Canterbury Medical Research Foundation Conference report:

Sarah Wright, PhD student, C/-Van der Veer Institute.

The 10th International Conference of Alzheimer's and Parkinson's disease, AD/PD 2011, Barcelona Spain, 9th- 13th March 2011.

I received a CMRF travel grant-in-aid which enabled me to attend the Alzheimer's and Parkinson's disease (ADPD 2011) conference in Barcelona and present a poster. Delegates of this conference are both clinicians and scientists who seek to further understanding of these two neurodegenerative diseases and improve the outcome of patients. The conference not only combined the two diseases, but also was a mix of clinical and scientific research. 2500 participants predominantly from Europe and the USA attended this conference with over 800 posters presented.

Highlights of the conference included a keynote address from Professor RS Frackowiak who revealed a project with access to all MRI brain scans of people over 50 years in Switzerland hospitals performed in order to outline the structure of the aging brain. A study of this magnitude has not been performed to date.

The presentation of my poster entitled *'Reflexive saccades in Alzheimer's disease using fMRI'* was a success with two research groups from London, Canada and Genoa, Italy interested in our research and future networking. Our focus on sensorimotor function in Alzheimer's disease was interesting to many at the conference as the majority of research groups focussed on the change in cognition measured by neuropsychological tests and Alzheimer's disease. A copy of the poster is attached.

It was an invaluable experience for my career, learning and networking with the top clinicians and scientists in the field of Alzheimer's disease. I am very grateful for the travel grant-in-aid from the CMRF which allowed me to attend this excellent international conference.

REFLEXIVE SACCADES IN ALZHEIMER'S DISEASE USING FMRI.

S.L. WRIGHT[1,2], M.R. MacASKILL[1,2], R. WATTS[1,3], L. LIVINGSTON[1,2], B. DEAVOLL[5], J. DALRYMPLE-ALFORD[1,4] and T.J. ANDERSON[1,2].

[1]Van der Veer Institute for Parkinson's and Brain Research, Christchurch, [2]Medicine, University of Otago, Christchurch, [3]Physics and Astronomy, University of Canterbury, [4]Psychology, University of Canterbury, [5]Canterbury District Health Board.

Introduction: Reflexive saccades are normally subserved by a fronto-parietal network consisting of the frontal eye field (FEF), supplementary eye field (SEF) and parietal eye field (PEF). Alzheimer's disease (AD) subjects exhibit prolonged latency in this 'reflexive' saccade paradigm. The sole previous study (Thulborn et al. 2000) to probe the function of reflexive saccades in AD using fMRI, found a left parietal lobe dominance in the AD group.

Methods: Fifteen AD and 16 control subjects performed the step reflexive task during 3T fMRI in a blocked design comprising 27 s blocks of step reflexive vs. predictive vs. fixation, repeated four times. fMRI data were analysed using SPM5 (Wellcome Department of Cognitive Neurology, University College London, UK) standard procedures and normalised to an elderly template (Lemaitre et al. 2005). All subjects completed a neuropsychological battery of global cognition (MMSE; Montreal Cognitive assessment, MoCA; ADAS-cog). The neuropsychological tests were grouped into the following domains, and a domain score formed by taking the mean of the z-scores of each of its constituent tests: *Visuo-spatial*, comprising the JLO, and VOSP; *Executive function*, comprising Letter fluency, Category fluency, Action fluency, Stroop inhibition; *Attention and working memory* comprising the TEA map search, Stroop colour and word naming.

Results: Saccade latencies were significantly delayed in AD (mean latency ± standard deviation, AD = 245±90 ms, Control = 210±56 ms, Figure 1). The AD group demonstrated a significant correlation with the MoCA and latency (p=0.05): for every MoCA point drop, there was an approximate increase in latency of 100 ms. There was a significant correlation between the latency and visuo-spatial domain scores in the AD group (p=0.03). This is consistent with the visuo-spatial demands of reflexive saccades. There was not a significant correlation for either the domains of executive function or attention and working memory.

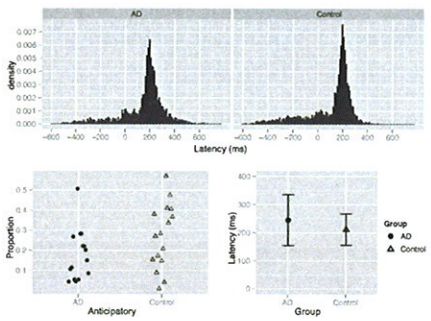

Figure 1 The histograms (10 ms bin width) show the distribution of the latencies of all reflexive saccades (top panel). The left lower panel shows the distribution of the proportions of anticipatory saccades for each group. The right lower panel shows a significant difference in the mean latencies reactive saccades (those with latencies >90 ms), p=0.04 (AD = 245±90 ms, Controls=211±56 ms). The error bars display the standard deviation of each group.

The AD group exhibited increased activity during the reflexive task compared to fixation in the following regions: bilateral FEF, DLPFC, SEF, SPL, thalamus, right supramarginal gyrus, right precuneus, right middle temporal gyrus, and the right occipital gyrus (Figure 2). In the Control group, regions that were more active when performing the reflexive task, compared with fixation were the bilateral FEF, SEF, supramarginal gyrus, thalamus, right DLPFC, right SPL, and right insula (Figure 2).

Direct comparison of the reflexive task between the AD and Control groups showed the AD group had more activity in the middle temporal gyrus bilaterally and reduced activity in the right FEF, left supramarginal and left occipital gyri compared with the Control group (Figure 3).

References

Claeys, K. G., Lindsey, D. T., De Schutter, E., & Orban, G. A. (2003). A higher order motion region in human inferior parietal lobule: Evidence from fMRI. *Neuron, 40*, 631-642.

Corbetta, M., Akbudak, E., Conturo, T. E., Snyder, A. Z., Ollinger, J. M., Drury, H. A., et al. (1998). A common network of functional areas for attention and eye movements. *Neuron, 21*, 761-773.

Lemaître, H., Crivello, F., Grassiot, B., Alpérovitch, A., Tzourio, C., & Mazoyer, B. (2005). Age- and sex-related effects on the neuroanatomy of healthy elderly. *Neuroimage, 26*, 900-911.

Nobre, A. C., Gitelman, D. R., Dias, E. C., & Mesulam, M. M. (2000). Covert visual spatial orienting and saccades: Overlapping neural systems. *Neuroimage, 11*, 210-216.

Perry, R. J., & Zeki, S. (2000). The neurology of saccades and covert shifts in spatial attention: An event-related fMRI study. *Brain, 123*, 2273-2288.

Thulborn, K., Martin, C., & Voyvodic, J. (2000). Functional MR imaging using a visually guided saccade paradigm for comparing activation patterns in patients with probable Alzheimer's disease and in cognitively able elderly volunteers. *AJNR. American Journal of Neuroradiology, 21*, 524-531.

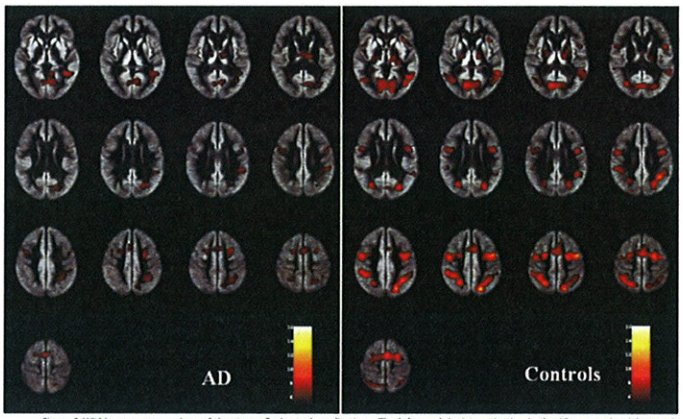

Figure 2 Within-group comparison of the step reflexive task vs. fixation. The left panel depicts activation in the AD group; the right panel depicts activation in the Control group. The colour bar indicates t-values from 5 (red) to 16 (yellow). Images are overlaid on the mean normalized grey matter image for all subjects, with a 5 mm gap between slices.

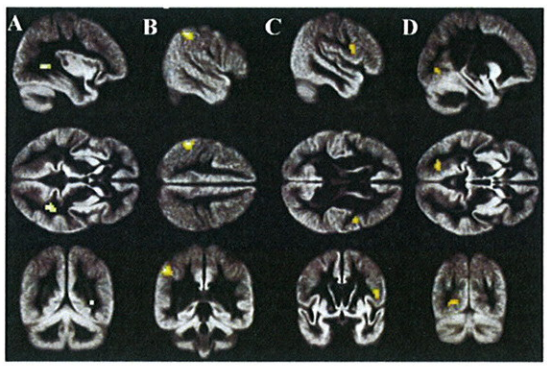

Figure 3 A) corresponds to increased activity in the right middle temporal gyrus in the AD group compared to the Control group. B, C and D correspond to regions of reduced activity in the AD group compared with the Control group and represent the left supramarginal gyrus, right FEF and left occipital gyrus respectively in the reflexive task compared to fixation

Discussion: Visuo-spatial attention was impaired in our AD group and was likely to have exerted a significant effect upon their performance of these sensory-driven reflexive saccades. Increased activity in the middle temporal gyrus in the AD group, may reflect compensatory recruitment and reliance on the lower-order movement processing system, due to reduced resources available in the posterior parietal (supramarginal gyrus and IPL) higher order processing complex.

Perry et al (2000) found that the right supramarginal gyrus is involved in both saccades and attention shifts and is suggested to play an 'alerting' role, where it notifies other regions of a potentially salient visual stimulus, as well as its role in motion processing (Claeys, Lindsey, De Schutter, & Orban, 2003). Middle temporal gyrus activation that extends into both the superior and inferior temporal gyri has been suggested to be associated with covert shifts in visual attention (Corbetta et al., 1998; Nobre, Gitelman, Dias, & Mesulam, 2000). The FEF is crucial to the generation of saccades, and the reduction in activity in the right FEF may be associated with impaired reflexive saccade performance in the AD group.

Conclusion: In AD, increased activity in the middle temporal gyrus and reduced activity in the FEF and supramarginal gyrus may be due to the increased demand of spatial attention in the reflexive task. Increased neuronal resources are required for the AD group to perform the task, reflected by 'over-activity' of the middle temporal gyrus, however a ceiling-effect is reached in the FEF and supramarginal gyrus because of the underlying structural damage to the neural networks in AD, thus insufficient neuronal compensation takes place. This study is the first to directly compare the AD and Control groups while performing reflexive saccades, and has found robust differences between the groups in the temporo-parietal and frontal cortices, compared with previous findings of within-group left parietal lobe dominance.

Acknowledgements: Thank you to the Neurological Foundation of New Zealand for funding this project and providing a travel grant-in-aid to attend this conference. Thanks you to the Canterbury Medical Research Foundation for providing a travel grant-in-aid to attend this conference.