

COGNISION™ for use in Clinical Diagnostics



NEURODIAGNOSTIC CHALLENGES

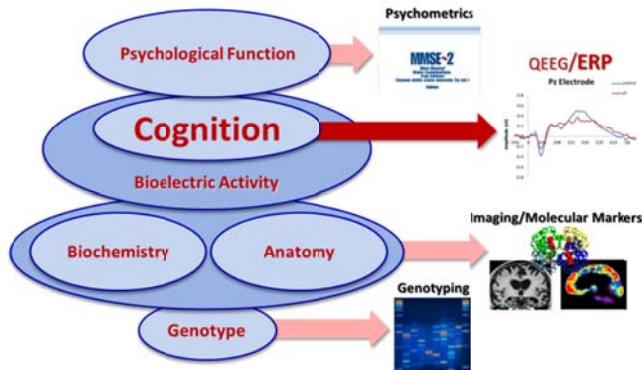
Diagnosing patients with cognitive disorders such as Alzheimer's dementia is notoriously difficult, especially in the early phases of the disease. This may limit a patient's own understanding of their condition and reduce their ability to benefit from the earliest possible interventions. Furthermore, providing an exceptional level of patient care may be impractical in the current reimbursement environment.

The solution to this dilemma would be a sensitive and reliable test of cognitive impairment which can be easily integrated into any physician's practice and which can be reimbursed at an economically viable rate.

Fortunately, with the recent technological advances embodied in Neuronetrix's COGNISION™ System, that solution is available now.

THE NEURO-BIOMARKER LANDSCAPE

Providing an accurate diagnosis generally relies upon a physician's assessment of a variety of complex medical tests. These tests often provide a "biomarker", or *measure of a physiologic process*, which is linked in some way to the disease. Because of cost/reimbursement pressures it is important for the physician to select only the most appropriate and cost-effective biomarker test at each stage of the suspected disease.



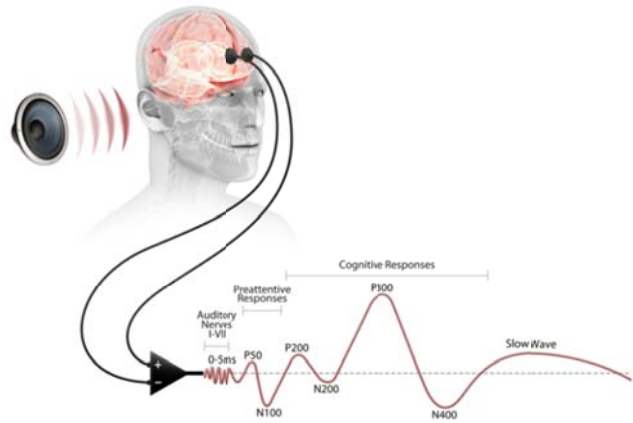
For complex cognitive disorders, such as Alzheimer's dementia, it is especially important to evaluate biomarkers of the cognitive deficits which present as the major clinical symptoms.

While there are biomarkers which can be used to evaluate risk factors for dementia such as genotyping — and other biomarkers which are measures of the anatomy or biochemistry of the brain such as amyloid imaging or cerebral spinal fluid assays — none of these are direct measures of cognitive dysfunction which is the core criteria of Alzheimer's dementia.

Neuropsychological assessments can be used to measure cognitive function but they are not measures of brain physiology. Only electrophysiological techniques such as event-related potentials (ERP) and quantitative EEG (QEEG) provide physiologic biomarkers of cognitive processes, or **cognitive biomarkers**.

COGNISION™ & COGNITIVE BIOMARKERS

The COGNISION™ System provides a series of EEG-based measurements which directly reflect cognitive processing performance. These cognitive biomarkers are automatically extracted from data recorded during a 25-minute — FDA approved — test which can be administered by any clinical tech after only a few hours of training.



BEST PRACTICE AND CLINICAL NECESSITY

The tests performed by the COGNISION™ System have been recommended as part of the NINCDS-ADRDA "best practice" criteria in; Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease¹. Additional support for tests of this type was provided in the Alzheimer's Association's new guidelines published in 2011. In their FAQ regarding the Publication of New Criteria and Guidelines for Alzheimer's Disease Diagnosis, April 2011², they recommend "biomarkers showing that nerve cells in the brain are injured or actually degenerating".

A COGNISION™ test directly reflects neuronal function and is abnormal in neurodegenerative diseases. This information may be useful to better understand complex cognitive problems in many patients.

- Discriminate dementia with an organic etiology from psychiatric disorders such as pseudodementia.³
- Positive test for early cognitive impairment consistent with Alzheimer's dementia.⁴
- Nominal results provide very high specificity which could reduce the number of patients who might otherwise be unnecessarily referred for extensive neuropsychological evaluations.⁴
- May be useful to limit the number of patients who might otherwise be unnecessarily referred for PET imaging in the

absence of any physiologic evidence of cognitive impairment.

- Provides a sensitive longitudinal measure to track or identify the early signs of cognitive decline in otherwise healthy subjects. This would help physicians to determine when and how to actively manage the disease.⁵
- Provides a sensitive measure of drug effects which can be useful for drug selection and/or to provide feedback to the patient regarding the value of maintaining treatment.⁶

PRACTICAL OFFICE IMPLEMENTATION



Easy-to-use Device

The brain of the COGNISION™ System is an easy-to-setup, wireless, handheld device which controls the test and records the electrophysiological data.

Web-based Architecture

Software to order and run a test and to review the test results can be used from any Windows® PC and all data is stored in a HIPAA-compliant manner in the cloud.

Automated Patient Report Generation

Results and relevant measures from the COGNISION™ test are presented in a pre-formatted patient report that can be edited by the treating physician to include clinical findings.

EEG/EP Patient Report

Physician/Practice Information: Louisville Neurology 1044 E Chestnut St Louisville KY 40204		Patient Information: Name: John Doe ID: 123-45-6789 Birth Date: 01/14/1948		
Study Technician: Mary Jones		Study Information: Ordered By: Dr. John Smith Order Notes: Test required to evaluate self-reported dementia symptoms in depression syndrome.		
Treating Physician: John Smith, MD		Data-Set ID: 1817 Date Uploaded: 11/18/2014		
Electronic Signature				
Test Notes: Patient was having trouble understanding the task requirements.				
Study Findings: P300a was significantly delayed over the frontal lobe indicating moderate cognitive slowing. MMN was recruited at all midline locations indicating reduced memory encoding performance. Task performance accuracy was reduced consistent with Alzheimer's dementia.				
Study Protocol: Auditory_Oddball_Active_3_01/EEG				
Test Name	Test Description	Patient Instructions		
Auditory_Oddball_Active_3_01	2-deviant auditory oddball paradigm with button press task. 75 x 1.000Hz Standard tone, 15 x 2.000Hz Target tone, 10 White Noise burst. Resting state EEG -10 minutes.	Press button with dominant hand when hearing the high tone. Close eyes during test.		
EEG				
Study Results:				
TASK PERFORMANCE				
Feature	Value			
Button Press Accuracy (%)	84.1			
False Alarms (%)	0.3			
Median Reaction Time (ms)	459			
ERP FEATURES				
Feature	Stimulus	Amplitude (µV)	Latency (ms)	Avg Amplitude (µV)
P50	Standard	1.23	45.6	78.9
N100	Standard	1.23	45.6	78.9
P200	Standard	1.23	45.6	78.9
P50	Target	1.23	45.6	78.9
N100	Target	1.23	45.6	78.9
P200	Target	1.23	45.6	78.9
N200	Target	1.23	45.6	78.9
P70	Target	1.23	45.6	78.9
Slow Wave	Target	1.23	45.6	78.9
P50	Distractor	1.23	45.6	78.9
N100	Distractor	1.23	45.6	78.9
P3a	Distractor	1.23	45.6	78.9
EEG FEATURES				
Feature	Peak Frequency (Hz)	Power		
Alpha Band	0.6			

COGNISION™ PatientReport 1

BILLING & REIMBURSEMENT

A COGNISION™ testing session consists of three distinct procedures:

1. Pure tone audiometry to assess hearing deficits which are often comorbid with dementia and can confound the clinical workup.
2. 25 minutes of EEG recording which includes both P300 and resting-state EEG tests.
3. EEG digital analysis to help identify important features of the EEG useful in evaluating cognitive function.⁷

These procedures are reimbursed by Medicare when coded with the established codes and performed to support a diagnosis of Alzheimer's or other dementia. The total reimbursement for the procedure generally exceeds \$700.

If a longer resting-state EEG test is clinically indicated and extends beyond 20 minutes, for example to allow for both eyes-open and eyes-closed testing, the 2nd procedure listed above can be split and billed using two distinct codes; 95816 (EEG 20-40 minutes) and 92585 (Auditory evoked potentials for evoked response audiometry and/or testing of the central nervous system).

Procedure Code		Disease Code		Reimbursement*
CPT	Descr	ICD-10	Descr	Rate
92552	Pure tone audiometry	G30-31	MCI & Alzheimer's Disease	\$32.20
95816	EEG 20-40 minutes	F01 - F09	Other Dementias	\$374.57
95957**	EEG digital analysis			\$325.60
Reimbursement Total				\$732.36

* Average reimbursement rate based on CMS localities
 ** As of January 1, 2016, a Florida LCD (Medicare local coverage determination) limits the use of 95957 to cases of epilepsy and/or cerebral vascular disease. It is important to review the LCD for complete indications and limitations.

PRACTICE REVENUE

Practices that see one or more dementia patients per day on average can net in excess of \$7,000 per month in COGNISION™ procedure revenues.

Practice Revenue Example (20 procedures/month)	
Procedure Reimbursement	\$732.36
Labor & Overhead Costs	-\$50.00
Rental Cost	-\$37.25
Patient Report Cost	-\$295.00
Net Revenue per Procedure	\$350.11
Practice Revenue Per Month	\$7,002.20

SELECTED REFERENCES

1. McKhann (1984). Clinical diagnosis of Alzheimer's Disease - Report of the NINCDS-ADRDA Work Group under the auspices of Dept. of HHS Task Force on AD. Neurology, 34, 939-944.
2. FAQ - Publication of New Criteria and Guidelines for Alzheimer's Disease Diagnosis, April 2011, The Alzheimer's Association.
3. Patterson (1988). Latency variability of the components of auditory event-related potentials to infrequent stimuli in aging, Alzheimer-type dementia, and depression. Electroencephalography and Clinical Neurophysiology.
4. Cecchi (2015). A clinical trial to validate ERP markers of Alzheimer's disease in outpatient settings. Submitted to Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring.
5. Ball (1989). Longitudinal P300 Latency Changes in Alzheimer's Disease. Journal of Gerontology, 44(6), 195-200.
6. Leiser (2011). Aligning strategies for using EEG as a surrogate biomarker: Biochemical Pharmacology, 81(12), 1408-1421.
7. Nuwer, M. (1997). Assessment of digital EEG, quantitative EEG, and EEG brain mapping, Neurology, 49(1), 277-292

CONTACT

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