The Christchurch Neurotechnology Research Programme
— *NeuroTechNZ*™ —

Richard Jones
Director

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Introduction

The *Christchurch Neurotechnology Research Programme* ('*NeuroTech*' & *NeuroTechNZ*™) was formally established in February 2001 (although its had a long informal history) as a formal joint venture between Canterbury District Health Board (CDHB – Medical Physics & Bioengineering [MPBE], Neurology), University of Otago, Christchurch (UOC – Medicine), and University of Canterbury (UC – Electrical & Computer Engineering [ECE], Psychology). *NeuroTech* was initially based in MPBE at Christchurch Hospital but moved into the new *Van der Veer Institute for Parkinson's and Brain Research* at 66 Stewart Street in May 2004. It remains administratively under, but autonomous from, MPBE.

Neurotechnology can be broadly defined as 'Technology for investigation, quantification, monitoring, and treatment of the nervous system and its disorders'. Within this, *NeuroTech*'s vision is to focus on neurotechnology concerning the brain via three broad long-term objectives:

- Undertake cutting-edge research leading to the development and validation of innovative neurotechnology, particularly techniques and devices aimed at accident prevention and improved rehabilitation which can 'make a difference' to humankind by preventing loss of life and injury and by maximizing quality of life.
- Maximize the health and financial benefits of the innovative neurotechnology through commercialisation – IP protection, pre-market prototype development and validation, and product manufacture and sales on the global market.
- Maintain an awareness of other research projects in the Van der Veer Institute and, where appropriate, foster collaborations with researchers so as to identify and stimulate basic and applied brain research which might lead to potential products suitable for channelling through *NeuroTech* for commercialisation.

NeuroTech's key personnel are:

Staff

- Associate Professor Richard Jones – Neuroengineer/scientist and Director of Programme, CDHB & UOC & UC
- Dr Paul Davidson – Neuroengineer/scientist and Deputy Director of Programme, CDHB & UOC & UC
- Dr Carrie Innes – Neuroscientist and CMRF Postdoctoral Research Fellow, CDHB
- Stephanie van Bolderen – Personal Assistant, CDHB

Postgraduate students (+ degree sought)

- Malik Peiris – PhD, Electrical & Computer Engineering, UC
- Daniel Myall – PhD, Medicine, UOC
- Amol Malla – ME, Electrical & Computer Engineering, UC
- Govinda Poudel – PhD, Medicine, UOC
- Petra Hoggarth – MA, Psychology, UC
- Stephanie van Bolderen – Graduate Diploma in Management (Marketing), Commerce, UC

Affiliated staff & Research Fellows

- Associate Professor Philip Bones – UC
- Associate Professor John Dalrymple-Alford – VdVI & UC
- Dr Michael MacAskill – VdVI & UOC
- Dr Marcus Heitger – VdVI & UOC
- Dr Richard Watts – VdVI & UC
- Dr Richard Green – UC
- Grant Carroll – CDHB
- Professor Tim Anderson – VdVI & UOC & CDHB

NeuroTech is primarily funded by the Foundation for Research Science and Technology (FRST) from which current funding ends 30 September 2007. Funding beyond then has been sought via a Full Proposal to FRST earlier this year (following acceptance of last year's Concept Proposal), the outcome of which is advised mid-July. *NeuroTech* was successful in gaining funding over the past year from Lottery Health Research and University of Otago. Funding applications have also been made to Marsden Fund, Canterbury Medical Research Foundation, and Neurological Foundation, from which outcomes are awaited. Just being invited to submit a Full Proposal to Marsden, following our Preliminary Proposal in February, is considered quite an achievement (although it doesn't buy the groceries).

Research Activity

NeuroTech's research largely falls with four Sub-Programmes (of which only the second currently receives funding from FRST), of which the following outlines activity and achievements over the past year.

A. Driving Assessment Research Programme

Carrie was formally awarded her PhD in 2006 and is currently funded via a prestigious of 3-year Canterbury Medical Research Foundation Postdoctoral Research Fellowship which commenced February 2006. Her Fellowship was to allow her to continue her research in off-road driving assessment & prediction as well as commence research into lapses of responsiveness.

Building on research during her PhD project, Carrie has initiated four further research studies aimed at validation and improvement of our Canterbury Driving Assessment Tool's (*CanDAT*™) ability to predict capability to drive safely on the road based primarily on performance on a battery of computerized tests of sensory-motor and cognitive function (*SMCTests*™):

- Study 1 – Validation and improvement of the Full Assessment version of *SMCTests* (i.e., for specialist driving assessment therapists) on the full car-rig assessment system (affectionately known as *Chrissy*) at Burwood Hospital's Driving and Vehicle Assessment Service (DAVAS) in Christchurch. The study involves independent off-road and on-road assessments of 200 referrals of persons with definite or suspected brain disorders.
- Study 2 – Identical to the DAVAS study except for off-road assessment being on *CanDAT* (Chrissy's portable descendant) and undertaken by O'Leary Driving Assessment Services in Wellington.
- Study 3 – Validation and improvement of the briefer Screening Assessment version of

Figure 1. Paul being 'assessed' by Carrie on *CanDAT*.

CanDAT (i.e., primarily for medical practitioners [GPs and physicians] who have a mandatory responsibility to assess and certify driving abilities for older-aged drivers and for persons who have some form of neurological or musculoskeletal disorder) at Pegasus Health's new – and, as far as we aware, the world's first – driving screening service specifically for GPs (at 24 Hour Surgery, Christchurch). This study involves a pilot of 200 referrals to the new service from the ~240 GPs under Pegasus's umbrella.

- Study 4 – Validation and improvement of the prediction models in both the Full and Screening Assessment versions of *CanDAT* when applied to a population of 60 healthy older-aged persons. This study is being undertaken by Petra as her 'part-time' MA project in Psychology at UC (which we aim to upgrade to a PhD in August), while also undertaking her Postgraduate Diploma in Clinical Psychology. Petra is supervised by Richard, Carrie, and John and is based at the Institute. In addition to the full set of tests on *CanDAT*™ and a blinded on-road assessment, Petra will assess participants on a range of standard tests in the area of cognition/dementia, anxiety, aggression, and mood.

A considerable amount of work has gone into taking the hardware and software of *CanDAT* to a streamlined and robust pre-market prototype for off-road driving assessment (Figure 1). Paul led the technical development of *CanDAT*, based upon a modified steering wheel and foot pedals from USA, a laptop, separate screen, and, most importantly, *SMCTests*. Under Paul's guidance, Roger Bellamy made a major contribution to the system software (Roger left us in December 2007). MPBE's Mechanical Section (Johann Bader, Nevill Turner) and Clinical Engineering Section (Kathryn Greenfield, Richard Dove) provided mechanical and electrical/electronic/safety input to the small-scale manufacture of *CanDAT*s for sale (on a

Figure 2. Carrie and Paul at CDHB's 2006 Q&I Awards Function.

cost-recovery basis only) to collaborative-research beta sites for the necessary validation/improvement studies described above. We have also developed a good relationship with Christchurch manufacturer Shape Technology Ltd who are keen to take on the role, if needed, of larger-scale manufacture of *CanDAT* systems for taking to the international market – a necessary step in getting the benefits of our driving assessment research out into the big world. We are also putting considerable energy into finding an international company with distribution and support channels to our end-users (primarily OTs and GPs), necessary for successful global commercialisation (i.e., marketing, sales, and support) of *CanDAT*. So far, we have not found a company with a sufficiently good 'fit' between *CanDAT* and the company's current product lines and channels – this, in itself, supports our view of a largely unmet world-wide need and market for such devices.

Another boost for our Driving Assessment Research Programme and *CanDAT* came in August 2006 when we were awarded Runner-up in CDHB's Quality & Innovation Awards (clinical/diagnostic category) for our submission 'Canterbury Driving Assessment Tool (*CanDAT*™) – Increasing the safety and accuracy of driving assessment of people with brain disorders' (Figure 2).

Carrie's research into using computerized sensory-motor and cognitive tests to predict the driving ability of persons with brain disorders has been recognized by acceptance of a paper for publication in *Journal of the Neurological Sciences*.

B. Lapse Research Programme

Several long-term projects are under way looking at various aspects of complete lapses of responsiveness (Figure 3). These lapses can be anywhere from 1 to 20 s duration and due either to *microsleeps*, where the brain turns off for a few seconds due to a brief shut-down in our arousal system, or *lapses of sustained attention*, which can occur even when a person is not drowsy. Our Lapse Research Programme is looking at various aspects of lapses and drowsiness, including (1) detection and prediction of lapses from electrophysiological and video data, (2) characteristics of lapses, such as rate, duration, changes over time, and differences between individuals, and (3) underlying mechanisms in the brain.

Malik is close to submitting his PhD on characteristics and EEG-based detection of lapses (he changed from full- to part-time on taking up a full-time research position at Fisher and Paykel Healthcare in Auckland in July 2006). An important paper on Malik's work was published in *Journal of Sleep Research* in August 2006, which focused on the high incidence and characteristics of lapses in non-sleep-deprived healthy subjects. Also in August, Richard

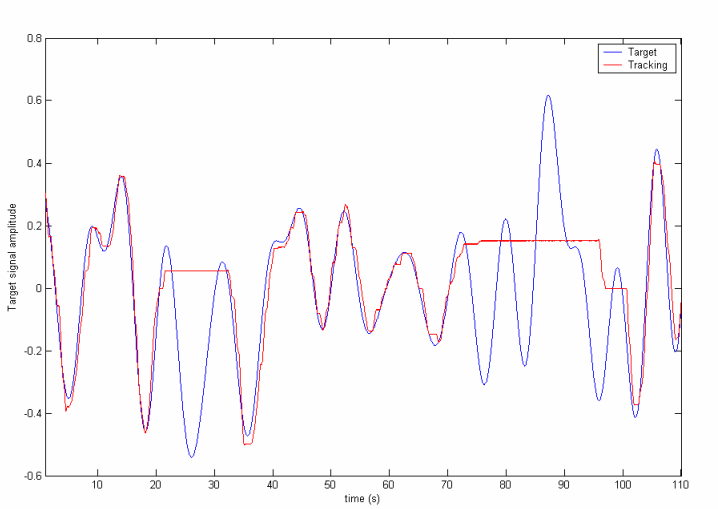

Figure 3. Some more extreme lapses seen in a non-sleep-deprived healthy subject undertaking a 1-h long tracking task in Malik's study (14 of the 15 subjects lapsed at least once and, on average, at a rate of ~40/hour.

presented a paper at *EMBC 2006* in New York on an aspect of Malik's research looking at ability to detect lapses from spectral changes in the EEG.

Amol is currently writing up his ME thesis on a computer-vision-based system he has developed for automated detection of drowsiness and lapses by measuring eye closure from video images of a person's face (Figure 4).

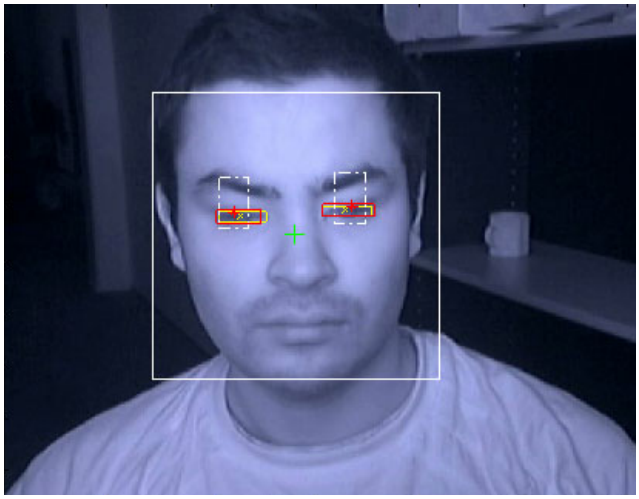

Figure 4. Automated identification of face and eyes leading to measurement of eye-closure.

Govinda has made substantial progress towards our aim of finding out just what does happen in the brain during lapses. His PhD project will investigate lapses via fMRI, 64-channel EEG, video of eyes, and visuomotor performance on a continuous 2D tracking task – all being carried out concurrently while in a 3T MRI scanner for up to an hour (Figure 5). This is a very exciting, – but also very challenging – project and, hence, we've roped in some new and keen co-researchers due to their specialist expertise and experience: Richard Watts (MRI) and Michael Hlavac (sleep disorders) from Christchurch; Leigh Signal (sleep-wake research) from Wellington; Tzzy-Ping Jung (ICA and drowsiness) from San Diego; Fabio Babiloni and Laura Astolfi (sim-fMRI+EEG and directed transfer function analysis) from Rome. Govinda has completed a major literature review and research proposal and built a mock MR scanner in the

Institute so that we can carry out preliminary studies and subject familiarisations with an MR scanner without incurring the high costs needed to do the same in the real scanner. He has also developed a novel 2-D tracking task able to detect behavioural lapses with high temporal accuracy. Understanding just what happens in the brain between arousal, attention, default mode, and other networks in the brain during lapses is of considerable interest in its own right but it also has the potential to provide important information for use in substantially

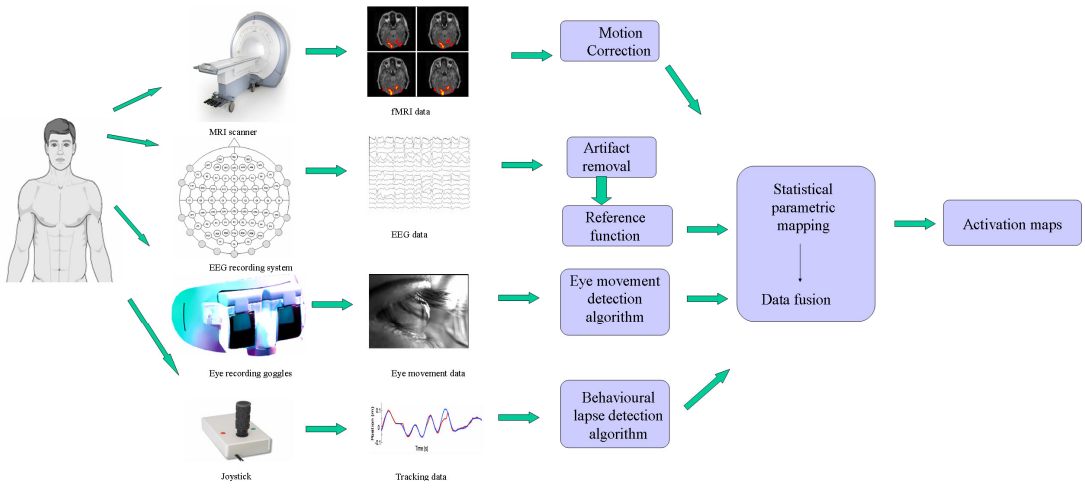

Figure 5. System for concurrent measurement of fMRI, EEG, video, and 2-D tracking.

improving the accuracy of detection and, hopefully, prediction of lapses solely from the EEG.

Our ability to carry out simultaneous fMRI+EEG investigations of the brain during lapses is only possible due to (i) the installation in late 2006 of a GE 3T MRI scanner immediately below the Institute in Hagley Radiology and (ii) a successful application to Lottery Health Research (led by Paul) for $76,000 to purchase a Neuroscan MagLink system to allow us to measure 64 channels of EEG while a person is in the undergoing fMRI. This new tool for investigation of functional activity in the brain is currently the ultimate tool for non-invasive investigations of the brain.

Carrie's research in the Programme has taken a major shift and is now focused on looking at what happens in the brain just prior to the *end* of a lapse. This will tie in closely with Govinda's study and aims to answer the question 'Once a person has gone into a lapse, why does he/she come out of it rather than continue to meet the brain's presumed need to sleep or, at least, rest?'

Paul provides critical input into all of the above projects and is also forging new directions in his own research in this area focused on the detection of lapses. His detection system based on recurrent neural networks is able to detect lapses from EEG better than any other system in the literature. A paper on this work has appeared in the prestigious *IEEE Transactions on Biomedical Engineering* (May 2007). However, as impressive an achievement as this is, the level of accuracy of detection is still too low to be viable as a device for accurate detection of lapses in, say, various transport sectors. Paul is forging a new direction for lapse detection based on the development of a head-mounted device and a more multi-modality approach to detection, with sensors for EEG, video-based eye closure, a MEMS gyroscope, an auditory warning output, signal/image processing electronics, and a power supply. This is an exciting new approach but still very much in the proof-of-concept stage.

C. Traumatic Brain Injury Research Programme

Marcus has not long completed the first two years of his Postdoctoral Fellowship from UOC and has not long been advised of this having been extended for a further two years. His work continues to focus on the subtle deficits which occur following mild TBI. He has demonstrated that sub-clinical motor deficits can be detected in patients who were otherwise considered to have had no long-term adverse effects due to their mild head injury (e.g., concussion and subsequent visit to an Emergency Department). Furthermore, Marcus has shown that some of these deficits will not have completely recovered several months after the accident. He has also shown that the early subtle oculomotor, somatomotor, and visuoperceptual deficits are predictive of outcome, including postconcussion syndrome. These findings are being further validated through further more extensive studies of acute TBIs and of patients referred to the Burwood Head Injury Clinic several months after their injury due to non-resolving sequelae. Once validated, these techniques have the potential for incorporation into devices which can predict outcome following mild head injury with substantial possibilities for commercialisation. Marcus's research has lead to a further two publications – *Brain Injury* and *Journal of the Neurological Sciences* – over the past year.

Back in 2004, Marcus was successful in gaining funding from the CMRF for a project aimed at using advance MR imaging techniques to study anatomical and physiological changes in persons who had sustained a mild TBI. This project was put on hold pending arrival of the 3T MR scanner. Now that the scanner has arrived and been commissioned (in Hagley Radiology), this imaging study will soon be up and running.

D. Virtual-Environment Neurorehabilitation Research Programme

Not deterred by a series of substantial technical challenges, Daniel has developed an impressive 3-D multi-sensor/multi-display platform for studies of movements in a virtual environment (Figure 6) – based in our Movement & Virtual Environment (MoVE) Lab at the Institute. Daniel is close to submitting a manuscript on this system, with examples from several pilot applications, to an international journal in neural engineering.

Figure 6. Near-field and head-mounted-display virtual environments.

With this new system, Daniel, Michael, Tim, and Richard have instigated a major research study involving 24 patients with Parkinson's disease and matched controls. The study, nearing completion of its data-collection phase, comprises 4 sessions per subject, several movement and adaptation paradigms (including visual/memory-guided movements and response delays), ballistic and smooth arm movements, and on- and off-medication; this all happens in a virtual environment in which all sorts of

manipulations (some obvious to subject, some not) can be made to the target, the visual environment, and to the target-response dynamics. Results from the study will be used to gain a fuller understanding of movement deficits in PD and to test and improve a computational model of the brain and its ability to account for the various deficits seen in PD.

By way of a head-mounted display, the MoVE system also has capabilities for investigating lower-limb dysfunction, such as postural sway and ambulation, in a fully immersive virtual environment. Peter Steenbergen, from University of Twente (Enschede, The Netherlands), made good progress in this area during his 4-month Biomedical Engineering Workshop Training with us. Still early days but we are keen to apply these techniques in the investigation of balance and gait disorders.
