defined character profile (according to the DSM IV) such as psychopathy, for example, it is impossible to infer motives or intent solely based on anatomical or functional brain abnormalities. It is still a challenge for forensic neuroimaging to determine whether there is a unique brain signature that characterizes psychopaths, violent individuals and murderers, for example. Apart from identifying neural signatures of psychological disorders, few people who engage in violent terrorist behaviour are also psychopaths or psychologically disordered. Would it be possible to characterize the personality profile of a terrorist? And once such a profile has been identified, will it be possible to correlate this personality with a particular neural signature? Can scientists use research on moral reasoning to identify a terrorist with a violent intent? Terrorist acts may be considered immoral in specific cultures; however, immoral behaviour to one person might be moral behaviour to another. Hence, using neuroimaging techniques to determine criminal/violent intent based on moral reasoning seems impossible. At the moment, ERP appears to be the most promising neuroimaging tool in detecting whether people have specific knowledge about terrorist activities or a crime scene, for example. The P300 response takes advantage of the fact that the terrorist has detailed knowledge of terrorist activities stored in his/her brain and an innocent person does not. However, to administer this test, prior knowledge of the subject's potential involvement in terrorist activities would be necessary.

Technology Readiness Levels Assessment

While not all applications of neurofunctional imaging can easily be predicted at this time, several key applications, which may be disruptive to the military and other institutions, can be identified. The following list provides examples of such applications.

Table 4 Technology Readiness Levels

Application	2005	2010	2015	2020	2025	2030
Hand-held Anatomical Imaging						
Hand-held Functional Imaging						
Brain-Machine Interfaces						
Brain-Computer interfaces						
Interrogation / Lie Detection						
Determining Intent						
Remote Imaging / Detection						

Technology Readiness Levels Key

Level	Color	Description
1		Basic principles observed and reported
2		Technology concept and/or application formulated
3		Analytical and experimental critical function and/or characteristic
4		Component and/or breadboard validation in laboratory environment
5		Component and/or breadboard validation in relevant environment
6		System/subsystem model or prototype demonstration in relevant environment
7		System prototype demonstration in an operational environment
8		Actual system completed thorough test and demonstration
9		Actual system proven through successful mission operations

Hand-held anatomical and functional imaging - Hand-held devices for either anatomical or functional methods would allow more mobility. While currently it is difficult to imagine these devices doing any more than surface imaging, improvements in detection techniques of the major imaging methods, in particular two areas, optical and magnetic resonance, are likely to bring about some form of hand-held devices. An initial attempt at such a device for MRI has been developed in the lab of Bernard Blumich in Germany (Prado, et al, 2000; Casamova, et al, 2003;

Perlo, et al, 2004) and used to image the Achilles tendon (Miltner, 2003). This device, called the NMR Mouse, is based on the same principles of the inside-out magnet (Prammer, 2004) used in oil logging. DARPA has also been investing in research to develop a hand-held MR imaging device. Another very recent technological development with MR is the ability to detect MR signal using a noncryogenic atomic magnetometer (Savukov and Romalis, 2005). This device does not need a magnet nor does it utilize sensors that operate at liquid nitrogen or helium temperatures. This device can also be used for MEG detectors and would eliminate the need for cryogens. For handheld devices, MR is likely to cover the anatomical approaches while optical and EEG imaging are the most likely candidates for functional devices. The technology for hand-held devices is sufficiently advanced to anticipate that through concerted effort these devices will achieve widespread use in the next 30 years.

Brain-Machine interfaces - Brain machine interfaces have been the primary application of functional neuroimaging outside of knowledge-gathering and medical diagnostics. In order to avoid the use of implanted electrodes, EEG-based neurofunctional imaging methods have been developed. EEG has been the primary candidate because it is inexpensive and the seemingly closeness of the technology to that of implanted electrodes. However, the challenge to discern single-events from the noisy signals has hindered the use of anything but very strong signals. Progress in biomedical signal processing and localization of these signals is improving with great speed as desktop computing power increases. There are several companies that sell multi-electrode devices and even some that claim they can be used to control computers with thought. Cortek Solutions (www.corteksolutions.com) markets such a device developed by g-tek in Austria. While this device may be premature, it does illustrate the push to commercialize such technology not only for research use but even as a home product. Optical imaging in the near-infrared has been proposed as a brain-machine interface (Coyle, et al, 2004). In addition, MRI has also been used to move around a cursor on a computer (Yoo, et al, 2004) but without the device becoming much smaller or unless it is used for control of machines at a remote location, functional MRI is not expected to be of much use.

Brain-Computer interfaces - This is a more sophisticated approach with respect to the above referenced Brain-Machine interface as it implies two-way communication, the person controlling the computer while the computer provides responses by methods other than visual feedback on the computer screen. Initial attempts at this have been developed for surgical procedures and provide feedback to the surgeon through tactile sensory input. However, no work has yet been done using direct electrical signals sent to the brain. There is work being done to grow brain cells on computer chips, which might act as an interface into the brain, but this approach is outside the scope of a neuroimaging assessment. Cyberkinetics, a company in the United States, has produced “Braingate”, which is an implantable electrode for controlling a brain computer interface. This device has been implanted into a paralyzed man and allows him to do some simple tasks such as change the channel on his TV. The role of neuroimaging in the chip development will be to gather enough knowledge about how information flows in the brain to determine how one might use such a device to intervene in the brain. At the University of Florida, Thomas DeMarse of the Biomedical Engineering department has used neurons from an excised rat brain to interact through a multi-electrode array with an F-22 fighter jet simulator on a desktop computer. The neurons receive information from the simulator and then respond. He is using this model to understand what happens in the neurons between the input of signals and what then comes out. Another group led by Theodore Berger at the University of Southern

California in Los Angeles has been using microchips to collect signals from one part of the brain and then pass these signals to the next section of the brain. This may be a good first step to making a two-way interface but it does not require that the chip interpret or encode the signals, they are simply passed on.

Transcranial magnetic stimulation may provide another means to input signals into the brain. It has been able to interrupt thought processes without direct contact with the brain. Whether this technology can do more than interrupt thoughts is not obvious. However, it has impacted the treatment of depression and so research into its mechanism of action as well as how to interrupt specific thoughts is likely to continue.

Interrogation / Lie Detection - There is an increasing focus on the notion of 'brain fingerprinting' (Farwell and Smith, 2001). The concept of brain fingerprinting is essentially predicted on the notion that 'guilty knowledge' can be determined on the basis of specific changes in ERPs. Farwell explains that the fundamental difference between a terrorist and an innocent suspect is that the terrorist has detailed knowledge of terrorist activities stored in his/her brain and an innocent person does not. An ERP trace called the P300 is elicited 300 milliseconds after an event. The P300 generally occurs when a stimulus holds specific significance for a subject, such as knowledge of a crime scene or terrorist activities, for example. (http://www.brainwavescience.com/)

Determining Intent – To date, inferring mental events from brain images is limited to experimental conditions with well-defined trials, precisely known timing, a limited number of events and cooperating subjects (Dehaene et al., 1998). Thus, it is apparent that there are many challenges to overcome before neuroimaging techniques can be used to infer criminal/violent or terrorist intent. Although forensic neuroimaging has initiated studies into the neural signatures of psychopaths and murderers, a causal link between violence and abnormal brain structure or function is difficult to establish. In order to determine a neural signature of terrorist intent, a common neural activity pattern of terrorist intent would have to be identified. This neural activity pattern will be influenced by experience and many other factors such as moral reasoning or genetics, for example. An alternative to fMRI in determining terrorist intent is ERP. Using ERP as counter-terrorist measure is not measuring intent *per se,* but the subject's familiarity with detailed knowledge of the terrorist activity/crime. This measure makes a determination of "information present" or "information absent" and provides a statistical confidence for this determination.

Remote Imaging / Detection – Very little of this report has focused on the issue of detecting brain thoughts at a distance. While brains clearly generate electromagnetic waves, these waves are very weak. EEG and MEG work by detecting these weak waves but require very sensitive and specialized equipment. It is more likely that a chemical signal from the body will be detected at a distance. That being said, it is possible that some as yet undetected phenomena can be detected at a distance. Molecular imaging might play a role here. If an agent that is very specific to a neuroreceptor or combination of receptors is developed and this agent has attached to it nanoparticles that emit a signal, then one might be able to build a detector that registers this signal. However, many technological as well as biological hurdles must be overcome in order for this to become a reality. Imaging or detection methods that have not yet been investigated on biological systems may have a role to play here as well.

Recommendations

It is important to realize that the ability to make measurements in neurofunctional imaging has greatly outstripped our ability to understand what those measurements mean. In addition, the cost of medical care is really pushing the development of faster and cheaper instrumentation. Thus the area of neuroimaging instrumentation development is heavily invested on the corporate and government levels. Where development is slow in specialty applications such as hand-held detectors, implantable devices and the application of non-medical imaging techniques to biological systems. Much of this type of development is being funded by DARPA (Defense Advanced Research Projects Agency) in the United States. There are several solicitations by DARPA at the moment that are of interest here. The HAND (Human Assisted Neural Devices, www.darpa.mil/dso/thrust/biosci/hand.htm) program headed by COL Geoffrey Ling, M.D., Ph.D., is working to develop a new hand prosthetic device using a multidisciplinary, multipronged approach. The idea is that a new device, which is capable of the necessary force and sensory feedback to truly make a prosthetic hand useful, will be developed in four years time. A solicitation (www.darpa.mil/dso/solicitations/prosthesisPIP.htm) has recently been issued for this program. Other areas of DARPA research related to neurofunctional imaging and the technology applications listed above are provided in Table 5. Some of these areas might be of interest to DRDC for joint research with DARPA.

The major area where advances could significantly affect the timelines provided above is that of neurocognitive function. A better understanding of how the brain works - what causes particular memories to occur in association with specific stimuli, how the biochemical processes interact with thought, etc – leads directly to better interpretations of neurofunctional imaging results and thus better application of these methods to a host of applications. Developing tools to allow sophisticated tasks to be performed and monitored during neurofunctional imaging experiments will go a long way to aid in developing this understanding.

Table 5 DARPA Solicitations Related to Applications of Neurofunctional Imaging

Name of Program	Link to Solicitation	Short Description of Program
Engineered Biomolecular nano-devices/system	www.darpa.mil/baa/baa05-16.htm	Development and demonstration of chip scale array platform that integrates scalable biological ion channel device architectures to enable direct, real-time conversion of biomolecular signals to electrical signals
Neurotechnology for intelligence analysts	www.darpa.mil/baa/baa05-19mod1.html	Use real-time analysis of EEG (any neurophysical signal that occurs in milliseconds) to extract when an analyst detects a target rather than waiting for a cognitive response or other physiological response.
Defense Sciences Research and Technology	www.darpa.mil/baa/baa05-19pt1.html	Advanced signal processing techniques for the decoding of neural signals in real time, specifically those associated with operationally relevant cognitive events, including target detection, errors, and other decision-making processes; and Novel interface and sensor designs for interacting with the central (cortical and subcortical structures) and peripheral nervous systems, with a particular emphasis on non-invasive and/or non-contact approaches
Biologically-Inspired Cognitive Architectures	www.darpa.mil/baa/baa05-18.html	Develop and evaluate psychologically-based and neurobiologically-based theories, design principles, and architectures of human cognition. In a subsequent phase, the program has the ultimate goal of implementing and evaluating computational models of human cognition that could eventually be used to simulate human behavior and approach human cognitive performance in a wide range of situations.

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Expert Assessment of Neuroimaging and Brain−Computer Interface (U)

4. AUTHORS (First name, middle initial and last name. If military, show rank, e.g. Maj. John E. Doe.)

Lizann Bolinger; Ryan D'Arcy; Yannick Marchand; Bram Ramjiawan; Uta Sboto−Frankenstein

5. DATE OF PUBLICATION (Month and year of publication of document.)	6a NO. OF PAGES (Total containing information, including Annexes, Appendices, etc.)	6b. NO. OF REFS (Total cited in document.)
October 2005	30	

7. DESCRIPTIVE NOTES (The category of the document, e.g. technical report, technical note or memorandum. If appropriate, enter the type of report, e.g. interim, progress, summary, annual or final. Give the inclusive dates when a specific reporting period is covered.)

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