

Apolipoprotein E4 status is Associated with Agitated Behavior in Nursing Home Residents with Dementia

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Background

Multiple factors contribute to the development of behavioral symptoms in dementia (BSD). One such factor may be the apolipoprotein E (APOE) genotype. Although the role of APOE polymorphisms in the development of Alzheimer's disease (AD) has been studied extensively, the relationship of APOE and BSD has received only limited attention. The role of APOE genotype in moderating behavioral symptoms and psychopathology has been studied in community dwelling persons with AD, using caregiver proxy reporting, however, this relationship has not been studied in the nursing home population. Information related to APOE genotype and the relationship to BSD would add needed data to assess risk factors for behavioral symptoms.

Behavioral Symptoms of Dementia are a significant clinical problem in nursing homes with a prevalence ranging between 30% and 84% [1, 2]. While classifications and names may vary across studies, behaviors generally include four broad categories: physically aggressive, physically nonaggressive, verbally aggressive and verbally nonaggressive [3, 4]. The most frequent behaviors include problematic vocalization, restlessness, wandering, and pacing. In two prevalence studies of BSD, 38% of nursing home residents had repetitive purposeless activity, 29% had problematic vocalization, 18% acted inappropriately, and 9% wandered [5, 6]. Several studies have examined the association of resident characteristics such as mental status, dementia diagnosis, age and gender to behavioral symptoms of dementia [4, 7], with varying results. Given that the risk of AD is 47% in those persons exhibiting one $\epsilon 4$ allele rising to 91% in those exhibiting two $\epsilon 4$ alleles and BSD are highly prevalent, few studies have included genetic variability, as one of the resident characteristics that may be associated with the frequency and intensity of behavioral symptoms [8-10].

Several studies using proxy reporting have explored the relationship between APOE and BSD in community dwelling persons with dementia with mixed findings [9-12]. These recent studies indicate that the risk for BSD, such as restlessness, pacing and vocalization, may be increased relative to the APOE genotype. To date no studies have assessed this relationship using direct observation in nursing home residents with AD. The purpose of the study was to describe the association between BSD and ApoE genotype.

Methods

This study employed a comparative non-randomized two-group design (BSD versus non-BSD group). The independent variable was the APOE genotype, obtained by buccal swabs. The dependent outcome variable was a cluster of six agitated behaviors (restlessness, escape restraint, tapping and banging, searching and wandering, pacing and walking, and vocalization) measured using the Modified Agitated Behavior Rating Scale (mABRS) [13]. Participants A comparative sample of residents, with and without behavioral symptoms, with moderate to severe dementia and who met inclusion criteria were selected from the 130 residents screened. Nursing staff screened residents for participation in the study using the Brief Agitated Rating Scale (BARS) screening tool [14]. Criteria for participation included: > 65 years; living on the

unit for at least 2 months [15]; stabilization on anti-psychotic medication for at least 1 month; continued residency in the nursing home for the duration of the study; a diagnosis of dementia, according to the DSM-IV criteria [16], a Mini Mental State Exam (MMSE) [18] score < 21 (range 0-30), and for those residents who exhibited BSD, a score of >15 on the BARS [14]. Residents were excluded if they had acute psychiatric or physical illness; mental retardation or developmental delay, a stroke that caused gross motor, visual or sensory impairment, and end-stage or Parkinson's dementia (as reported in the participant's medical record).

Once proxy consent was obtained from families, 36 participants (21 with BSD and 15 with no BSD) were enrolled into the study, out of a total of 79 who met the criteria and were approached for consent. Since we were able to obtain genotyping on only 34 residents, only these residents are included in the analysis. Research Assistants observed and recorded resident behavior every 20 minutes between 8:00 am and 8:00 pm daily for 5 days. Buccal swabs were obtained for later APOE genotyping prior to the observation period.

Results

Of the 34 participants aged 71- 102 (M = 87.9, SD = 6.8), 86 % were female and 47% had at least one $\epsilon 4$ allele. Participants had an average MMSE score of 10.43 of a total possible score of 30 (SD + 7.4, range 0 – 21), indicating moderate to severe dementia, and a mean of 3.92 medical comorbidities (SD + 1.96, range 0 – 6). Twenty-three residents (63.9%) showed cardiovascular problems such as hypertension (36%), while 22% were diagnosed with depression. Sixty-nine percent of residents were prescribed analgesic, 36% an antipsychotic, 17% an anxiolytic, and 75% an antidepressant.

ANOVA for repeated measures was used to test the association between APOE4+/4- and behavioral symptoms. Mean behavior scores were grouped according to the presence or absence of APOE 4 (4+ = .45+.34), (4- = .24+.16). There was a significant difference in total behavioral symptoms, driven by restlessness and vocalization ($F_{1,30} = 4.40, p = .04$), between those who had an APOE $\epsilon 4$ allele (3/4, 4/4) present compared to those who did not. Odds ratio of 1.71 (95% CI, .42-6.96), supported these findings. Restlessness (manual manipulation) was significantly inversely correlated with MMSE score ($r = -.37, p = .03$) but not APOE genotype.

Conclusions: The 47% of participants with at least one allele is consistent with a diagnosis of AD. Findings indicate that the presence of the APOE4 allele increased the risk for behavioral symptoms in nursing home residents with dementia, and that those persons with a diagnosis of dementia and a lower mental status, reflected in the MMSE score, were more prone to restless behavior. Genotyping may prove useful to identify individuals at risk for behavioral symptoms.

References

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