Application of EEG, Evoked Potential and Event Related Potential protocols in Psychiatry

ANT – Advanced Neuro Technology
Netherlands

www.ant-neuro.com
Application of EEG, Evoked Potential and Event Related Potential protocols in psychiatry

1. Short introduction into neurophysiological assessment ................................................................. 2
   1.1. Introducing EEG recording, EEG spectrum analysis and Event Related Potential analysis .......... 2
   1.2. Description of several EP and ERP protocols with relevance to psychiatry ............................. 4
2. Rationale of the use of EEG/EP/ERP protocols in psychiatry .......................................................... 7
   2.1 Improved diagnostic precision ........................................................................................................ 7
   2.2. Better predicted treatment response ............................................................................................ 11
   2.3. Shortened time to final diagnosis and most effective treatment .................................................... 12
   2.4. Ability to provide alternative treatment: Neuro-Feedback ........................................................... 13
   2.5. A final reason to use neuro-physiological assessment in psychiatry ......................................... 13
3. The Cognitrace system ..................................................................................................................... 14
   3.1. Introducing Cognitrace ................................................................................................................ 14
   3.2. Cognitrace system overview ....................................................................................................... 16
   3.3. Attractive features of Cognitrace for clinical practice ................................................................. 18
   3.4. Selected user list of hospitals, institutes or practices .................................................................... 20
4. General conclusions ............................................................................................................................... 21
5. Main references .................................................................................................................................... 22

ANT – Advanced Neuro Technology
Phone    US     +1 (608) 824 0903
          Europe   +31 (53) 436 5175
Internet  www.ant-neuro.com
Email     info@ant-neuro.com
1. Short introduction into neurophysiological assessment

1.1. Introducing EEG recording, EEG spectrum analysis and Event Related Potential analysis

By placing electrodes on the scalp it is possible to record the electrical activity of the brain; this is called an electro-encephalogram (EEG). What are recorded by means of an EEG are probably reflections of temporal and spatial summation of synchronized postsynaptic cortical potentials (Schaul, 1998; Luck, 2005). Specifically, EEG data represent the synchronous activity of large cortical groups of neurons, measured as integrated electrical signals on the scalp (Figure 1).

EEG activity can be subdivided into various types of frequency rhythms or bands. Research has indicated that different EEG frequency bands are associated with different mental states (e.g., Demos, 2005). For example, alert mental states (i.e., being attentive) are reflected in higher frequencies, fast wave activity, known as beta waves. In-alert mental states (i.e., being inattentive, distracted) are reflected in lower frequencies, slow wave activity, known as theta waves. Accordingly, a relationship has been found between abnormal mental states on the one hand and abnormalities in specific frequency bands on the other hand (e.g., Demos, 2005). For instance, attention problems in individuals with attention deficit/hyperactivity disorder (ADHD) are often associated with an increased power in the theta band combined with a decreased power in the beta band (Lubar, 1995; Barry et al., 2003; Butnik, 2005). EEG frequency or spectrum analysis entails e.g.: 1) Subdivision of the EEG into different frequency bands, such as delta, theta, alpha, beta and gamma; 2) Estimation of the absolute or relative power in a band; 3) Calculating the ratio between bands; 4) Investigating left/right symmetry and 5) Investigating coherence (i.e., synchronization between channels).

Event Related Potential (ERP) analysis allows the investigation of specific types of information processing by the brain. An ERP is a change in electrical brain activity stereotyped and time-locked to an event (e.g., stimulus), although it can also occur for omission of an expected stimulus. ERPs are small relative to the spontaneous brain activity (background EEG), that is they have a low signal-to-noise ratio. To increase the signal-to-noise ratio an often-used method is ERP averaging. This can be done when the same stimulus is presented many times. ERP averaging makes use of the fact that the ERPs are time-locked to the stimulus but the background EEG is not.

ERPs are wave patterns that are characterized by three parameters: 1) Polarity (positive or negative, which is often indicated by the letter in the ERP name); 2) Latency (the moment of peak occurrence after stimulus presentation, which is often indicated with the number in the ERP name) and 3) Scalp distribution.

The temporal resolution of ERP analysis is much higher than that of other neuro-imaging methods like functional
MRI, SPECT and PET (i.e., it is in the order of milliseconds). Compared to those techniques ERP analysis lacks spatial resolution due to the following facts: 1) the conducting properties of the brain attenuate and blur the scalp signal 2) there are silent brain sources which can not be measured on the scalp and 3) there is noise inherent to any real life measurement. However, during the last years, several promising algorithms have been developed to overcome this problem (i.e., MNE, sLORETA, swLORETA, LAURA, ECD). A main advantage of ERPs is their non-invasiveness, experimental flexibility and low costs. Moreover, they can easily be used for children and psychiatric individuals as well.

ERPs allow the investigation of: 1) Basic functional pathways by recording of early ERPs or ‘evoked potentials’ (EPs) in response to clicks or tones (Auditory EP, AEP), flashes or a pattern reversal (Visual EP, VEP) or electrical stimulation (Somatosensory EP, SEP); 2) Cognitive pathways by recording of ERPs related to the execution of attention, emotion or memory tasks.

(For further reading: e.g., Luck, 2005)

Figure 1. EEG consists of the synchronous activity of large (cortical) groups of neurons, measured as integrated electrical signals on the scalp.
1.2. Description of several EP and ERP protocols with relevance to psychiatry

**LDAEP (Loudness dependent AEP)**
The ‘LDAEP’ assesses the increase in amplitude of the N1, a negativity in the EP around 100 ms after stimulus presentation, and the subsequent positivity (P2) elicited by increasing tone loudness/sound level during auditory stimulation (e.g., Mulert et al., 2002; Linka et al., 2005) (Figure 2).

Figure 2. The N1 amplitudes at several electrode positions (negativity is presented upwards) in response to five different sound levels.

(Figure is copied from Linka et al., 2005).

**P50**
P50 assessment entails the recording of a very early positivity, occurring in the EP already 50 ms after stimulus presentation, in reaction to short tones presented in pairs. Typically there is a lower P50 amplitude in response to the second tone of the pair (S2 in Figure 3) relative to that in response to the first one (S1 in Figure 3). This suppression of the P50 amplitude in response to the second tone, also called the ‘P50 suppression ratio’ (S1-S2 in Figure 3), is thought to be related to filtering of irrelevant auditory information (e.g., Freedman et al, 1999).
Figure 3. The P50 amplitude at a temporal electrode position in response to two tones that were presented in pairs. The EP elicited by the first tone of the pair (S1) is presented in blue and the EP elicited by the second tone (S2) is given in red. The dashed line represents the difference between the EPs in response to S1 and S2 (the P50 suppression ratio).

![Figure 3](image)

(Figure is made by Advanced Neuro Technology, Enschede, Netherlands)

**MMN**

The Mismatch Negativity or MMN is a negative ERP component that is recorded between 100-200 ms in response to low-probability deviant sounds in a sequence of standard sound stimuli, when attention is directed elsewhere. The deviance between sounds can for example be defined by a frequency (pitch) difference or a duration difference. The MMN is considered as the 1st step in the processes leading to conscious detection of differences in auditory context, i.e. the mnemonic comparison of a given stimulus with a previous one which has already build up a trace in memory. The violation of the previously formed memory trace produces the MMN. Recently, it has been demonstrated that not only physical characteristics of the stimulus but also abstract properties can lead to the MMN. The MMN is best seen in the difference wave between the ERP in response to the standard and deviant sounds (e.g., Tervaniemi et al., 1999; Kujala et al., 2007) (Figure 4).

![Figure 4](image)

(Figure is copied from Kujala et al., 2007).

**P300**

The P300, a positive ERP component around 300 ms after stimulus presentation, is typically generated in an auditory ‘oddball’ protocol in response to attended low-probability (deviant) target stimuli requiring an overt response (Figure 5). Typically the P300 amplitude in response to the low-probability target stimuli will be higher...
relative to that in response to the standard stimuli. The P300 is considered to be related to the maintenance of working memory when the mental model of the stimulus environment is updated (Donchin and Coles, 1988).

Figure 5. A graphic explanation of the protocol typically used to evoke a P300 component (i.e., an auditory ‘oddball’ protocol). In blue the ERP in response to standard stimuli is given and in red the ERP in response to low-probability target stimuli is given.

(CN V)

The Contingent Negative Variation (CNV) protocol entails the recording of the brain response to a warned reaction time task. Figure 6 shows a graphic explanation of the CNV protocol. Typically the ERP measured with a CNV protocol is divided into three different components or processes: 1) The one following the warning stimulus (S1 in Figure 6), which is related to the orientation response and to the S1 processing, 2) The CNV itself, which precedes the imperative stimulus (S2 in Figure 6) and which is related to motor preparation, time evaluation and S2 expectation and 3) The one following the motor act, the Post Imperative Variation, which is related to appraisal of the motor response and coping with the task. This latter component can be negative or positive depending on task performance (PINV and PIPV, respectively in Figure 6) (Timsit Berthier and Gerono, 1998; Rockstroh et al. 1982).

Figure 6. Graphic illustration of the protocol typically used to evoke a Contingent Negative Variation (CNV).
2. Rationale of the use of EEG/EP/ERP protocols in psychiatry

EEG/EP/ERP protocols are important clinical tools in psychiatry, primarily because of their role in the investigation of brain function. Research has shown that cortical neuronal dysfunction plays a major role in many psychiatric disorders (e.g., Pogarell et al., 2006; Halford, 2003). Current clinical practice often overlooks the use of neurophysiological protocols in the evaluation of psychiatric disorders. However, the correct application and interpretation of such protocols can offer several significant advantages. Neurophysiological assessment can result in:

1. Improved diagnostic precision
2. Better prediction of treatment (drug) response
3. Shortened time to final diagnosis and most effective (drug) treatment
4. Ability to provide alternative treatment: Neuro-Feedback

In the following paragraphs point by point a short clarification is given by presenting examples derived from clinical practice and the scientific literature.

2.1 Improved diagnostic precision

Since the advancement of neurophysiological measurement techniques a large number of studies have been conducted with the aim to find abnormalities in specific neurophysiological protocols among the main psychiatric disorders. Indeed, this has resulted in evidence that main psychiatric disorders are related with abnormalities in specific EEG/EP/ERP protocols (e.g., Hansenne, in press). However, research has also shown that certain neurophysiological abnormalities occur in multiple psychiatric disorders. In other words, although neurophysiological protocols are sensitive to psychiatric disorders, they may lack specificity. Nevertheless, we propose that the use of a combination of neurophysiological protocols could provide adequate diagnostic precision (see also Hansenne, in press). We would suggest the use of ‘disorder-specific protocols’ consisting of a combination of several EEG, EP or ERP protocols. Below for several psychiatric pathologies a disorder-specific protocol is described (see also listed in Table 1).

A. Schizophrenia:

It has been shown that, relative to healthy individuals, schizophrenic individuals show a decreased P50 suppression ratio (e.g., Freedman et al., 1999). Moreover, this impaired P50 suppression ratio has been
proposed as an endophenotype for schizophrenia, since it is present in patients with chronic schizophrenia, as well as in unaffected first-degree relatives and seems to be unaffected by typical antipsychotic medication (e.g., Price et al., 2006). Like a reduced P50 suppression ratio, a reduction in the MMN and P300 amplitude have also been proposed as endophenotypes for schizophrenia (e.g., Price et al., 2006; for clarification of these ERP protocols see again 1.2.). Price et al. (2006) sought to compare and combine data from probands & family members of schizophrenic patients and healthy subjects who were all assessed on each feature with an electrophysiological battery consisting of four protocols among which the P50, MMN and the P300 auditory oddball protocol (Figure 7). The conclusion of this study was that a multivariate endophenotype, based on a weighted combination of electrophysiological features, provides greater diagnostic classification power than any single endophenotype. This is due to low correlations between measures. Importantly, a high classification power was found, in the order of 70-80 %. Concluding, the P50, MMN and the P300 in combination seem to be useful for the assessment of schizophrenia.

Figure 7. The MMN and P300 components measured in probands and family members of schizophrenic patients and in healthy controls.

(B. Attention Deficit/Hyperactivity Disorder (ADHD):

In a review by Barry et al. (2003) on electrophysiology in ADHD, it was concluded that in terms of resting EEG, the parameters most reliably associated with ADHD are elevated relative theta power, reduced relative alpha and beta power, and elevated theta/alpha and theta/beta ratios (Figure 8). In the same review, it was concluded that among the ERP deficits that have been associated with ADHD one of the most robust deficits is a decreased P300 auditory oddball amplitude (for explanation of this protocol see 1.2. or Figure 5) recorded posterior over the scalp. We propose that a combination of Quantitative EEG (QEEG) measures and the P300 auditory oddball protocol may provide a useful diagnostic tool in the assessment of ADHD.)
Figure 8. Distribution of the power in the different EEG frequency bands in a subject with ADHD. It can be observed that there is great power in the theta band while there is little power in the beta band, which is assumed to be characteristic for subjects having attention problems.

(Figure copied from Demos, 2005)

C. Depression:

Evidence suggests that electrophysiology in depression is characterized by a decreased CNV (e.g., Timsit Berthier et al., 1987 and in preparation; for explanation of the CNV protocol see 1.2. or Figure 6). Additionally, often in depressive patients a Post Imperative Negative Variation, a PINV, correlated with slow reaction time occurs (Figure 6, on the left). In controls instead there is a return to baseline after the imperative stimulus (e.g., Timsit-Bertier 1987 and in preparation). Also, a disturbed loudness dependence of the auditory N1/P2 response (LDAEP) has been described in relation to depression (e.g., Pogarell et al., 2006; Linka et al., 2005; for explanation of the LDAEP protocol see 1.2.). When depression is assumed in a certain patient, the use of the CNV and the LDAEP protocols could provide more certainty.

D. Alzheimer disease:

Individuals with Alzheimer disease generally show reduced P300 amplitudes and elevated P300 latencies to task-relevant stimuli (e.g., Pogarell et al., 2006; for explanation of a typical P300 protocol see 1.2. and Figure 5). Further, in terms of resting EEG these patients usually show a decreased mean frequency of the EEG, an elevated delta and theta power and a decreased alpha and beta power. Moreover, a decreased EEG complexity, measured by EEG coherence analysis, has been related to Alzheimer disease (e.g., Jeong, 2004; Hegerl and Möller, 1997).
Table 1: Proposed Disorder-Specific Protocols

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Schizophrenia</th>
<th>ADHD</th>
<th>Depression</th>
<th>Alzheimer’s Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Decreased P50 suppression ratio</td>
<td>Elevated relative theta power in the resting EEG</td>
<td>Decreased Contingent Negative Variation (CNV) amplitude</td>
<td>Decreased mean frequency of the resting EEG</td>
</tr>
<tr>
<td></td>
<td>Decreased Mismatch Negativity (MMN) amplitude</td>
<td>Decreased relative alpha/beta power in the resting EEG</td>
<td>Occurrence of a Post Imperative Negative Variation (PINV) correlated with slow reaction time (RT)</td>
<td>Elevated delta and theta power in the resting EEG</td>
</tr>
<tr>
<td></td>
<td>Decreased P300 auditory oddball amplitude</td>
<td>Elevated theta/alpha and theta/beta ratios</td>
<td></td>
<td>Decreased alpha and beta power in the resting EEG</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Decreased P300 auditory oddball amplitude</td>
<td>Decreased EEG complexity (measured by EEG coherence analysis)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Decreased P300 amplitude (to task-relevant stimuli)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Elevated P300 latency (to task-relevant stimuli)</td>
</tr>
</tbody>
</table>

**Words of warning:** It should be noted that the use of ‘disorder-specific protocols’ is a preliminary proposal. Further (validation) research is important. Additionally, the order of the individual protocols within the above suggested disorder-specific protocols may be of importance (in relation to fatigue, alertness, etc.). It may be sensible to start with active protocol (in which an overt response is requested) and end with passive one (e.g., start with the P300 and end with the P50 protocol).
2.2. Better predicted treatment response

Converging arguments from experimental studies support the hypothesis that the amplitude of P300 and CNV as well as the loudness dependence of the auditory N1/P2 response (LDAEP) are regulated by central catecholaminergic and serotoninergic neurotransmission (e.g., Linka et al., 2005; Pogarell et al., 2006; Timsit-Berthier, 2003; Mulert et al., 2007; for an explanation of these ERP protocols see 1.2.). Figure 9 shows an illustration of the relation between serotonergic neurotransmission and the LDAEP. The catecholaminergic and serotoninergic systems are also the target of several psychotropes. Therefore, neurophysiological assessment may offer reliable indicators to predict both favorable responses and drug intolerance in psychiatric patients. Importantly, neurophysiological assessment could provide a method to objectively monitor drug effects, which is presently lacking in psychiatric practice.

Figure 9. The association between serotonergic neurotransmission and the loudness dependence of the auditory evoked potentials (LDAEP, N1 and subsequent P2): a strong serotonergic neurotransmission (i.e., high firing rate of brainstem serotonergic neurons) is associated with a weak loudness dependence of N1/P2 amplitudes of the primary auditory cortex (left), and vice versa (right).

(Figure copied from Pogarell et al., 2006)
Examples from the Literature:

- In depressed patients, a significant relationship between a strong LDAEP, indicating low serotonergic function, and a favorable response to selective serotonin reuptake inhibitors (SSRIs) has been demonstrated (e.g., Pogarell et al., 2006; Linka et al., 2005; Mulert et al., 2007).
- As is described in 2.1. Alzheimer patients generally show reduced P300 amplitudes, which is thought to be related to a cholinergic dysfunction in these patients. Interestingly, it has been found that Alzheimer patients with higher P300 amplitudes before treatment with cholinesterase inhibitors (CEIs) show a better response to treatment, as evidenced by their scores on dementia rating scales (e.g., Pogarell et al., 2006).

2.3. Shortened time to final diagnosis and most effective treatment

Apart from being more objective, neurophysiological assessment may also provide answers much faster concerning both the diagnosis itself as well as the most effective pharmacologic treatment.

Early diagnosis:
There is a need for reliable and efficient biological markers for early detection of people at risk for neuro-degeneration (e.g., Parkinson`s disease, various types of dementias) for the administration of neuro-protective treatment. Evidence suggests that neurophysiological measures such as the P300 combined with QEEG parameters may be much more effective for early detection of neuro-degeneration than conventional techniques (Hegerl and Möller, 1997; Pogarell et al., 2006; Jeong, 2004).

Shortened search for effective drug treatment:
A child with ADHD undergoes, on average, about nine years’ worth of treatment before the most effective treatment is found (personal communications with doctors). Patients with depression must often try several different antidepressants before the correct medication is found. This time-consuming procedure may lead to increasing distress to the patients; the risk of self-harm, suicidality, and chronicity may increase as well (e.g., Pogarell et al., 2006). The use of a neurophysiological parameter for reliable prediction of individual responses to different drugs would allow immediate provision of adequate and effective drug treatment. This would help to shorten the disease process and thus to prevent the risk of chronicity or sustained therapy-resistance.
2.4. Ability to provide alternative treatment: Neuro-Feedback

Neuro-feedback utilizes the relationship between abnormal mental states and brain wave frequencies. The goal of neuro-feedback is to train clients to normalize abnormal EEG frequencies and to increase awareness of how a normalized EEG pattern “feels.” More specific, the aim is to teach clients how to produce a more optimal pattern of brain waves in order to attenuate or abolish an existing abnormal mental state.

Neuro-feedback uses basic principles of biofeedback to provide clients with immediate feedback of brain electrical activity, which should lead to their learning to regulate mental states. By using electrodes attached to the scalp, electrical activity of the brain is sent to and processed by an electroencephalograph and computer. Data are displayed to the client in a format resembling that of a video game. The game action is controlled by clients who meet preset training parameters. Each time the brain waves find their way to the preset state, the client is quickly rewarded with positive feedback. As clients learn to regulate their mental activity in this manner, pathological symptoms can diminish (e.g., Butnik, 2005 and Demos, 2005).

There is clinical evidence that neuro-feedback can be an effective treatment for several disorders: e.g., ADHD, Learning Disorder, Anxiety, Post traumatic Stress Disorder, addiction, epilepsy, victims of closed head injuries and headaches (e.g., Demos, 2005). However, it should be noted that neuro-feedback treatment is still considered controversial. There are already some scientific studies showing promising results (e.g., Raymond et al., 2005; Levesque et al., 2006; Heywood and Beale, 2003), but there are inconsistencies and currently methodologically well-organized large-scale validation studies are lacking. Nevertheless, neuro-feedback could be a promising alternative treatment method (see also 3.1).

2.5. A final reason to use neuro-physiological assessment in psychiatry

Neurophysiological findings can provide insight into the natural history of the disorder. Accordingly, the discussion of neurophysiological findings with the patient (and relatives) might help to increase the understanding and acceptance of the disorder, modify the subjective experience of the disorder and increase the compliance to treatment.
3. The Cognitrace system

3.1. Introducing Cognitrace

Cognitrace is the clinical neuro-psychiatry system developed by the Dutch company, Advanced Neuro Technology (ANT). It provides the user with EEG, EP, and ERP protocols (see chapter 1 for an introduction into these techniques) that can be used with psychiatric disorders such as schizophrenia, ADHD, depression and Alzheimer disease (see Table 1 for protocols of value for these disorders). Cognitrace uses dedicated protocols for both recording and analysis. The streamlined workflow provides an easy-to-use and efficient environment for patient management, data acquisition, analysis, reporting and archiving. Importantly, Cognitrace is CE approved and has received FDA 510(k) approval.

Cognitrace consists of complete sets of measurements for neuro-psychiatry:

- **EEG**: Data is collected from multiple electrodes using a comfortable cap over a certain period of time (typically a few minutes). The data is automatically cleaned from artifacts that occurred during the recording (eye movements etc.), which can be reviewed by the technician or doctor. Next spectrum analysis is performed to map the electrical activity of the brain. Different frequency bands are displayed (alpha, beta, theta, delta) and can be automatically analyzed against age-matched reference data (find more details in 3.3.).

- **VEP**: Light stimulation of the patient is performed using a photic flash device. The recording is carried out at multiple electrodes; following this, artifact detection & rejection is done and the data is averaged. VEP averages are displayed and the results are compared with a VEP normative data set.

- **AEP**: This protocol is similar to the VEP only this time auditory stimuli (beeps) are presented to the patient. The AEP averages can also be compared with an AEP normative data set.

- **P50**: During this protocol the patient will listen to short tones presented in pairs and the processing of the brain is again recorded at multiple electrodes. After recording the automated reporting tool processes the data and presents a printable report to the technician or doctor. This report will consist of the averages elicited by the first and second tone, and the difference waves calculated by subtracting the averages elicited by the first and second tone. These difference waves can be used to analyze auditory sensory gating in patients.

- **P300 (Auditory oddball paradigm)**: A low and high pitch tones are presented to the patient. The order of presentation is pseudo-random with a likelihood of 20 against 80 for the high tones. The patient is asked to respond to the high pitch tones by clicking on a response pad. Reaction time and correctness are recorded with the continuous EEG. After the recording has been done, a report is generated which shows the brain responses at different electrodes together with reaction time data and spectra plot.
• **Visual P300 (Visual oddball paradigm):** This protocol is similar to the auditory P300 protocol only the audio presentation is replaced by visual presentations on a monitor.

• **CNV:** The patient receives a warned reaction-time task. Again, for this protocol, reaction time and correctness are recorded together with the EEG. After the recording the automated reporting tool processes the data and presents a printable report to the technician or doctor.

• **VEP to pattern reversal:** This protocol is similar to the VEP protocol with the photic device, only this time the patient is stimulated with a checkerboard pattern-reversal.

Recently the following protocols have also been added to the Cognitrace system:

• **SEP:** Electrical pulses are given to the patient and somatosensory processing of the brain is recorded at multiple electrodes.

• **MMN:** This component can be measured in Cognitrace in response to the processing of low-probability deviant sounds varying in *frequency* or in *duration* from the standard sounds presented to the patients. After recording the automated reporting tool processes the data and presents a printable report to the technician or doctor.

• **LDAEP:** The loudness dependence of the N1 and subsequent P2 can be measured in Cognitrace in response to five different sound levels. Also, a device to calibrate sound level is available.

• **Neuro-feedback:** Both a visual and auditory EEG-feedback protocol has been implemented in Cognitrace. To obtain more information on these protocols, please ask ANT.

A recording session that includes for example the EEG, VEP, AEP, P300 (auditory and visual) and CNV protocols takes about 45 minutes (patient preparation, instructions and recording time). The offline analysis procedure adds another 15 to 30 minutes depending upon the type of patient and the number of stimulation protocols done for this patient. In clinical application the report is automatically created.

In addition to the above mentioned standardized recording protocols the system can be used for other protocols like:

• Regular clinical EEG recordings (eyes open, eyes closed, photic stimulation at different frequencies, optionally with digital video)

• Sleep recordings (requires bipolar and auxiliary inputs on the amplifier, optional)

Moreover, Cognitrace can be extended with the *Evoke experiment generator tool* which allows the user to design and customize the stimulation protocols. These stimulations can be included in the standardized recording protocols.

The basis of the Cognitrace system is provided by the *Eemagine EEG software.* The workflow philosophy of Eemagine EEG contributes to the efficiency of the Cognitrace system. Well-defined templates outline the
workflow of the recording, analysis and reporting. The highly interactive and intuitive display of patient information, EEG traces, voltage and spectral analysis maps makes the review of results simple. Needless to say that all results are documented automatically. Cognitrace is the ideal neurophysiologic system for psychiatric research and patient evaluation.

3.2. Cognitrace system overview
Table 2. Cognitrace System elements

<table>
<thead>
<tr>
<th>Recording and Stimulation</th>
<th>Analysis and reporting</th>
<th>Language supported</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 24 channel amplifier</td>
<td>• 3d mapping of voltage (EEG) and FFT results</td>
<td>• English</td>
</tr>
<tr>
<td>• Impedance LEDs on front amplifier</td>
<td>• Spectral analysis (online and offline)</td>
<td>• Dutch</td>
</tr>
<tr>
<td>• PC for recording and stimulation</td>
<td>• Statistical analysis</td>
<td>• French</td>
</tr>
<tr>
<td>• Patient administration database</td>
<td>• Offline averaging and signal conditioning</td>
<td>• German</td>
</tr>
<tr>
<td>• Recording software</td>
<td>• Automatic report generation for clinic application</td>
<td>• Spanish</td>
</tr>
<tr>
<td>• Online averaging</td>
<td>• EEG, EP reference database (optional)</td>
<td></td>
</tr>
<tr>
<td>• Stimulus presentation software</td>
<td>• Spike detection (optional)</td>
<td></td>
</tr>
<tr>
<td>• Response keypad</td>
<td>• Review stations (optional)</td>
<td></td>
</tr>
<tr>
<td>• Audio card and headphones</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Device to calibrate sound level (optional)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Photic flash (optional)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Electrical stimulator (optional)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• CRT for visual presentations of stimuli (optional)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Color Printer (optional)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Caps (optional)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Starter kit for caps (optional)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
3.3. Attractive features of Cognitrace for clinical practice

Reference data for EEG Eyes open/closed, AEP and VEP protocols

ANT has normative reference data available for statistical comparison between normal subjects and the patients. The reference data is divided into age groups: 5-7, 7-9, 9-13, 14-19, 20-29, 30-39, 40-49, 50-59, 60-69, and 70-79 years. Deviations are shown in z-score units. The reference database is an optional item that can be purchased with the Cognitrace system. When this database is purchased a comparison to normative reference data is automatically done during the analysis of the EEG, AEP and VEP protocols.

Patient Management & Administration

The patient management database in Cognitrace is for the administration of patients, data as well as for the analysis and report done for these patients. The database lists all patients and the recordings, analysis and reports corresponding to each patient. The database can be running on the Cognitrace system or installed on a centralized server. The patient information along with the recordings can be accessed from the recording system as well as from any review station or other system running an up-to-date internet browser.

Network integration

Cognitrace can be set up to be running within the local area network of the department. With this EEG’s and EP’s can be reviewed over the network. All analysis, results and reports are automatically updated in the patient management database.

Cognitrace philosophy – open system

The Cognitrace system is a direct result of ANT’s experience in the field of cognitive psychology. Since several years ANT is one of the leading manufacturers of cognitive EP/ERP research equipment. This includes systems for acquisition, cognitive stimulation and analysis. All of ANT products are designated for research applications, with the exception of Cognitrace system.

The basis of the Cognitrace system is the research ERP system that ANT developed. For Cognitrace, the research system has been downscaled in terms of number of recording channels and functionality. Furthermore, it has been made more user-friendly and efficient for clinical application.

Cognitrace is an open and modular system that can be easily adjusted and customized. Moreover, it can be extended with additional components such as the experiment generator for those users that wish to use the system for a wider range of patients/applications.
**Training**

With each Cognitrace system, a one-day training session is included. This training day can be either split in two half days of 4 hours or used in one whole day. This depends on the preference of the customer and is discussed at the time of purchase. Moreover, the type of training also depends on the equipment purchased.

Typically a training session includes:
- EEG recordings, impedance test, patient preparation and instruction, start recordings
- Patient Database management, create/edit patient
- Review of data, EEG/AEP/VEP analysis
- Reporting, edit reports

The contents of the training may be varied upon the experience of the customer. For instance, in case the customer has experience in EEG recording less time will be spent on this topic, and more time will be directed towards other subjects.

**Internet Support**

ANT offers to all of its customers Internet Support. This tool uses advanced communication technology which facilitates an instantaneous connection between ANT and your PC, in order to provide remote technical assistance.

Internet Support features include; remote application and screen sharing, file transfer, text chat and voice chat (VoIP). ANT virtually teleports your desktop to their Internet Support Team allowing them to take control of a remote PC, provide advice and communicate as if they were right there sitting beside you. This means instantaneous customer support for you and no more expensive travel or downtime waiting for assistance. With our internet support you resume working productively almost instantaneously.

Highest security has been one of primary concerns throughout the development of this Internet Support. Our 256bit AES encryption and strict security measures incorporated refuse unauthorized personnel access to your data, patient information, programs and systems: you do not have to open ports, change your network or firewall configuration or modify NAT tables.

The Cognitrace system is always delivered with a free headset with microphone to make it possible to communicate with the Internet Support Team.
3.4. Selected user list of hospitals, institutes or practices

- St. Elizabeth ziekenhuis, Dr. Monte, Zottegem, Belgium
- Hôpital Brugmann, Dr Verbanck, Belgium
- Private usage: Dr. G. de Bruecker, Lede, Belgium
- ASZ Ziekenhuis, Aalst, Belgium
- Psychiatrie Ziekenhuis, Lede, Belgium
- Heilig Hart Ziekenhuis, Roeselare, Belgium
- Hôpital Charleroi, Charlois, Dr. Libois, Belgium
- Hôpital St. Luc a Bouge, Belgium
- Private usage: Dr. E. Bouillon, Blaton, Belgium
- Private usage: Dr. G. Otte, Gent, Belgium
- Hôpital Charleroi, Charlois, Belgium
- Psychiatrie Guislain, Dr. Otte, Gent, Belgium
- CHU Saint-Antoine, Paris, Dr. C. Peretti, France
- Private usage: Dr. H. Matthis, Gossau, Switzerland
- Granada, Spain
- Anti-aging Centre, Athens, Greece
- Path Medical Center, Dr. Braverman, New York NY, USA (four systems)
- Spring Mountain Treatment Center, Dr. Matthews, Las Vegas NV, USA
- Curamed, Cherry Hill NJ, USA
- HBM Center, New York, NY, USA
- Sun City, PH, USA
- Chesapeake Neurology Insitute MD, USA
- Neurology Institute, Voorhees, NJ, USA
- Wayne State University, Dr. N. Boutros, Detroit MY, USA
- UHS Meridell Achievement Center Texas, Liberty Hill, TX, USA

and more …
4. General conclusions

To summarize, the Cognitrace system of ANT can have an important role in psychiatry, because:

- It offers an objective measurement of abnormalities and is fully adapted to the needs of a clinical environment.
- It provides disorder-specific neurophysiologic protocols which can contribute to the early detection and diagnosis of several psychiatric disorders and to a fast and objective selection of treatments.
- Discussion of neurophysiological findings with the patient (and relatives) might help to increase the understanding and acceptance of the disorder, modify the subjective experience of the disorder and increase the compliance to treatment.
- It gives the possibility of giving additional, alternative treatment protocols such as Neuro-Feedback.

Cognitrace

mapping cognition to the brain
5. Main references


• Butnik SM. Neurofeedback in adolescents and adults with attention deficit hyperactivity disorder. JCLP/In Session 2005, 61, 621–625.

• Demos JN. Getting started with neurofeedback. W.W. Norton & Company, 2005.


• Halden JJ. Neurophysiologic correlates of psychiatric disorders and potential applications in epilepsy. Epilepsy and Behavior 2003, 4, 375-385.


• Linka T, Muller BW, Bender S, Sartory G, Gastpar M. The intensity dependence of auditory evoked ERP components predicts responsiveness to reboxetine treatment in major depression. Pharmacopsychiatry 2005, 38, 139-143.


• Luck, SJ. An Introduction to the event-related potential technique. The MIT Press, 2005.


• Price GW, Michie PT, Johnstone J, Innes-Brown H, Kent A, Clissa P, Jablensky AV. A multivariate electrophysiological endophenotype, from a unitary cohort, shows greater research utility than any single feature in the Western Australian family study of schizophrenia. Biological psychiatry 2006, 60, 1-10.


• Timis-Berthier M. Neurophysiological aspects of depression. In preparation.

