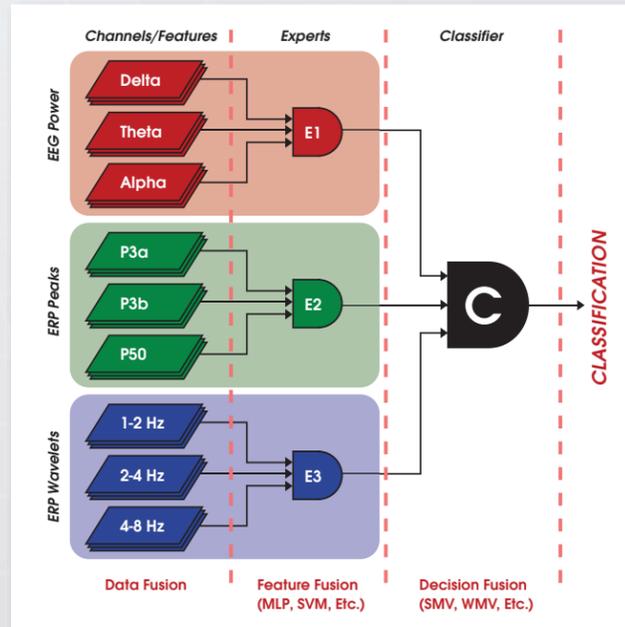


BIOMARKER FUSION CLASSIFICATION

The complexity of assessing all possible combinations of qEEG & ERP biomarker features scales up with the addition of each potential feature. Neuronetrix has implemented a flexible architecture to facilitate automated classification of aEEG/ERP data using artificial neural networks. The **COGNISION™ Classifier** module enables rapid testing and validation of meaningful combinations of qEEG/ERP biomarkers.

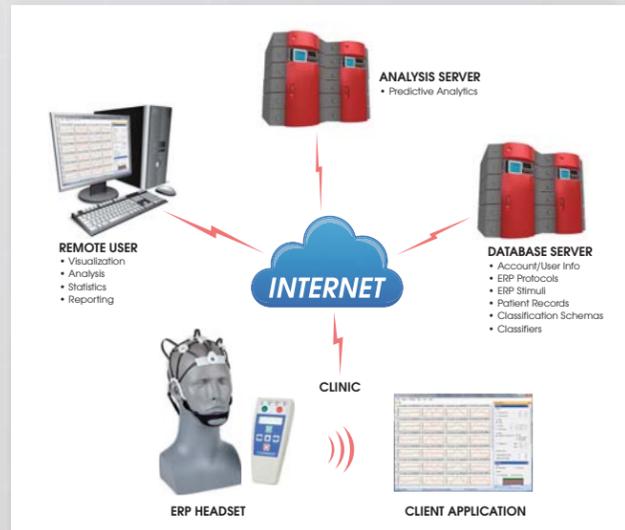
Features of the **COGNISION™ Classifier** module include:

- Database: Entire classification system is built on the **COGNISION™ Patient Manager** database so all clinical biomarker information can be used in the classification model
- Meta Modeling: Easy and intuitive definition of classification model architecture (Class-Set, Feature Set, Training Set, Experts, Validation, etc.)
- Data Fusion: Can combine data from qEEG and ERP tests (spectral properties, amplitude vs time, areas under the curve, wavelets, etc.)
- Feature Fusion: Automatically extracts and combines groups of features using optimized experts (Support Vector Machine, Multi-Layer Perceptron, Random Forrest, etc.)
- Decision Fusion: Combines decisions from multiple experts for final classification (Weighted Majority Voting, Stacked Generalization, etc.)
- Model Validation: Implements automatic k-fold validation



COGNISION™ APPLICATIONS

- Cognitive Research
- Large-scale Therapeutic Trials
- Clinical Investigations of Cognitive Disorders



SCIENTIFIC & CLINICAL REFERENCES

Luck S. J., Mathalon D. H., O'Donnell B. F., Hamalainen M. S., Spencer K. M., Javitt D. C., Uhlhaas P. J., A Roadmap for the Development and Validation of Event-Related Potential Biomarkers in Schizophrenia Research, *Biological Psychiatry*, 70(1), 28-34 (2011)

Leiser S. C., Dunlop J., Bowlby M., Devilbliss D. M., Aligning strategies for using EEG as a surrogate biomarker: A review of preclinical and clinical research, *Biochem Pharmacol* (2010)

Javitt D. C., Spencer K. M., Thaker G. K., Winterer G., Hajos M., Neurophysiological biomarkers of drug development in schizophrenia, *Nat Rev Drug Discov*, January;7(1):68-83 (2008)

Polich J. & Herbst, K.L. P300 as a clinical assay: rationale, evaluation, and findings. *Int. J. Psychophysiol.* 38, 3-19 (2000)

Jackson C., Snyder P. J., Electroencephalography and event-related potentials as biomarkers of mild cognitive impairment and mild Alzheimer's disease, *Alzheimer's & Dementia* 4, S137-S143 (2008)

Duncan C. C., Barry R. J., Connolly J. F., Fischer C., Michie P. T., Näätänen R., Polich J., Reinvang I., Van Petten C., Event-related potentials in clinical research: guidelines for eliciting, recording, and quantifying mismatch negativity, P300, and N400. *Clin. Neurophysiol.* 120, 1883-1908 (2009)

Polikar R., Topalis A., Green D., Kounios J., Clark C.M. Comparative multifresolution analysis and ensemble of classifiers approach for early diagnosis of Alzheimer's disease. *Computers in Biology and Medicine* 37(4), 542-558 (2007)

Bewernitz, M., Derendorf, H. Electroencephalogram-based pharmacodynamic measures: a review. *International Journal of Clinical Pharmacology and Therapeutics*, 50(3), 162-184 (2012)

Olichney, J. M., Yang, J.-C., Taylor, J., Kutas, M. Cognitive event-related potentials: biomarkers of synaptic dysfunction across the stages of Alzheimer's disease. *Journal of Alzheimer's Disease*, 26 Suppl 3, 215-228. (2011)

Broglio, S. P., Moore, R. D., & Hillman, C. H. A history of sport-related concussion on event-related brain potential correlates of cognition. *International Journal of Psychophysiology*, 82(1), 16-23 (2011)

Onofrij, M., Thomas, A., Iacono, D., Luciano, A. L., & Di Iorio, A. The effects of a cholinesterase inhibitor are prominent in patients with fluctuating cognition: a part 3 study of the main mechanism of cholinesterase inhibitors in dementia. *Clinical Neuropharmacology*, 26(5), 239-251 (2003)



EVENT-RELATED POTENTIALS & QUANTITATIVE EEG

for the evaluation of cognitive function

THE COGNISION™ SYSTEM

Recent scientific studies using complex electrophysiological measures have detected brainwave signatures for many neurological processes. Neuronetrix has translated these scientific advances into an easy-to-use system to rapidly test and evaluate a variety of cognitive functions. The company's **COGNISION™ System** automatically performs a selection of standardized qEEG/ERP tests, and then uses proprietary pattern recognition algorithms to automatically classify the subject's brainwave signatures.

Advanced features include:

- Wireless, battery-powered system for use in an office environment
- Subject-friendly headset fits a large range of head sizes
- Calibrated insert earphones ensure consistent auditory stimuli
- Active electrodes provide high SNR and fewer artifacts
- Integrated action buttons for subject responses
- Convenient Hydro-Dot® Biosensors are easy to apply and deliver very low skin contact impedance

Specifications:

- Channels: 7- Fz, Cz, Pz, F3, P3, F4, P4
- Sampling Rate: 125/250 samples/sec
- Band Pass: 0.3-35/70 Hz
- CMRR (50/60 Hz): >130 dB
- Noise (RTI): <1 μV_{RMS}

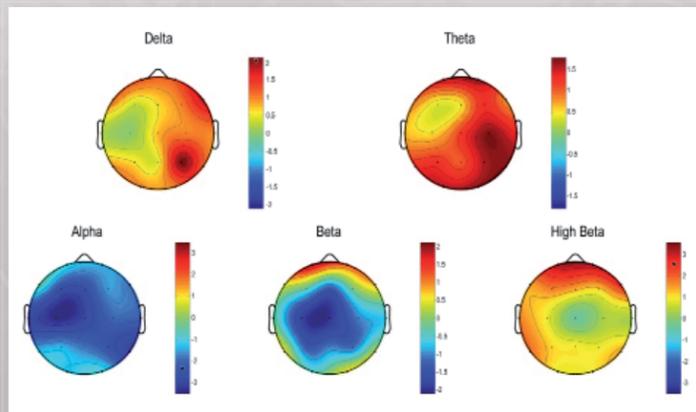


BIOELECTRIC MEASURES OF BRAIN FUNCTION

Quantitative electroencephalography (qEEG) and event-related potentials (ERP) have been studied extensively as useful tools for the evaluation of cognitive function, early detection of neurological disease, and evaluation of the effects of psychoactive compounds.

QUANTITATIVE EEG

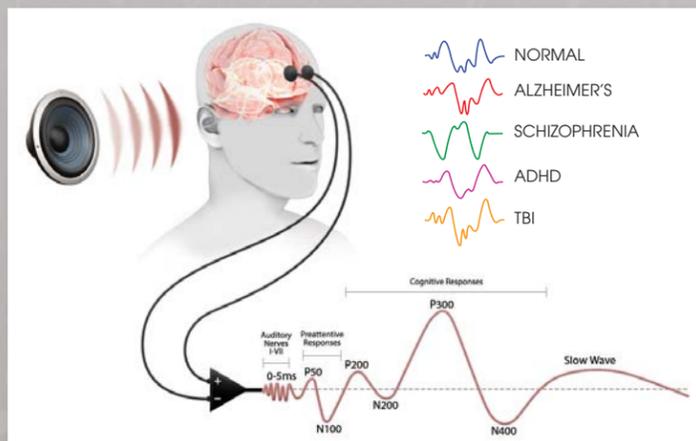
Certain characteristic frequencies of the EEG can be representative of specific cognitive states such as sleep, attentiveness, relaxation, etc. The analysis of the spectral content of the EEG is called quantitative EEG (qEEG). qEEG can be used to evaluate a range brain functions.



EVENT-RELATED POTENTIALS

Event-related Potentials (ERP) are part of the EEG generated by sensory and cognitive processing of external stimuli. The stimuli can be auditory, visual, or tactile and are generally arranged in a long sequence of many repetitions. These sequences can be designed to probe specific cognitive processes such as selective attention, memory encoding, or semantic processing.

The ERP provides a real-time electrophysiological biomarker of the underlying cognitive processes. These measures can provide important information about how the brain normally processes information and about how this processing may go awry in many neurological or psychiatric disorders.

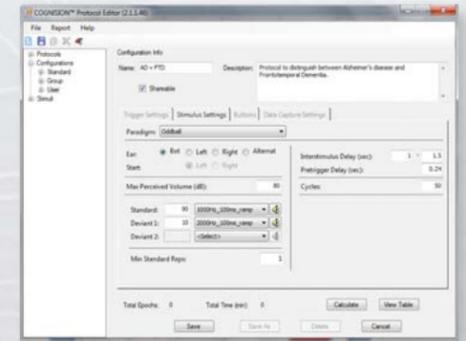


COGNISION™ QEEG/ERP PROTOCOL EDITOR

The **COGNISION™ System** uses an online library of standard ERP protocols. These protocols use auditory and/or visual stimuli which are also stored in the library. Additional protocols can be created by the user using predefined paradigm templates. These new protocols may then be shared with other users of the system.

Protocol definitions include: Predefined paradigms include: Stimuli include:

- Stimulus Settings
- Sequencing
- Timing
- Epoch Grouping
- Analysis Logic
- Single Stimulus
- Equal Probability
- 2-3 Deviant Oddball
- Match-mismatch
- Standard EEG
- Auditory
- Visual
- Combined

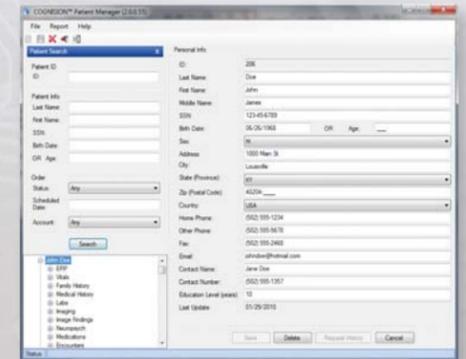


COGNISION™ PATIENT MANAGER

Management of vast amounts of personal, clinical, and biomarker data in longitudinal, multi-center studies present a formidable logistical challenge. Neuronetrix has developed a **Patient Manager** module to simplify storage/sharing of such data, thereby promoting collaborative research and facilitating complex data-mining functions.

Features of the **COGNISION™ Patient Manager** include:

- HIPAA-compliant security
- Centralized biomarker database for all relevant neurological markers (Vitals, Family History, Medical History, Labs, Imaging, Image Findings, Psychometrics, Medications, and Patient Visits)
- Context-based SQL search functions
- De-identified data sharing
- Internet-based architecture for instant data access and visualization

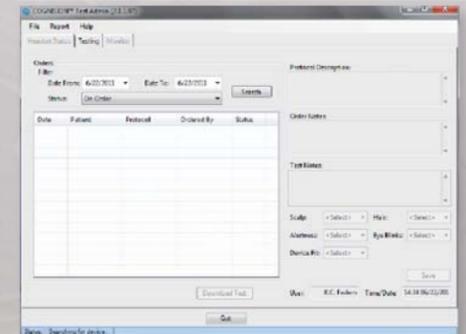


COGNISION™ TEST ADMIN

COGNISION™ tests are "ordered" in advance through the **Patient Manager** module and can be performed at any site which has a **COGNISION™ System**. The tests are administered by looking up which tests have been scheduled to be performed at a particular site and for a particular subject. The tests are then downloaded into the headset and performed.

Features of the **COGNISION™ Test Admin** module include:

- Notification of tests to be performed
- Specific tests identified for each subject
- Real-time display of test data, artifacts, and task responses
- Confirmation of test completion



COGNISION™ ERP VIEWER

The **COGNISION™ Software** includes an expert application to view and analyze qEEG/ERP data. Raw, average, grand average, and group average waves can be displayed. All preprocessing functions can be stored and automatically applied to facilitate rapid qEEG/ERP interpretation. The **Viewer** module is fully integrated with the **Patient Manager** and **Classifier** modules.

COGNISION™ Viewer display functions include:

- Raw EEG/ERP, average, difference, grand average, and grand difference waves
- Power spectrum
- Wavelet transforms
- Automatic paradigm grouping
- Normalization: amplitude, offset, and drift
- Sinc(x) function interpolation
- Automatic peak detection

