Event-related potentials and reaction time can distinguish healthy aging from mild Alzheimer's disease

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PGDS. PGDS catalyzes the conversion of prostaglandin H2 to PGD2 which spontaneously converts to PGJ2, Δ⁵PGJ2 and ultimately 15dPGJ2, a potent apoptotic agonist. The isolated native PGDS protein showed apoptotic activity in a TUNEL assay performed on LLC-PK1 cells. A recombinant (r) form of human PGDS was isolated from E. coli and polyclonal antibodies raised against it in rabbits. Western blot analysis, utilizing the rPGDS antibodies as a probe, showed a strong signal at 29 kDa in SDS-PAGE separated AD plasma. There were increases in the apoptotic indices (AI; % of cells in apoptosis) after a 2 h exposure of LLC-PK1 cells to AD plasma (AI: 4.4±3.0, 40.2±1.6), PGDS (AI: 22.9±1.1), the end product Δ⁵PGJ2 (AI: 22.5±1.1), and camptothecin (AE: 21.3±4.1), when compared to control plasma (AI: 9.4±2.5), or untreated LLC-PK1 cells (AI: 7.2±0.7). The cyclooxygenase (COX)-1 and COX-2 inhibitor indomethacin, the COX-2 specific inhibitor NS-398, anti-trans retinoic acid, and anti-PGDS antibody all significantly (p<0.05) reduced the induction of apoptosis by AD plasma (43, 58, 54, 44% reductions respectively) and rPGDS (51, 76, 65, 59%), but not Δ⁵PGJ2. Our findings provide a novel mechanism for the expanding body of evidence that non-steroidal anti-inflammatory drugs, which inhibit the substrate for cyclooxygenase, might serve as a biomarker.

Poster Presentation: Brain-Behavioral Relationships II

1042 NORADRENERGIC CHANGES AND AGGRESSIVE BEHAVIOR IN PATIENTS WITH DEMENTIA.

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In addition to cognitive impairment there are various behavioural syndromes that may be present in subgroups of Alzheimer’s disease (AD) patients and it has been suggested that patients with ‘non-cognitive’/behavioural disturbances may have different neurochemical changes than patients with AD alone. The locus coeruleus (LC), the major source of noradrenaline (NA) projection neurons in the brain, is known to be damaged in AD. Despite substantial neuronal loss, it has been hypothesised that there is an increase in the activity of the surviving NA neurons. The integrity of the NA system was therefore investigated in patients with AD, non-AD dementia and controls and possible relationships between changes in the NA system and the presence of behavioural syndromes in AD were examined. High affinity α2 receptor sites in three cortical regions (BA21, 22 and 40) of AD, non-AD dementia and control patients. It was found however, that there was a significant loss of LC cells in AD, the greatest cell loss occurring within the rostral portion of the nucleus (50%) with a relative sparing of caudal cells. A significant difference was also seen in the mid-temporal cortical NA concentration (31% decrease) in AD patients, although this was less pronounced than in the median raphe nucleus. The data is consistent with a compensatory activation of the remaining LC NA neurons, which may lead to increases in both NA concentration and numbers of cortical NA terminals. There was a significant positive correlation between the presence of aggressive behaviour during the course of the illness and both magnitude of residual LC cell loss and decreased mid-temporal NA concentration, suggesting that decreases in NA activity may lead to aggressive behaviour in a sub-group of AD patients. This study may have implications for the treatment of behavioural syndromes, particularly aggression, in AD patients.

1045 EVENT-RELATED POTENTIALS AND REACTION TIME CAN DISTINGUISH HEALTHY AGING FROM MILD ALZHEIMER’S DISEASE.

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Objective: To examine the utility of multivariate measures of event-related brain potentials and reaction time (RT) to accurately classify healthy elderly subjects and mild Alzheimer’s disease (AD) subjects. Background: Studies using the detection of a rare target stimulus have found group differences in RT and brain potentials (P300 and readiness potential or RP) between AD and elderly controls. However, these individual measures do not have the requisite sensitivity or specificity to be useful for defining an individual as having AD. The purpose of the present experiment was to determine if a multivariate approach using RT, RP, and P300 would improve sensitivity and specificity. Methods: We studied healthy controls (n = 18; M age 69.7 ± 7.3), and AD patients (n = 11; M age 72.0 ± 9.0; Mini-mental status = 23.3 ± 2.9). Healthy controls were screened using a battery of neuropsychological tests. In the target detection task subjects listened to a sequence of 300 tones. Frequent (1000 Hz; n = 240) and target (2000 Hz; n = 60) tones were presented in a random order. The subject's task was to quickly press a button when a target was presented. Behavioral measures were reaction time and accuracy. EEGs was continuously recorded from 7 sites using standard techniques. Evoked potentials to target and frequent tones were averaged off-line. Linear discriminant analysis was used to predict group membership (AD or control) for each subject on the basis of their RT, and P300 latency. Results: There were significant univariate differences in reaction time (p < .01), RP amplitude (p < .02), and P300 latency (p < .01) between controls and AD. Median z-scores for AD relative to controls were 1.4 (RT), -1.1 (RP), and 1.6 (P300 latency). Discriminant analysis showed 81.8 % sensitivity (correctly classified AD) and 100% specificity (correctly classified controls). Conclusions: We identified significant differences between healthy controls and AD patients on three measures using a task that is easy to perform. The combined use of RT, RP, and P300 latency was capable of distinguishing mild AD patients from age-matched subjects with a high degree of accuracy. The method may have promise for distinguishing normal aging from early AD.