

SCD *plus*, APOE4, and amyloid interrelations in a memory clinic population

a Bayesian network approach

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BACKGROUND

Subjective Cognitive Decline (SCD) *plus* is a consensus-based set of features linked to higher Alzheimer's disease (AD) risk.^{1,2}

These features are typically studied as isolated risk factors, but in practice could be viewed as an inter-related system due to their co-occurrence.³

Bayesian networks can quantify evidence for and against existence of conditional dependence,⁴ providing a robust picture of relations within the SCD*plus* construct and with other AD (bio-)markers.

AIM

To investigate the conditional relationships among SCD *plus* features, APOE4 carriership, and amyloid pathology in a cognitively unimpaired memory clinic population.

SAMPLE

Table 1. Sample characteristics of individuals with SCD from the Amsterdam Dementia Cohort (n=347)

Age M±SD, range	62±8 (44-82)
Male	192 (53%)
Years of education	12±8 (5-17)
APOE4 carrier (n=318)	124 (34%)
Amyloid positive* (n=255)	73 (29%)

Presence of SCD*plus* features

Complaints are persistent	172 (50%)
Complaints pertain to memory	240 (70%)
Informant confirmation of decline	90 (26%)
Onset in the past 5 years	294 (85%)
Onset after the age of 60	130 (37%)
Feeling worse than peers	193 (56%)

*evaluated based on CSF or PET according to local guidelines, with PET as leading.
The SCD*plus* feature "Seeking out medical help" was not included in the network, as this was a memory clinic sample.

METHODS

Participants: 347 individuals with SCD from the Amsterdam Dementia Cohort, see Table 1.

Measures: Six SCD*plus* features (see Table 1) derived from the Cognitive Change Index and clinical interview. Amyloid status was based on CSF or PET.

Analysis: Conditional relationships (edges) between variables were analyzed with Bayesian graphical modeling³ in Rstudio, using Bernoulli priors. Bayes Factors (BF) were computed to quantify the evidence for every potential edge.

Edges were classified as present, absent, or inconclusive, using a Bayes Factor (BF₁₀) threshold of 10. (i.e., posterior inclusion probability > 90% or <10% respectively).

RESULTS Network evidence

Strong evidence for conditional (in)dependence:

- Presence of 8 associations (positive/negative); BF > 10
- Absence of 3 associations (red); BF < 0.1, with borderline strong evidence for absence of another 3 associations (red-dotted); BF 0.12-0.15.

Strongest edge: Complaints pertain to memory - Persistence

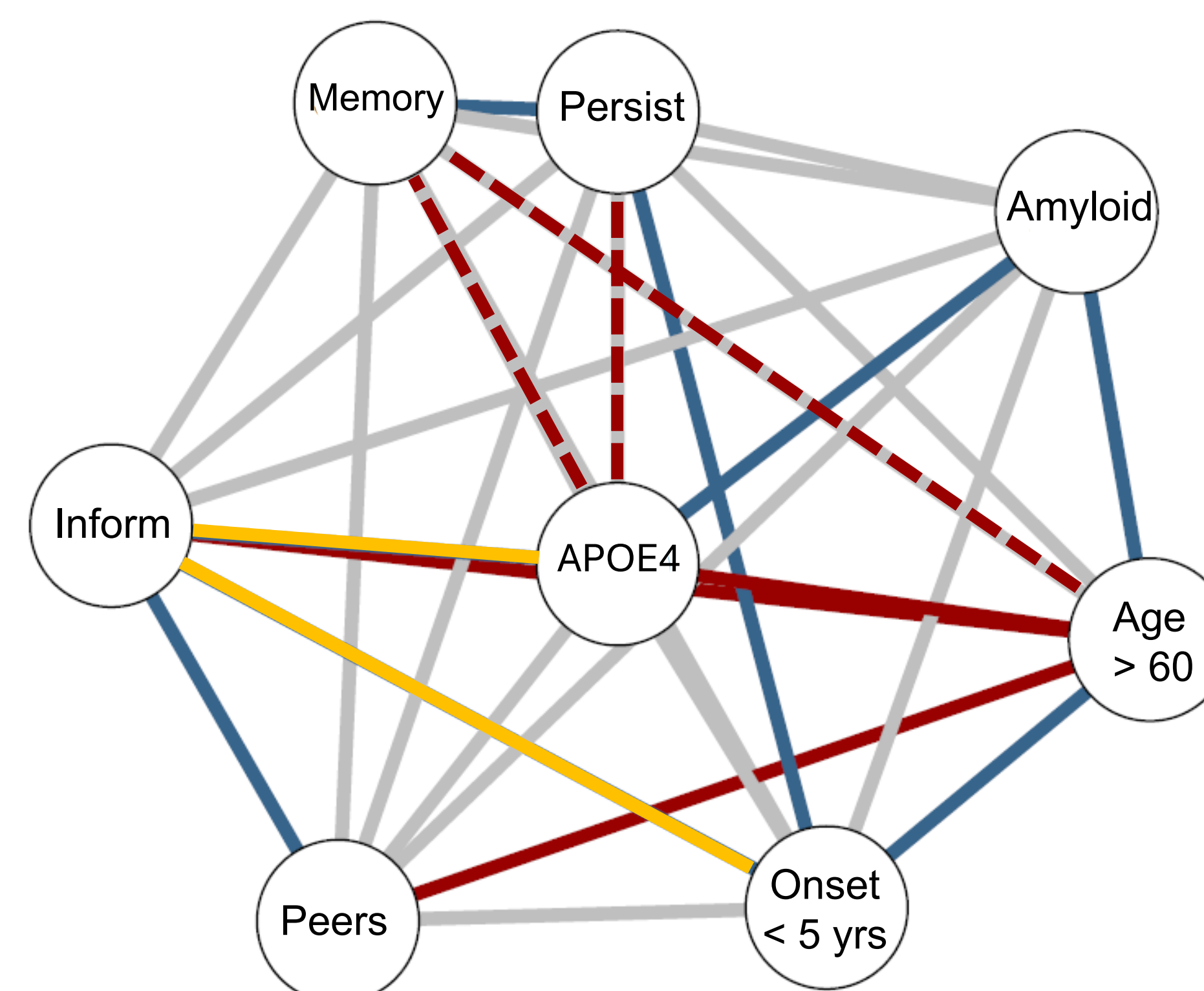


Figure 1. Visualization of the network based on edge evidence in the data. Blue and yellow edges indicate strong evidence for a positive and negative association respectively between the variables (i.e., conditional dependence, BF > 10), red edges indicate strong evidence for absence of an association between the variables (i.e., conditional independence, BF < 0.1), grey edges indicate inconclusive edges; insufficient evidence for or against an association (BF > 0.10 and < 10).

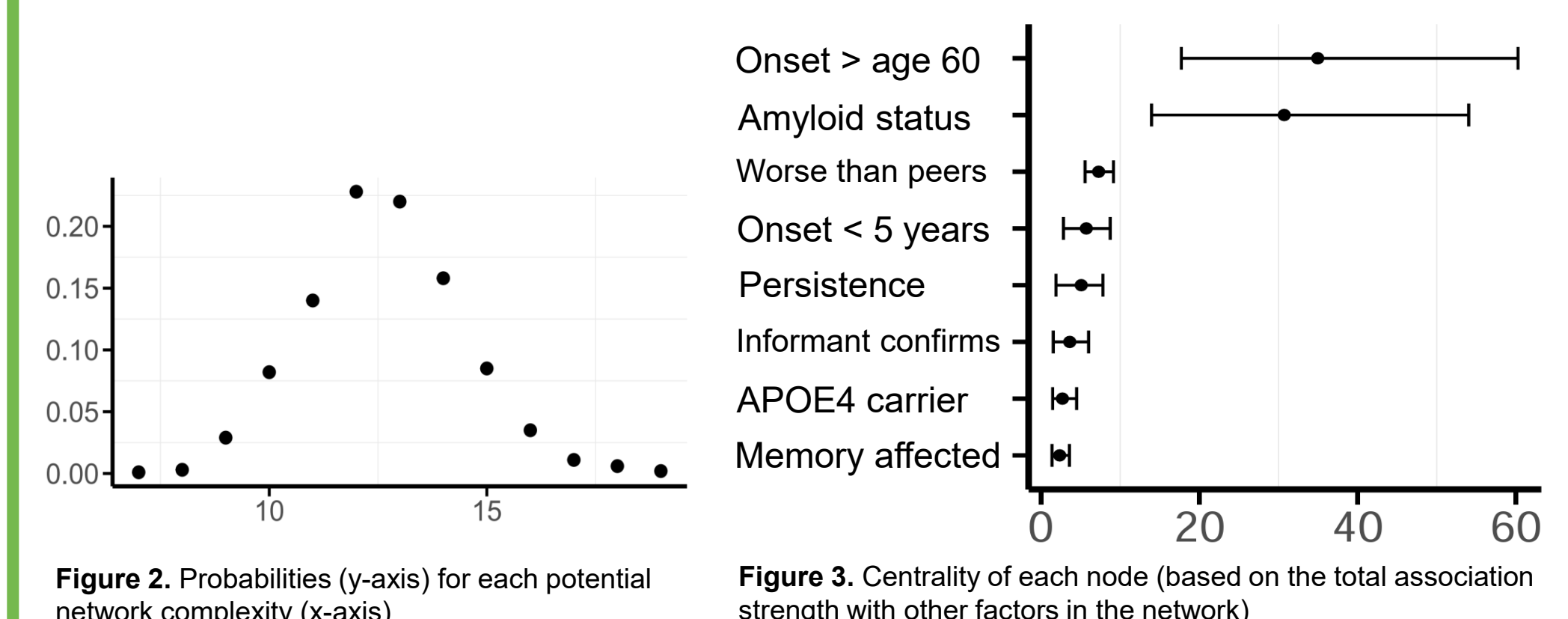
Memory = Complaints pertaining to memory, Persist = Persistent experience of decline, Inform = Informant confirmation of decline, Peers = Feeling worse than peers, Onset = Onset within the last 5 years, Age > 60 = Onset after age 60, APOE4 = APOE4 carrier, Amyloid = Amyloid positive

RESULTS Network interpretation

The most likely network structure contained 12-13 associations (43-46% density; Fig 2).

Existing associations were mostly positive, i.e., presence of one SCD*plus* feature was related to a higher likelihood of another feature. However, informant confirmation was less likely in case of complaint onset < 5 years and APOE4 presence.

Age at onset was the most central SCD*plus* feature (Fig. 3), mostly due to its associations with amyloid and onset timing, followed by Feeling worse than peers. Complaints pertaining to memory were least central.



Conclusion

In a relatively sparse network, we found strong evidence for both **presence** and **absence** of interrelations among SCD*plus* features and between these features and biological AD risk markers.

Amyloid positivity was more likely in case of **complaint onset after age 60**.

APOE4 was largely isolated from SCD *plus*, but less likely if there was informant confirmation of decline.

The varied interrelations point to **heterogeneity** in the SCD*plus* construct and in terms of the **relevance of its features for biological AD markers**.