Statistical analyses

In order to determine the influence of educational status and individual dementia risk factors on subregional hippocampal and medial temporal cortical thickness we first estimated mixed general linear models, with averaged (across subregions) thickness as the dependent variable and education status (lower/higher) and risk factor status (low/intermediate/high) as between-group factors and age and gender as covariates. We also investigated a possible interaction between education and risk factor status. After we established significance with the multivariate F tests we conducted post hoc univariate tests including linear regression analyses to determine the influence of education on regional cortical thickness among patients differing in risk factor status. Gender and APOE allele distribution were compared with Chi-Square tests. Statistical analyses used a significance level of $p<0.05$.

RESULTS

Patients with higher or lower education did not significantly differ in age or gender distribution. The frequency of the APOE4 risk allele or the presence of the family history risk factor was also comparable between the groups (Table 1).

Table 1. Demographic characteristics and neuropsychological scores.

Characteristics and Measures	Lower education	SD	Higher education	SD	Significance (*p*-value)*
N	32		26		
Age (years)	71.8	± 7.0	73.8	±6.3	*0.25*
Female sex (no.)	18		9		0.1
Education (years)	11.5	± 1.2	16.2	±1.7	**< 0.001**
APOE status (no.)					
2,3	2		1		*0.68*
3,3	12		6		*0.24*
3,4	13		14		*0.32*
4,4	5		5		*0.72*
First degree family history of AD (no.)	9		13		*0.09*
MMSE (score range 0-30)	21.1	± 5.2	24.7	± 4.2	**0.033**

MMSE: Mini Mental State Examination; *Chi-Square tests for Gender and APOE status

Mean cortical thickness (averaged across all subregions) did not significantly differ between higher and lower educated patients (higher educated: 2,28 mm ± 0.12 mm, lower educated: 2,20 mm ± 0.17 mm). The mixed general linear models did not show main effects for education status and risk factor status, but revealed an interaction between both factors ($F=3.97$, $df=2,46$, $p=0.026$). Main effects for age and gender were not significant. Post hoc analyses (Figure 2) showed no correlation between the years of education and cortical thickness in all medial temporal lobe subregions among Alzheimer's disease patients carrying no genetic risk factors. In patients carrying either the APOE4 allele or having a first-degree family history of Alzheimer's disease, years of education and cortical thickness were positively correlated in the parahippocampal cortex (Pearson's $r=0.45$, $p=0.045$), and across all medial temporal subregions combined ($r=0.48$, $p=0.031$). The entorhinal cortex failed to reach significance ($r=0.44$, $p=0.053$). Among patients homozygous for the APOE4 allele or carrying both APOE4 and family history risk factors, years of education and cortical thickness were positively correlated in the hippocampus CA23DG region ($r=0.63$, $p=0.004$), subiculum ($r=0.47$, $p=0.044$), entorhinal cortex ($r=0.58$, $p=0.01$), perirhinal cortex ($r=0.73$, $p<0.001$), parahippocampal cortex ($r=0.72$, $p=0.001$), fusiform gyrus ($r=0.61$, $p=0.006$), and across all subregions combined ($r=0.77$, $p<0.001$).