



Neural Diagnostics Pty Ltd

EVestG™ (ElectroVestibulography)

In the absence of competing technology, research to date indicates NDPL's EVestG™ platform technology can objectively and in real time:

- Separate a wide range of Central Nervous System [CNS] disorders from healthy normals, including schizophrenia, depression, Parkinson's disease, Meniere's and Vertigo, and
- Measures the effects of drug and physical therapies on sufferers of CNS conditions.

EVestG™ has application to multiple sclerosis, Parkinsonian type disorders, and autistic spectrum disorders as well as to Alzheimer's disease and dementia.

THE PROBLEM OF CNS CONDITIONS

CNS conditions include Schizophrenia, Depression, Alzheimer's, Parkinson's disease, Autistic Spectrum Disorder, Multiple Sclerosis and Bi-Polar Disorder.

These disorders have sub-types which are difficult to separate one from another, yet each sub-type has a different treatment which, if misdiagnosed, extends the patient's suffering.

3% to 5% of the population in developed countries are being treated for these CNS conditions at any point in time, and 1 in 4 people globally will suffer from a serious CNS disorder in their life.

The majority of diagnostic tests are subjective and rely upon the scarce skill and restricted access to the relatively few psychiatric and neurological specialists for accurate diagnosis.

There is at present no objective, accurate, quick, convenient, inexpensive diagnostic system which pharmaceutical companies, neurologists, and psychiatrists can use in surgeries and clinics nor in clinical trialling of drugs, for initial screening or diagnosis of CNS conditions, and subsequently for targeting treatment and monitoring its effectiveness.

In nations with advanced healthcare systems, access to advanced imaging technology is available to a few; even then diagnosis is not assured.

Some CNS conditions take many months or even years before a final diagnosis can be made. Currently, in the case of Alzheimer's, diagnosis can only be confirmed after death.

The cost burden of CNS conditions for all nations is over US\$2 trillion per year in lost productivity, as well as in direct and indirect costs to diagnose, treat and manage sufferers.

Within these costs, pharmaceutical companies invest close to US\$1 billion and up to 12 years to bring a new CNS drug to market. Collectively, they spend close to US \$40 billion per year in trialling of all drug candidates in Phase 1 to 4 clinical trials.

Early diagnosis, intervention and targeted treatment are recognised as the best way to improve the health outcomes for sufferers, their carers and healthcare systems.



THE EVestG™ SOLUTION

Neural Diagnostics technology, **EVestG™**, is the first low cost, objective technique that will support specialist clinicians make faster diagnostic decisions and deliver better targeted clinical interventions than is currently possible, yet with equivalent or greater accuracy.

EVestG™ also facilitates more accurate and earlier assessment of the efficacy of new drug compounds and/or physical therapies in their development cycle. [See Figures 1,3 and 7]

The enhanced diagnostic decisions will be based on augmenting clinical experience with statistically robust information that correlates to electrophysiological biomarkers specific to each CNS condition, particularly to separate disorders with closely aligned symptoms.

The premise of **EVestG™** is that dizziness, loss of balance and motor disorders are defining symptoms of many CNS disorders and are issues associated with their treatment. Further the vestibular (balance) system has known bi-directional neural pathways to emotional, motor, pain, behaviour and other brain centres. Consequently, objectively measuring the neurological function of the vestibular system and its associated pathways can reasonably be expected to give an insight into the status and progression of CNS disorders should any be present.

EVestG™ results to date have so far borne this hypothesis out as being correct, as shown in the scatter plots for different disease EVestG biomarkers in Figures 2 to 7 below.

EVestG™ Technology

EVestG™ measures the brain's electrical activity before and after stimulation of the Vestibular System through use of sensors placed within each ear canal, while the patient sits in a tilt chair. The proprietary Neural Event Extraction Routine (NEER™) captures data related to proprietary objective biomarkers indicative of specific CNS disorders.

EVestG™ measurement takes less than 30 minutes and is painless to the patient throughout. Two fully operational facilities exist at Monash University and a leading research-based hospital, the Alfred in Melbourne, Australia.

Clinical Trials using EVestG™ are ongoing with over 200 data sets measurements recorded and analysed from CNS compromised subjects, including over 80 CNS sufferers covering the CNS disorders of schizophrenia, depression, Parkinson's disease, dissociation, Asperger's, positional vertigo, Meniere's disease. In addition, 57 healthy normal control subjects have provided at total of another 472 data sets, including replication studies which provide a strong base line data.

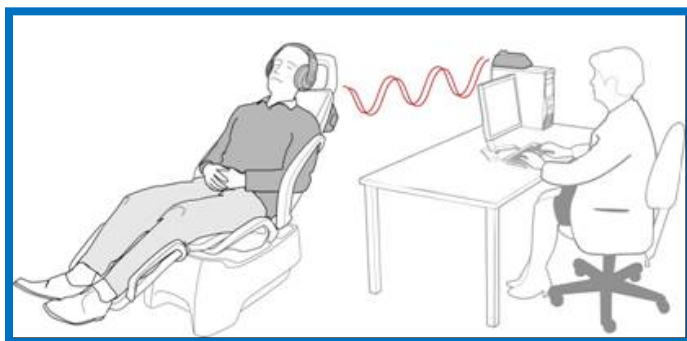
Over 700 data sets of EVestG™ waveforms, collectively give strong reproducible evidence of consistent waveforms unique to each of a number of CNS disorders that are calibrated against best practice current clinical diagnosis for those disorders. Preliminary data indicates confidence levels reaching 95% in separating healthy normal subjects from CNS sufferers. This confidence level is expected to increase as more data is gathered.

Collaboration with Texas Instruments

Neural Diagnostics has established collaboration with Texas Instruments Inc Dallas, to integrate their state-of-art chip technology to facilitate real-time signal processing and wireless communication. The outcome of this collaboration will be a miniaturised electronic unit in which the Neural Event Extraction Routine (NEER™) firmware will be embedded in the chip, which will also have wireless communication capability.

This EVestG base unit will be linked to the controls of an automated tilting chair, with sound attenuation earmuffs incorporating signal transponders communicating to a secure data processing and reporting centre, via a high-speed internet connection, as shown schematically in Figure 1.

Figure 1 EVestG Measurement Arrangement in Clinical Setting

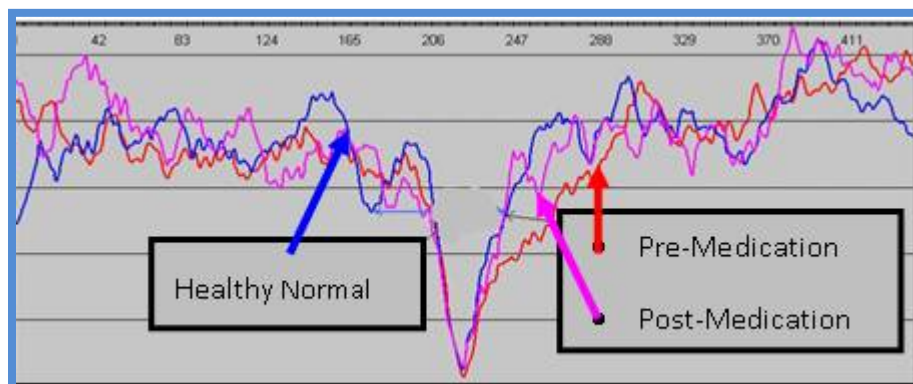


PROOF-OF-CONCEPT

Critical proof-of-concept studies have been carried out over the last two years at the Alfred Hospital with two ARC linkage grants and, based on these and other trials, an Australian National Health Medical Research Council (NHMRC) Development grant to test patient cohorts suffering from Unipolar and Bipolar Depression has been awarded. This is to be undertaken by Professor Fitzgerald at the Alfred Hospital Psychiatry Research Centre, Melbourne, Australia.

Figure 2 below shows an example of an EVestG wave form of a Parkinson subject taken before their early morning tablet of L-dopa and 60 minutes after medication, compared against a waveform from a healthy normal subject.

Figure 2 EVestG Waveforms for Parkinson Subject Before and After Medication [L-dopa]



Taking measurements of features from averaged waveforms similar to that shown above, consistent biomarkers have been extracted that correlate as surrogate endpoints to specific CNS conditions.

Results to date have also shown that EvestG is able to clearly separate healthy normals from sufferers of Schizophrenia, Parkinson’s disease [PD] and Meniere’s disease [MD]. Examples of the separations of Parkinson’s disease subjects before and after medication with L-dopa and from healthy normals are shown below in Figure 3.

Figure 3 EvestG™ Separation Biomarkers for Parkinson’s disease and healthy normals - Pre and Post Medication with L-Dopa

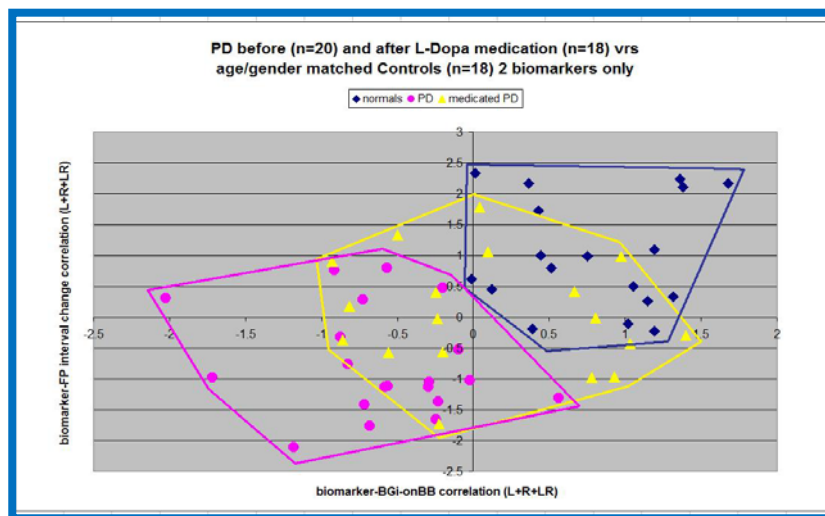
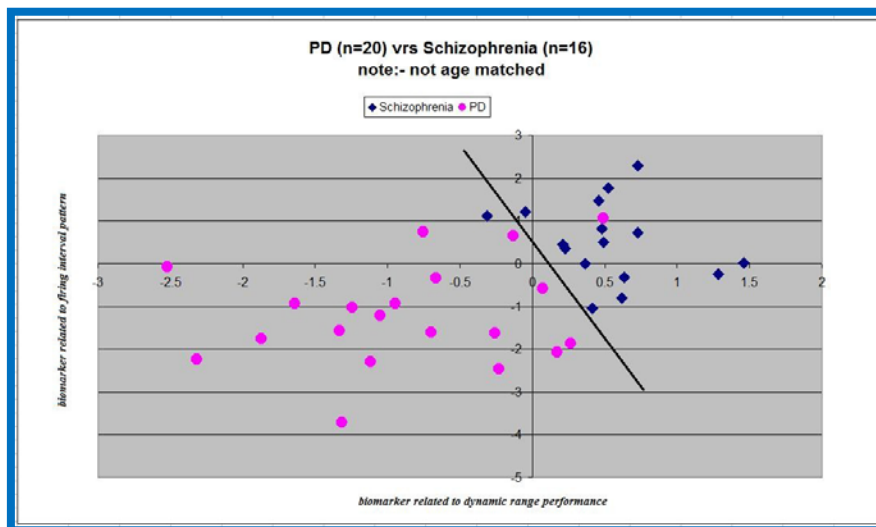


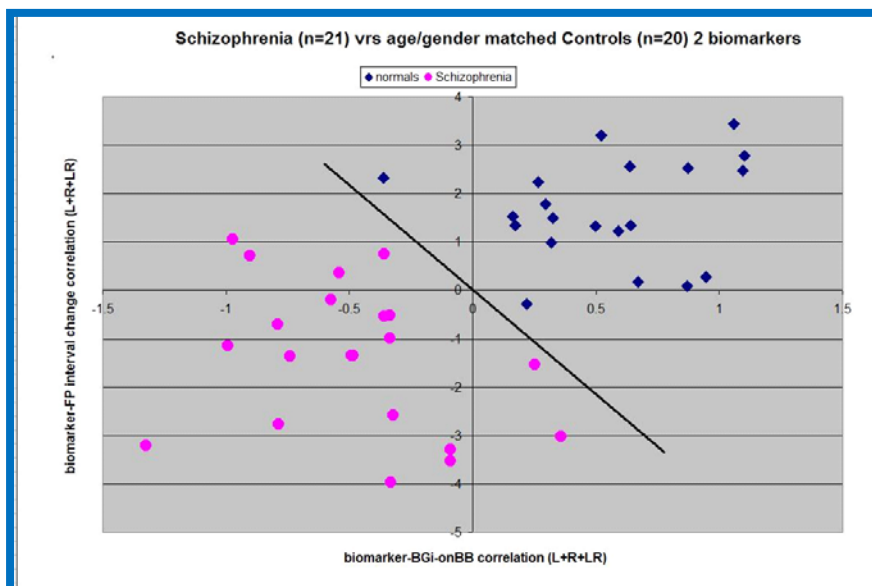
Figure 3 also raises the question as to whether EvestG, while separating Parkinson’s disease from healthy normals, can separate it from other CNS conditions. Figure 4 below suggests that this is the case, as seen in the example of separating people with Parkinson’s disease from sufferers of schizophrenia.

Figure 4 Parkinson’s disease Biomarker Separation from Schizophrenia.



In the same manner, Figure 5 shows results from an analysis of biomarkers that separate people with schizophrenia from healthy normals.

Figure 5 EVestG™ Separation Biomarkers for Schizophrenia and Healthy Normals



Figures 6 and 7 continue to highlight the versatility of EVestG to separate biomarkers for sufferers of uni-polar depression, and while there are only four data points, apparently from bi-polar subjects [manic / depressives] all from age and gender matched Healthy Normals

Figure 6 EVestG™ Separation Biomarkers for Uni Polar Depression and Healthy Normals with addition of 4 bi-polar sufferers

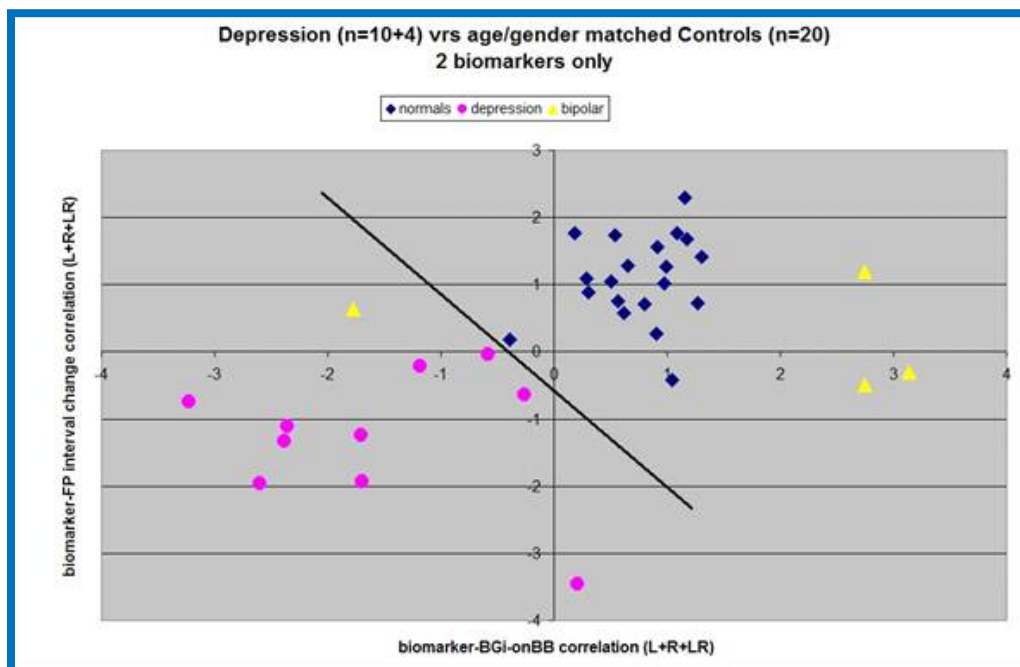
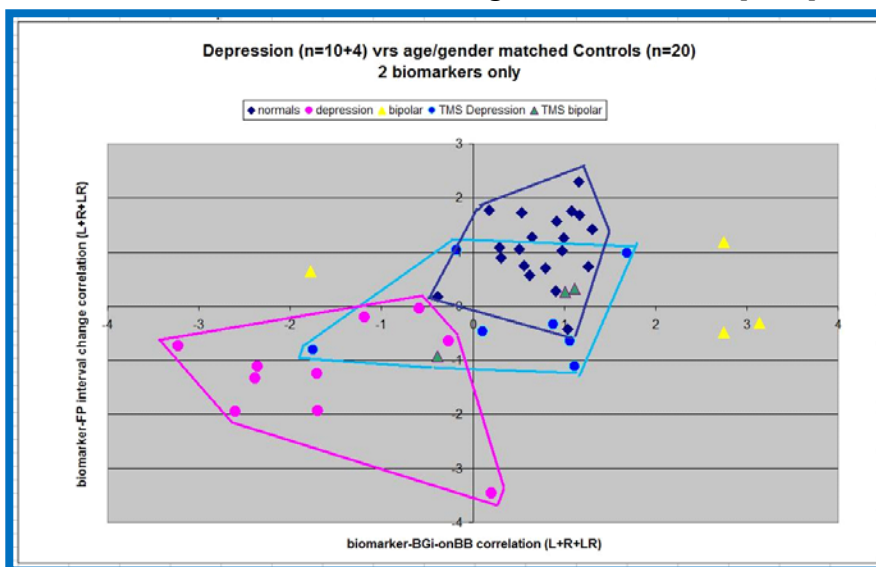
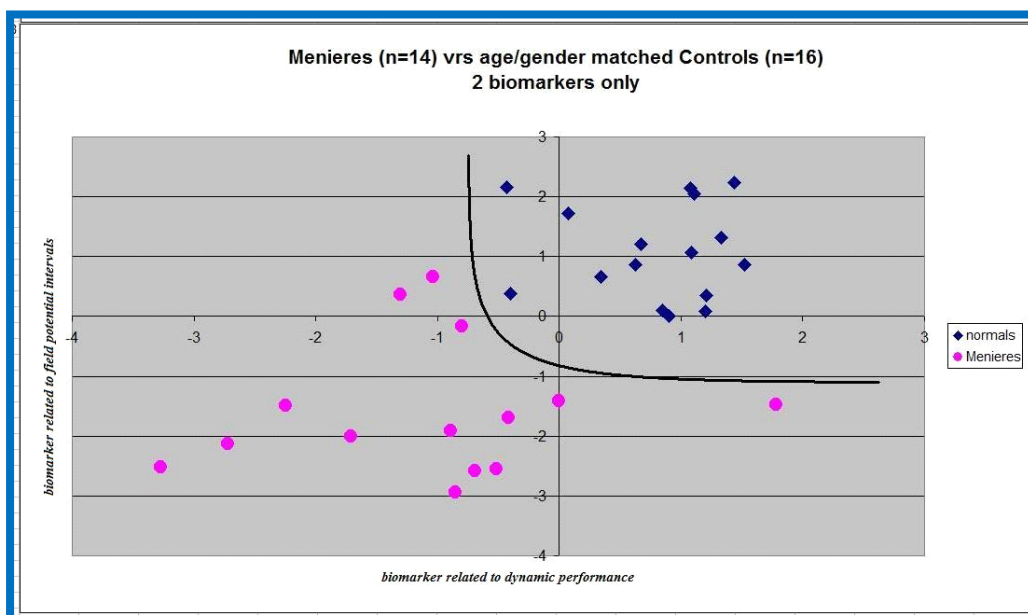


Figure 7 EVestG™ Separation Biomarkers for Uni- and Bi-Polar Depression Pre and Post Transcranial Magnetic Stimulation [TMS].



Other analyses also separate each of the above disorders from healthy normals and from other conditions, including Meniere’s disease, which is shown below in Figure 8

Figure 8 EVestG™ Separation Biomarkers for Meniere’s disease and Healthy Normals



Neural Diagnostics P/L current focus is to continue to build the statistical robustness of all the above results, as well as to expand the range of CNS disorders to which EVestG can be applied. These will include anxiety disorders, post-traumatic-stress disorder, autism spectrum disorder and multiple sclerosis.

Neural Diagnostics P/L is developing other biomarker measures that will augment its future research agenda.

KEY BENEFITS of EVestG™

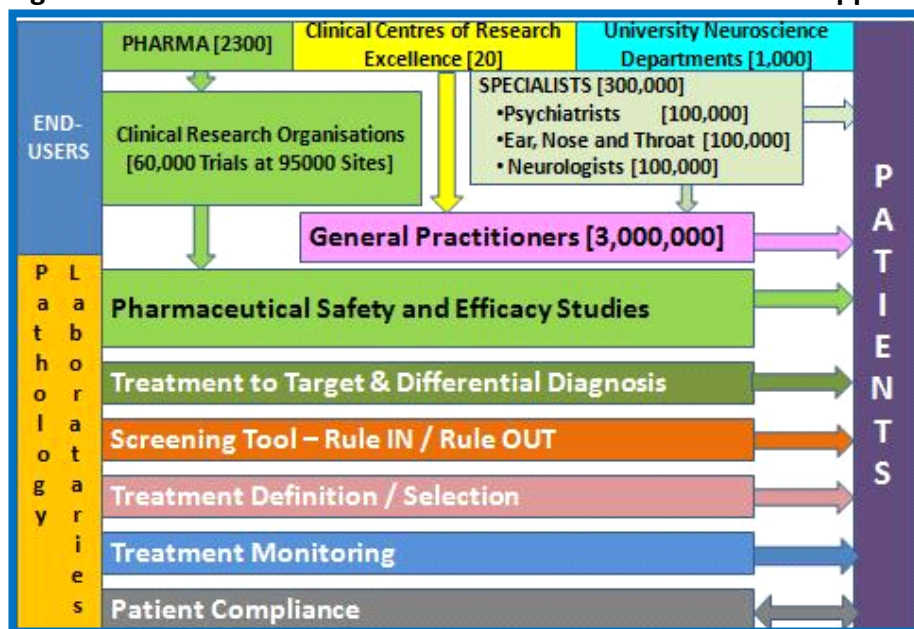
EVestG™ offers potential for:

- Quick, objective, and comparatively inexpensive service relative to other neural / brain functional measuring technologies, such as fMRI, EEG, and PET.
- Earlier diagnosis of CNS disorders which enables earlier intervention/treatment and opportunity for improved personalised outcomes across a wide range of mental and neurological illnesses.
- Objective measurement of changes to neural function during CNS clinical trials.
- The opportunity to objectively monitor effects of drugs and physical therapies in clinical interventions
- A simple automated test administered by Para-professionals.
- A painless and comfortable measurement process that is well accepted by patients.
- A culture, intellect and language neutral process for use with children and those with an intellectual disability, as it does not require their active participation in the measurement process.

TOTAL ACCESSIBLE MARKET

Figure 9 shows the general markets sectors for the EVestG™ diagnostic decision support service and associated applications in those segments.

Figure 9 Total Accessible Market Sectors for EVestG™ and its Applications



EARLY MARKET ENTRY

The initial market clinical application and entry point for EVestG™ is to differentiate between central and peripheral vertigos, including Meniere's and benign positional paroxysmal vertigo.