Genetic Effects on Visual N1 Amplitude and Latency.

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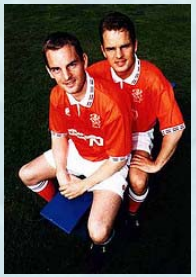
Reduced N1amplitude may be a biological marker of age related cognitive decline. We therefore investigated whether visual N1parameters are valid endophenotypes for this decline. First, we determined the heritability of N1 amplitude and latency. In addition, since the Apolipoprotein E gene (APOE) has been implicated in the onset of cognitive decline, we also investigated the effect of APOE genes on N1 parameters.

Participants were 665 twins and additional siblings (45% male) from the Netherlands Twin Registry (tweelingenregister.org), divided into two cohorts with ages around 25 and around 50. A proportion (422 subjects) were genotyped for APOE.



ERPs were calculated for nontargets from a visual oddball task with a minimum of 60 trials (silent counting).

Visual N1 is not a unitary concept. The Figure shows that, unlike the central auditory N1, an **early anterior N1** and a **late posterior N1** can be discriminated (consistent with Vogel and Luck, 2000). Anterior N1 was scored as the average N1 in a window from 88 to 168 ms. Posterior N1 was scored from 132 to 220 ms.

Age cohort differences show a negative shift with age at posterior sites (P7, O1, O2, P8) and a positive shift at the anterior leads (F7, F3, F1, Fz, F2, F4, F8). The shift covers a time range beginning at ca. 90 ms extending for at least several 100s of ms.

Does APOE ε4 influence the N1?

ε4 carriers show a significantly more negative anterior N1. The allelic effect of ε4 on amplitude is −.20 μV. The gene explains 6.8% of the total genetic variance (1.3% of the total variance.) ε4 carriers also show shorter N1 latency.

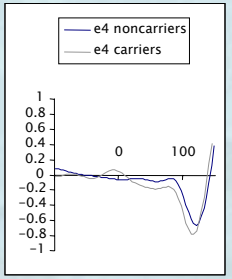
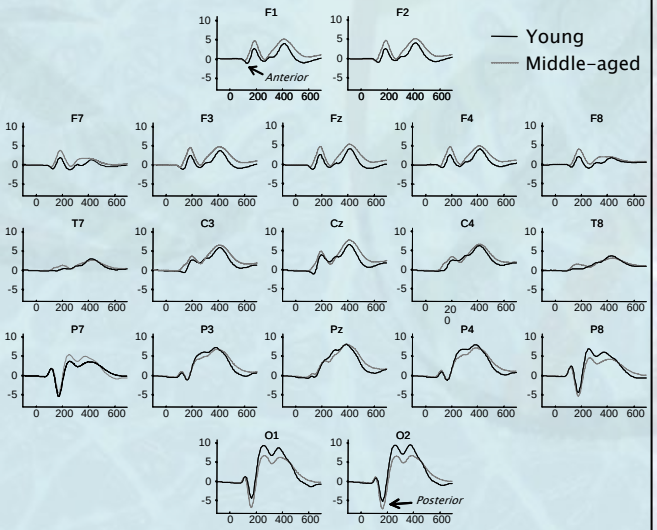


Figure: Grand average waves



CONCLUSIONS

-There are two visual N1 components: An earlier anterior and a later posterior N1.

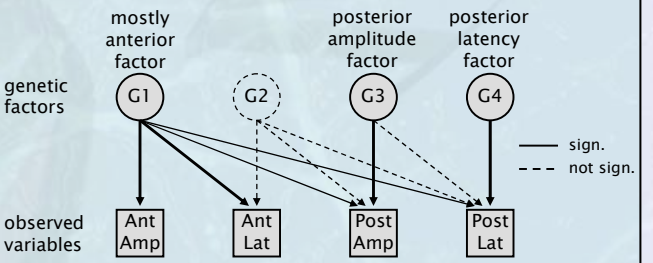
-Both components are heritable but influenced by genetically independent factors.

-The ApoE gene is part of the genetic factor influencing the anterior N1.

-ApoE E4 effects on amplitude—increased anterior N1—are opposite to the effects of age—decreased anterior N1.

Heritability can be determined by comparing monozygotic twin correlations to dizygotic and sibling correlations and is defined as the proportion of variance attributable to genetic expression. The Table shows significant heritability for anterior amplitude (20%), anterior latency (45%) and posterior N1 amplitude (50%) and latency (43%). No significant age cohort differences in heritability were found.

Multivariate modeling may be used to determine the the overlap of the genetic variance between the variables. A three genetic factor model gave the best fit to the data.



Varimax rotation of the above genetic factor structure resulted in a clear pattern with one factor for the anterior variables, one for posterior amplitude, one for posterior latency, and little to no overlap between these three. This result confirms the genetic independence of the anterior and posterior N1s.

Table: Loadings on the variables as percentage genetic variance explained.

	Factor 1	Factor 2	Factor 3	Factor 4	*heritability (h^2)*
Anterior amplitude	19%	1%	1%	1%	*22%*
Anterior latency	37%	2%	3%	2%	*45%*
Posterior amplitude	2%	0%	48%	0%	*50%*
Posterior latency	3%	40%	0%	0%	*43%*