Quantitative MRI and cognitive measures in patients with Alzheimer's Disease before and after Table Tennis

Study proposal for Andrew Battley and Ian Craigton-Chambers; BAT Foundation. By Dr Matthew Kempton, Prof Stephen Jackson, and Prof Steve Williams; King's College London

1. Background:

Alzheimer's disease is the most common cause of dementia and a leading cause of disability worldwide (Evans et al., 1989). The early stages of the disease are associated with deficits in memory but as the illness progresses common symptoms include confusion, language problems and irritability. Pharmacological treatments have been a major focus of research; however there is emerging evidence that other low cost therapies may be effective in playing a preventative role or slowing the progression of the illness.

Lack of physical exercise is a recognised risk factor for developing Alzheimer's disease and evidence from cohort studies suggest that exercise may be protective against developing dementia (Taaffe et al., 2008). In terms of an effective therapy once the illness has started, a randomised control trial of 3 months physical exercise in patients with Alzheimer's disease showed a number of benefits; patients in the exercise group and behaviour management group had better physical functioning, were more likely to be active during the day and had lower depression scores (Teri et al., 2003). Research such as the above led the National Institute for Health and Clinical Excellence (NICE) to recommend physical exercise for patients with dementia such as Alzheimer's disease (National Institute for Health and Clinical Excellence, 2011). Despite these encouraging findings, an observation study of NHS and private care centres in the UK revealed that on average those with dementia spent less than 12 minutes a day engaged in constructive activities (Ballard et al., 2001).

The benefits of physical exercise are likely to be mediated by changes in brain structure and function. Physical exercise has been shown to increase brain volume in elderly sedentary adults (Colcombe et al., 2006) as well as improving cognitive function specifically in the domains of executive function, visuospatial ability and cognitive control (Colcombe and Kramer, 2003). Animal studies have demonstrated that physical exercise increases cell proliferation and neurogenesis in the hippocampus, a region of the brain which is affected by Alzheimer's disease and is important in memory (van Praag et al., 1999). In addition a recent study revealed that the hippocampus in adults increased in volume after exercise, and that memory also improved (Erickson et al., 2011).

An excellent candidate for a type of physical exercise accessible to those at risk of developing Alzheimer's disease and those in the early stages of the illness is perhaps surprisingly, table tennis.

Table tennis is a fast moving, competitive and social activity which involves physical exercise, sustained attention and the development of visuospatial skills. The social and cognitive aspect of the sport has an added benefit as social networks may reduce the likelihood of developing Alzheimer's disease (Fratiglioni et al., 2004) and cognitive training may improve functioning (Sitzer et al., 2006). There have been a small number of preliminary studies directly examining the effect of table tennis in the elderly population. A Japanese study used table tennis in a neurological rehabilitation unit and observed that table tennis play was associated with an improvement in dementia and depression symptoms (Sato and Mori, 2004). In another Japanese study, elderly

table tennis players scored higher in a task of executive function and attention compared to non-table tennis players (Kawano et al., 1992). The Sport and ART Educational Foundation (SAEF, www.saef.us) in California, USA have developed the Alzheimer's Table Tennis Therapy Program to develop the sport in those with dementia and high risk groups. However the beneficial effects of table tennis in patients with Alzheimer's disease and its putative effect on brain structure and function has not been formally tested using objective measures such as MRI (magnetic resonance imaging) based techniques.

2. Methods:

2.1 Study Design:

The following study design has been selected:

Study A1: 32 Patients with mild Alzheimer's disease, 16 have table tennis intervention, 16 have no intervention "life as usual" (participants randomised to each intervention). All participants assessed twice (before and after 10 weeks of intervention)

2.2 Measures:

(Recorded both before and after intervention)
BOLD sections = new measures introduced in Feb 2016

Diagnostic Criteria
NINCDS-ADRDA Alzheimer's criteria

Cognition
Mini-mental state examination
Alzheimer's Disease Assessment Scale, cognition sub scale (ADAS cog) Clinical Dementia Rating
Trail making task (A and B)
Rey Auditory Verbal Learning task

Other
Questionnaire about enjoyment and performance in table tennis Geriatric Depression Scale (Yesavage et al 1982)
Elderly Fall screening test (Cwikel et al 1998) Blood pressure
Weight
Positive and Negative Affect Schedule (PANAS, Watson 1988)
UCLA Loneliness scale (version 3, Russell et al 1996)

MRI measures (1 hour scan)
High Resolution T1 structural scan –volume of the hippocampus and other relevant brain structures
Arterial Spin Labeling (ASL) – Blood flow at the hippocampus
Diffusion Tensor Imaging --- neuronal tract density between the hippocampus and the dorsal lateral prefrontal cortex (DLAPFC)
Resting state fMRI – functional connectivity between hippocampus and DLPFC Hippocampus fMRI task --- Neuronal activity of the hippocampus

2.3 Inclusion Criteria:
Patients with mild Alzheimer's disease: NINCDS-ADRDA probable Alzheimer's disease Age 65+
Mini mental state 18-24
Able to manage the physical aspects of table tennis
Able to have an MRI scan (no pacemaker or metal in body)

2.4 Outcome measures and hypotheses:

Primary outcome measures/ hypotheses
Hippocampal volume before and after table tennis as measured by structural MRI (increase in table tennis group)
Memory performance (increased performance in table tennis group)

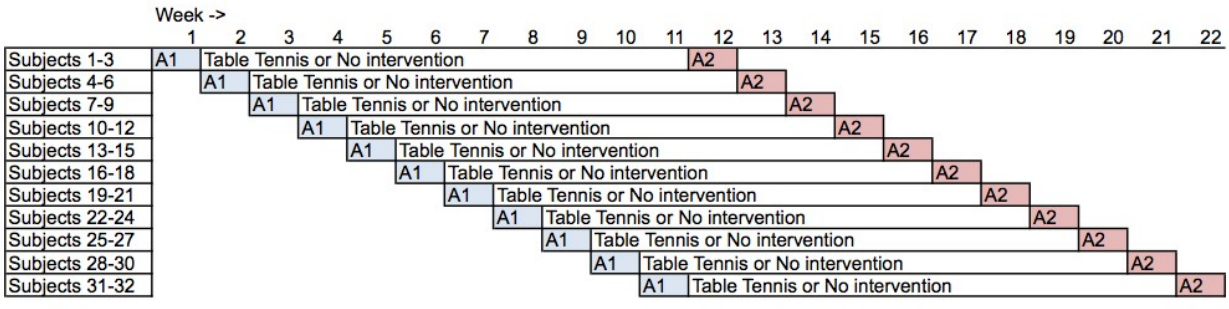
Secondary outcome measures/ hypotheses
Reduced Falls
Reduced blood pressure Less depression
Reduced negativity on the PANAS scale
Reduced loneliness as measured by the UCLA scale
MRI related: increased blood flow and activation in hippocampus, increased structural and functional connectivity between hippocampus and DLPFC

3. Logistics, Responsibilities & Timeline

KCL team responsible for application for ethical approval, taking informed consent, all assessments, data analysis and publication.

BAT foundation responsible for table tennis intervention (including equipment, transport for participants).The recruitment of participants require patients with Alzheimer's disease to be recruited by the BAT foundation via their contact with residential homes involved in their campaign.

Due to MRI availability of 3 scanning slots a week the table tennis training would need to be staggered, thus the experimental part of the study would take 22 weeks



3 Participants scanned a week
A1 = Assessmemt at Baseline
A2 = Assessment at Follow-up
Table tennis sessions are shown as 10 weeks here but could be shortened

References:

Ballard, C., Fossey, J., Chithramohan, R., Howard, R., Burns, A., Thompson, P., Tadros, G., Fairbairn, A., 2001. Quality of care in private sector and NHS facilities for people with dementia: cross sectional survey. Bmj 323, 426–427.

Colcombe, S., Kramer, A.F., 2003. Fitness effects on the cognitive function of older adults: a meta-analytic study. Psychol Sci 14, 125–130.

Colcombe, S.J., Erickson, K.I., Scalf, P.E., Kim, J.S., Prakash, R., McAuley, E., Elavsky, S., Marquez, D.X., Hu, L., Kramer, A.F., 2006. Aerobic exercise training increases brain volume in aging humans. J Gerontol A Biol Sci Med Sci 61, 1166–1170.

Erickson, K.I., Voss, M.W., Prakash, R.S., Basak, C., Szabo, A., Chaddock, L., Kim, J.S., Heo, S., Alves, H., White, S.M., Wojcicki, T.R., Mailey, E., Vieira, V.J., Martin, S.A., Pence, B.D., Woods, J.A., McAuley, E., Kramer, A.F., 2011. Exercise training increases size of hippocampus and improves memory. Proc Natl Acad Sci U S A 108, 3017–3022.
Evans, D.A., Funkenstein, H.H., Albert, M.S., Scherr, P.A., Cook, N.R., Chown, M.J., Hebert, L.E., Hennekens, C.H., Taylor, J.O., 1989. Prevalence of Alzheimer's disease in a community population of older persons. Higher than previously reported. Jama 262, 2551–2556.

Fratiglioni, L., Paillard-Borg, S., Winblad, B., 2004. An active and socially integrated lifestyle in late life might protect against dementia. Lancet Neurol 3, 343–353.

Kawano, M.M., Mimura, K., Kaneko, M., 1992. The effect of table tennis practice on mental ability evaluated by Kana-Pick-out test. International Journal of Table Tennis Sciences 1, 57–62.

National Institute for Health and Clinical Excellence, 2011. Dementia CG42 London: National Institute for Health and Clinical Excellence.

Sato, T., Mori, T., 2004. Clinical Brain Sports Medicine: The Effectiveness of Exercise Intervention on Brain Disease Patients: Utilizing Table Tennis as a Rehabilitation Program. Journal of the Society of Biomechanisms, Japan (SOBIM) 17, 1–8.

Sitzer, D.I., Twamley, E.W., Jeste, D.V., 2006. Cognitive training in Alzheimer's disease: a meta-analysis of the literature. Acta Psychiatr Scand 114, 75–90.

Taaffe, D.R., Irie, F., Masaki, K.H., Abbott, R.D., Petrovitch, H., Ross, G.W., White, L.R., 2008. Physical activity, physical function, and incident dementia in elderly men: the Honolulu-Asia Aging Study. J Gerontol A Biol Sci Med Sci 63, 529–535.

Teri, L., Gibbons, L.E., McCurry, S.M., Logsdon, R.G., Buchner, D.M., Barlow, W.E., Kukull, W.A., LaCroix, A.Z., McCormick, W., Larson, E.B., 2003. Exercise plus behavioral management in patients with Alzheimer disease: a randomized controlled trial. Jama 290, 2015–2022.

van Praag, H., Kempermann, G., Gage, F.H., 1999. Running increases cell proliferation and neurogenesis in the adult mouse dentate gyrus. Nat Neurosci 2, 266–270.