SCIENTIFIC LETTER

The effect of pacemaker mode on cognitive function

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There is increasing recognition of the interaction between cardiovascular disease and cognitive function.[1] The effects of cardiovascular performance on cognitive function remain unclear, however. This is relevant for patients who require pacemaker implantation for symptomatic bradycardia, as many such patients are elderly and the use of suboptimal pacing modes may expose them to intermittent hypotension and increased risks of atrial fibrillation. Intermittent hypotension, associated with impaired cerebral autoregulation in the elderly, may cause cerebral ischaemia, and atrial fibrillation is the predominant cause of multi-infarct dementia as well as a recognised risk factor for Alzheimer's dementia. Through these conditions pacing therapy may have an adverse effect on cerebral and cognitive function.

We therefore designed this study to assess the cognitive function of patients with symptomatic bradycardia after implantation of a permanent pacemaker and to test the hypothesis that single chamber ventricular (VVI(R)) pacing is detrimental to cognitive function when compared with atrial based pacing.

METHODS

Patients recruited to either of two multi-centre pacemaker trials (UKPACE or STOP-AF) at the Freeman Hospital in Newcastle upon Tyne, between January 1997 and May 1999, were invited to participate after randomisation to VVI(R) or atrial based pacing. Cognitive assessments were undertaken one month, one year, and two years after pacemaker implantation using CAMCOG (the cognitive section of the Cambridge examination for mental disorders of the elderly) and CANTAB (Cambridge neuropsychological test automated battery). CAMCOG is an interview based tool assessing orientation, language, recent memory, visual memory, remote memory, attention, calculation, praxis, abstract thinking, and perception. It discriminates between individuals with no or mild cognitive impairment and allows assessment of individuals with a wide range of cognitive abilities. CANTAB is a computerised tool that assesses learning and memory, attention and executive functions, and is sensitive to subclinical cognitive decline. Computerisation of testing allows complex stimuli to be generated and presented and responses to be recorded automatically and with precision. In addition it facilitates graduated levels of testing and collects detailed results which are analysed automatically. Touch screen technology allows precise, fast, and consistent testing while providing direct feedback to the subject without requiring verbal responses.

Data from subjects who completed all three assessments were analysed using general linear model analysis for repeated measures and, for the CANTAB data, using a principle component analysis to calculate composite cognitive function scores at each time point. Data published since the inception of the study allowed a retrospective power calculation to be made.[2] This suggested a study of 50 patients would have an 80% chance, at the 5% level, of detecting a meaningful difference in CANTAB scores.

RESULTS

Seventy four patients completed the three stages of cognitive assessment; 43 were male, mean age was 76 years (range 55–88 years), 36 patients were paced for sinus node disease, 38 patients for atrioventricular block, 41 patients were paced in DDD(R) or AAI(R) modes, and the remaining 33 patients in VVI(R). There were no significant differences in the demographic characteristics, co-morbidities (17% of VVI(R) *v* 27% of atrial paced had had atrial fibrillation and 34% of VVI(R) *v* 30% of atrial based were hypertensive), or use of medications between the groups in different pacing modes. Over the study period patients in the VVI(R) group had 59% ± 40% paced ventricular beats compared with 62% ± 30% in the atrial based group, $p = 0.8$.

CAMCOG scores at two years were predominantly dictated by the score at one month. Pacing mode had no significant effect on total CAMCOG scores although there was a trend towards a detrimental effect of VVI(R) pacing on the visual memory score (uncorrected $p = 0.02$, Bonferroni correction $p = 0.2$). Similarly initial performance had a profound effect on subsequent performance in CANTAB and there was a trend towards a reduction in the number of stages reached in the paired associates learning task. Mean (SD) score fell from 7.3 (1.1) to 6.7 (1.9) in the VVI(R) group but remained at 7.4 (0.8) in the atrial paced group, $p = 0.08$.

The effect of pacing mode on composite cognitive scores derived from CANTAB at each time point is shown in fig 1. Pacing mode had no significant effect on scores with the difference at two years between patients with atrial based and VVI(R) pacing estimated at 0.15 SD with 95% confidence interval (CI) of −0.61 to 0.30 SD, $p = 0.54$. Figure 1 suggests that scores one month after pacing affect subsequent performance. This was confirmed by regression analysis showing a significant effect of one month score on two year score ($R^2 = 0.63$, 95% CI 0.41 to 0.84, $p < 0.001$) but no effect of pacing mode on two year score ($R^2 = 0.13$, 95% CI −0.32 to 0.58, $p = 0.57$).

DISCUSSION

These data comprise the first evaluation of pacing mode on cognitive function. No significant effect was seen and the predominant factor influencing subsequent cognitive function proved to be cognitive performance at one month. A trend towards reduced function in visuospatial memory tasks, with VVI(R) pacing, was demonstrated in both CANTAB and CAMCOG. This is of some interest as defects in visuospatial memory have been identified as sensitive markers for the subsequent development of Alzheimer's dementia.[3]

Abbreviations: CAMCOG, the cognitive section of the Cambridge examination for mental disorders of the elderly; CANTAB, Cambridge neuropsychological test automated battery

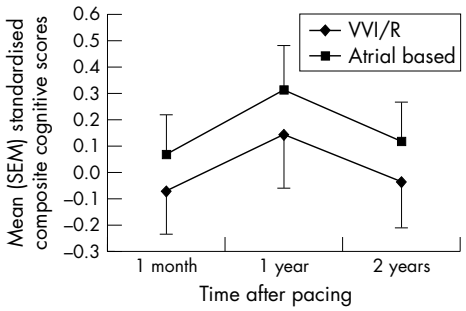

Figure 1 CANTAB scores after pacing.

Two studies have previously provided evidence that bradycardia per se impairs cognition. One, of 14 patients, has demonstrated an increase in regional cerebral blood flow and consequent improvement in cognitive function testing after pacemaker implantation for symptomatic bradycardia.[4] Another, of 19 individuals, has shown patients requiring pacemaker implantation to be cognitively impaired compared with sex, age, and mental status questionnaire matched volunteer controls, but to have no significant improvement in cognitive function over a six month follow up period after pacemaker implantation.[5] Neither of these studies made any assessment of the impact of pacemaker mode.

A number of other factors such as depression, hypertension, and atrial fibrillation may influence cognitive function or its assessment. Depression is a recognised confounder of cognitive assessment but in this study showed no correlation with CANTAB scores (Spearman's $\rho = -0.095$, $p = 0.3$ for the correlation between paired associates learning stages reached and a contemporaneous geriatric depression score). Atrial fibrillation and hypertension are recognised risk factors for cognitive decline. There were, however, no differences in their incidences at baseline and no differences in the incidence of paroxysmal, permanent atrial fibrillation, or other cardiovascular events after pacing.

Despite being adequately powered, this study has provided no evidence for a detrimental effect of VVI(R) pacing on cognitive function. There were apparent trends towards reduced function in the area of visuospatial memory, which warrant further examination. Future studies assessing neurocognitive decline following pacing should focus on changes within this cognitive domain. Currently, however, there is no evidence that VVI(R) pacing is detrimental to cognitive function in the two years after pacemaker implantation.

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