Christchurch Neurotechnology Research Programme

May 2009 – April 2010

www.neurotech.org.nz

Richard Jones
Director

Introduction

The *Christchurch Neurotechnology Research Programme* (‘*NeuroTech*’ – www.neurotech.org.nz) is a joint venture between CDHB (Medical Physics & Bioengineering, Neurology), University of Otago, Christchurch (Medicine), and University of Canterbury (Electrical & Computer Engineering], Psychology). *NeuroTech* is physically based at the *Van der Veer Institute for Parkinson’s and Brain Research* (VdVI).

- ***NeuroTech* personnel**

Staff

- Associate Professor Richard Jones – Neuroengineer/scientist and Director of Programme: Medical Physics & Bioengineering, CDHB; Electrical & Computer Engineering, UC; Psychology, UC; Medicine, UOC; VdVI
- Dr Carrie Innes – Neuroscientist, Postdoctoral Career Development Fellow (Accident Compensation Corporation): Medical Physics & Bioengineering, CDHB; VdVI
- Dr Govinda Poudel – Neuroengineer/scientist, Postdoctoral Research Fellow (Marsden): Medical Physics & Bioengineering, CDHB; VdVI

Students *(+ degree sought)*

- Daniel Myall – PhD, Medicine, UOC
- Petra Hoggarth – PhD, Psychology, UC
- Russell Buckley – MA, Psychology, UC
- Jie Chen – BE, Electrical & Computer Engineering, UC
- Chen Chen – BSc, Mathematics & Statistics, UC
- Jeremy Lane – Summer Student, Electrical & Computer Engineering, UC
- Agate Ponder-Sutton – Summer Student, Mathematics & Statistics, UC

Affiliated staff & Research Fellows

- Professor Philip Bones – Electrical & Computer Engineering, UC
- Professor Tim Anderson – Medicine, UOC; Neurology, CDHB; VdVI
- Associate Professor John Dalrymple-Alford –Psychology, UC; VdVI
- Dr Marcus Heitger – Medicine, UOC; VdVI

- Dr Richard Watts – Physics, UC; VdVI
- Dr Deak Helton – Psychology, UC
- Dr Michael MacAskill – Medicine, UOC; VdVI
- Dr Dominic Lee – Mathematics & Statistics, UC
- Dr Malik Peiris – ex- Electrical & Computer Engineering, UC
- Amol Malla – ex- Electrical & Computer Engineering, UC

Research Activity

A. Driving Assessment Research Programme

Carrie, Petra, John, and Richard have four research studies in progress aimed at (1) validation and improvement of our Canterbury Driving Assessment Tool's (*CanDAT*™) (Figure 1) ability to predict 'medical fitness to drive' and 'ability to drive safely' based primarily on performance on a battery of computerized tests of sensory-motor and cognitive function (*SMCTests*™) and (2) improving our understanding of the complex task of driving and the medical and non-medical factors which can prevent a person from driving safely:

- Study 1 – Determination of the accuracy of prediction models in both the Full and Screening Assessment versions of *CanDAT* when applied to a population of 60 healthy older-aged persons. Petra (supervised by Richard, Carrie, and John) has completed this study and has a paper in press in *Accident Analysis and Prevention*. In addition to the *CanDAT* tests and a blinded on-road assessment, Petra assessed participants on a range of standard tests of cognition/dementia, anxiety, aggression, and mood. Surprisingly, 16 of the participants failed the on-road test. Petra showed that, in this population, 'non-causal resource analysis' modelling is able to classify/predict Passes and Fails substantially better then 'binary logistic regression'.

- Study 2 – Petra has completed a two-year follow-up of driving accidents and traffic violations in the healthy older drivers study. The aim was to determine, as much as one can, the extent to which performance on the on-road assessment correlates with the true gold standard for safe driving of accidents and violations. The latter information is obtained from the participants themselves and from Land Transport NZ and the Ministry of Transport. This is the first study to have followed up on-road assessments in people

Figure 1. Carrie being tested by Petra on *CanDAT*.

for which there were no consequences from the assessment – i.e., persons who failed the on-road were permitted to keep driving. While the number of subjects, base rate for accidents/violations, and length of study limit the conclusions we can draw from this study, our results have shown no evidence of a difference between the on-road Pass and Fail groups! Petra presented preliminary results from the first year of the study at the *5th International Driving Symposium on Human Factors in Driver Assessment, Training, and Vehicle Design*, Big Sky, Montana, USA, in June 2009.

- Study 3 – Petra's third study focused on persons with mild cognitive impairment or early dementia referred for a driving assessment to Burwood Hospital's Driving and Vehicle Assessment Service. This study is looking at performance on *CanDAT* tests, several standard cognitive tests, and a blinded on-road assessment. These type of patients have previously proven particularly problematic as some have been found to perform poorly on *CanDAT* but still pass the on-road assessment. We aim to complete this study later this year.

- Study 4 – A large study aimed at acquiring independent off-road and on-road assessment data from 600 referrals of persons with definite or suspected brain disorders is well advanced. The data are being collected from three Occupational Therapy-based Driving Assessment Services in New Zealand: Burwood Hospital, O'Leary Driving Assessment Services (Wellington and Palmerston North), OTRS Group Ltd (Hamilton and South Auckland). The data from this study is bring used to determine and optimize the predictive accuracy of *CanDAT*. Several predictive models have been explored via a Final Year Project in Maths & Statistics, UC (Dominic Lee and Chen Chen), a Summer Studentship (Agate Ponder-Sutton), and substantial work by Carrie. This has led to a preliminary paper being presented by Carrie at the abovementioned Driving Symposium at Big Sky in June 2009 and a paper soon to be submitted which compares six classification/predictive modelling techniques: discriminant analysis, binary logistic regression, non-causal resource analysis, product kernel, kernel product, and support vector machine. Amongst other things, this has shown that while there is a substantial difference between these models in the accuracy with which they can model, and hence classify a training set, their ability to generalize to prediction of on-road performance in an independent test set is surprisingly similar.

In addition, Carrie had a paper published in *Behavioral Research Methods* on the performance of normal subjects on *SMCTests*. Richard gave a talk on the Christchurch Driving Research Programme at a Senior Drivers Workshop in Wellington in March 2010.

B. Lapse Research Programme

Several projects are under way looking at various aspects of complete lapses of responsiveness ('lapses'). These lapses can be anywhere from 1 to 15 s duration and are due to behavioural 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's long-term goals are broadly (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, (3) underlying mechanisms in the brain, and (4) factors affecting propensity to lapse.

Govinda (supervised by Richard, Carrie, and Phil) has made great progress towards finding out just what happens in the brain during lapses. His PhD project investigated lapses via

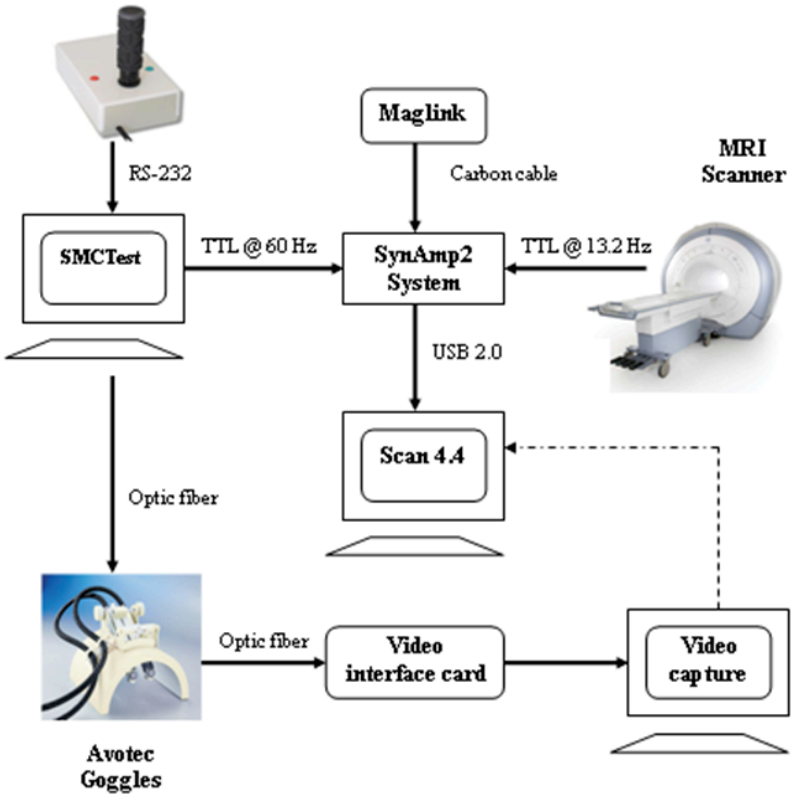

Figure 2. Schematic of simultaneous recording system.

fMRI, 64-channel EEG, video of eyes, and visuomotor performance on a continuous 2D tracking task – all carried out concurrently in a 3T MRI scanner for 50 min (Figure 2).

We collected data from 20 subjects. Despite the loud noise in the scanner (even with ear-muffs), 16 of our non-sleep-deprived subjects had microsleeps during their afternoon sessions, with an average 79 microsleeps per hour. Because slow eye-closure and sudden task non-responsiveness are strong behavioural indicators of microsleeps, Govinda put a lot of effort into understanding and quantifying the brain mechanisms underlying voluntary slow-eye-closure and task non-responsiveness during a visuomotor task. We now have group results of areas in the brain which have increased and decreased activity during microsleeps, as well as time-courses in areas of particular interest (Figure 3). During microsleeps, the BOLD signal (and, hence, neural activity) decreases bilaterally in the thalamus, posterior cingulate cortex, and striate cortex but increases in several cortical brain regions including the inferior frontal cortex, posterior parietal cortex, and occipital cortex. Furthermore, the extent of the decrease in neural activity in the thalamus increases with the duration of the microsleeps (Figure 3). Understanding just what happens in the brain between cortical arousal, attention, default mode, and other networks in the brain during lapses is of considerable interest in its own right but also has the potential to provide important information for use in substantially improving the accuracy of detection and, possibly, prediction of lapses solely from the EEG or in combination with video of the eyes. We have the only system in NZ able to carry out simultaneous fMRI+EEG investigations of the brain and consider sim-fMRI+EEG to be the ultimate tool for non-invasive investigation of the brain.

Carrie has contributed substantially to the sim-fMRI+EEG study, particularly in the demanding and time-consuming process of rating the simultaneous tracking and eye-video data for lapses. Her analyses have also shown that propensity for, and duration of, microsleeps and DIREs are correlated with scores on a subjective estimate of daytime sleepiness (Epworth Sleepiness Scale) but, surprisingly, not with other measures of sleep, such as sleep quality, disturbance, duration, and efficiency, and circadian type. This indicates

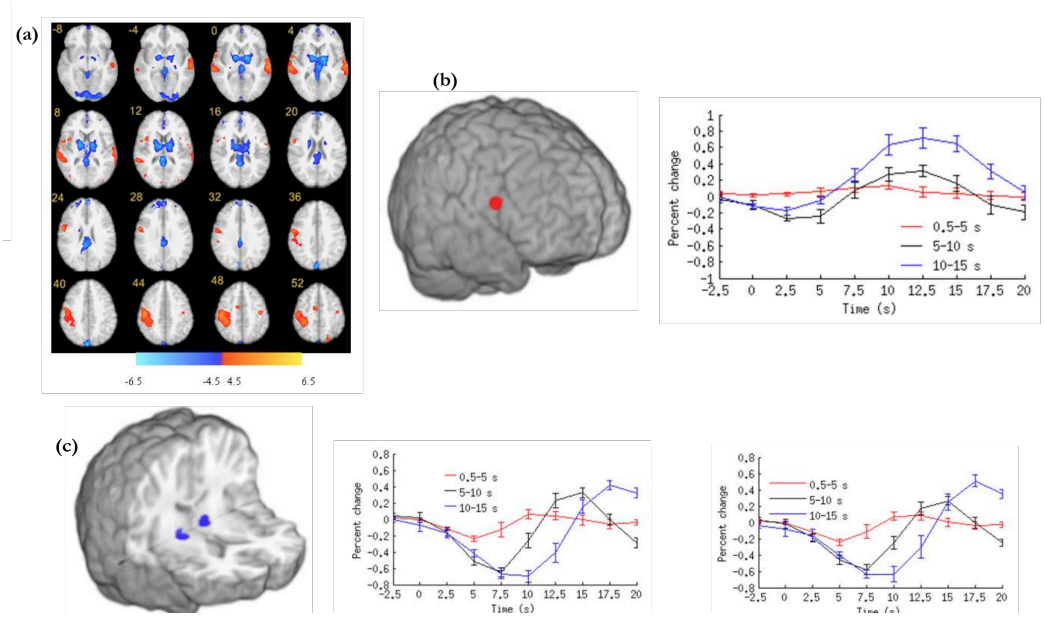

Figure 3. (a) Spatial map of activation (red) and deactivation (blue) during behavioural microsleeps obtained after group-level analysis. Time-resolved analysis of BOLD activity for three bins of 0.5–5 s, 5–10 s , and 10–15 s in the (b) right inferior frontal gyrus and (c) bilateral thalamus. Time-resolved analysis shows duration-dependent modulation in BOLD activity during microsleeps.

that propensity to fall asleep in situations in which sustained performance is required appears to be primarily a trait characteristic in normally-rested people. We have just submitted a paper on this work and findings.

Data collection in our follow-up Marsden-funded sim-fMRI+EEG study has not long commenced, which involves healthy participants coming in for 2 sessions: one in which they are normally-rested and the other in which their sleep during the prior night has been restricted to 4 hours. Like its predecessor, this study will allow us investigate even more closely important questions about (1) the timing and order of brain activity underlying lapses, (2) the mechanisms underlying the initiation and recovery from lapses, and (3) the underlying differences between microsleeps and lapses of attention. In addition, it will allow us to answer questions on the effect of sleep deprivation on the behavioural and neural mechanisms of microsleeps, attention lapses, and problem identification.

The data collection phase of Russ's MA project in Psychology (supervised by Richard, John, Carrie, and Deak) has not long commenced. His study is looking at the differences in propensity for microsleeps versus attention lapses on different types of tasks (2-D tracking vs. vigilance) and task complexity (independent tests vs. combined).

Jie Chen (supervised by Richard, Phil, and Govinda) completed his BE(Elect) project in 2009 aimed at automating the time-consuming human-expert rating of tracking performance and video of eyes for detection of lapses and their start- and end-points.

Overall, our Lapse Research Programme aims to (1) advance scientific understanding of the behavioural characteristics and underlying neural mechanisms of lapses and (2) develop lapse and drowsiness detection & prediction technology. Ultimately, its is hoped that this research will help in the prevention of serious/fatal accidents due to lapses, particularly in the transport sectors (truck & car drivers, pilots, air-traffic controllers, train drivers, health professionals), medicine (e.g., surgeons, anaesthetists), and industry (e.g., process control workers, nuclear plant operators).

Over the past year, Govinda submitted a superb thesis, was awarded his PhD, presented a paper at *EMBC'09* (Minneapolis), and has a paper in press in *IEEE Transactions on Neural Systems and Rehabilitation Engineering* and an abstract in press in *New Zealand Medical Journal*. With funding from Royal Society, Richard visited the Research Group and Neuroelectric Imaging Laboratory of Prof. Fabio Babiloni at the Santa Lucia Foundation – Scientific Institute for Hospitalisation and Treatment (National Hospital for Neuromotor Rehabilitation) in Rome in March 2010 and gave an invited seminar. He also gave an Invited Talk at a Workshop on 'Neurodynamic Insight into Functional Connectivity, Cognition and Consciousness' in Dubrovnik.

C. Traumatic Brain Injury Research Programme

From this research, we got a second paper published in the prestigious neurology journal *Brain*, this time on impaired eye movements in postconcussion syndrome. However, sadly, our research into the subtle/sub-clinical motor deficits following mild TBI has essentially come to an end following the departure of research leader, Marcus, to Belgium where he has taken up a research position in the Research Center for Movement Control and Neuroplasticity at the Katholieke Universiteit Leuven.

D. Virtual-Environment Neurorehabilitation Research Programme

Daniel and Michael's research study of 24 patients with Parkinson's disease and matched controls is now complete. The study involved 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 – all carried out in Daniel's 3-D multi-sensor/multi-display virtual-environment system. Amongst other things, the study has shown that Parkinson's patients retain artificially-induced changes in their arm dynamics (i.e., after-effects) substantially longer than control subjects. This has the potential for development of a novel neurorehabilitation approach to movement dysfunction in persons with Parkinson's disease. Daniel's analyses were based upon state-of-the-art mixed-effects models and, where appropriate, Bayesian prior estimates – all implemented in *R*.

Daniel has submitted a superb PhD thesis, is currently making some refinements to accommodate suggestions made by his examiners, and is close to being awarded his PhD. Several more publications are in the pipeline.

Publications & Presentations

Full papers in refereed journals –

Heitger MH, Jones RD, Macleod AD, Snell DL, Frampton CM, Anderson TJ (2009). Impaired eye movements in postconcussion syndrome indicate sub-optimal brain function beyond the influence of depression, malingering or intellectual ability. *Brain* 132: 2850-2870.

Poudel GR, Jones RD, Innes CRH, Watts R, Bones PJ (*in press*). Transient BOLD activity due to cued eye-closure and stopping during a continuous visuomotor task: A model-free investigation. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*.

Hoggarth PA, Innes CR, Dalrymple-Alford JC, Severinsen JE, Jones RD (*in press*). A multidomain approach to the determination of driving ability in healthy older adults. *Accident Analysis & Prevention*.

Full Papers in Published Conference Proceedings –

Innes CRH, Jones RD, Dalrymple-Alford JC, Severinsen J (2009). Prediction of driving ability in people with dementia- and non-dementia-related brain disorders. *Proceedings of 5th International Driving Symposium on Human Factors in Driver Assessment, Training, and Vehicle Design*, Big Sky, Montana, USA, 342-348.

Hoggarth PA, Jones RD, Innes CRH, Dalrymple-Alford JC (2009). Driving assessment and subsequent driving outcome: A prospective study of safe and unsafe driver groups. *Proceedings of 5th International Driving Symposium on Human Factors in Driver Assessment, Training, and Vehicle Design*, Big Sky, Montana, USA, 433-439.

Poudel GR, Jones RD, Innes CRH, Watts R, Signal TL, Bones PJ (2009). fMRI correlates of behavioural microsleeps during a continuous visuomotor task. *Proceedings of 31st Annual International Conference of IEEE Engineering in Medicine and Biology Society (EMBC 2009)*, Minneapolis, USA, 31, 2919-2922.

Published Abstracts –

Jones R, Poudel G, Innes C and Bones P (2010). Lapses of responsiveness: Their characteristics, detection, and underlying mechanisms. (Abstract). *Frontier Conferences*, doi: 10.3389/conf.fnins.2010.05.00008 http://frontiersin.org/conferences/individual_abstract_listing.php?conferid=944&pap=3707&ind_abs=1 [Presented at *Workshop of NeuroMath COST Action BM0601 on 'Neurodynamic Insight into Functional Connectivity, Cognition and Consciousness'*, Dubrovnik, Croatia, March 2010. (Invited Speaker)]

Poudel GR, Jones RD, Innes CRH, Bones PJ, Watts R (*in press*). Changes in BOLD activity during behavioural microsleeps (Abstract). *New Zealand Medical Journal*. [Presented at *Health Research Society of Canterbury Scientific Meeting*, Christchurch, March 2010]
