GWAS-by-Subtraction

Michel Nivard

Cognitive & Non-cognitive contributions to education

nature genetics

ARTICLES

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Investigating the genetic architecture of noncognitive skills using GWAS-by-subtraction

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Little is known about the genetic architecture of traits affecting educational attainment other than cognitive ability. We used genomic structural equation modeling and prior genome-wide association studies (GWASs) of educational attainment ($n = 1{,}131{,}881$) and cognitive test performance ($n = 257{,}841$) to estimate SNP associations with educational attainment variation that is independent of cognitive ability. We identified 157 genome-wide-significant loci and a polygenic architecture accounting for 57% of genetic variance in educational attainment. Noncognitive genetics were enriched in the same brain tissues and cell types as cognitive performance, but showed different associations with gray-matter brain volumes. Noncognitive genetics were further distinguished by associations with personality traits, less risky behavior and increased risk for certain psychiatric disorders. For socioeconomic success and longevity, noncognitive and cognitive-performance genetics demonstrated associations of similar magnitude. By conducting a GWAS of a phenotype that was not directly measured, we offer a view of genetic architecture of noncognitive skills influencing educational success.




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Cognitive & Non-cognitive contributions to education

Key resources for this paper:
FAQ/motivation: https://bit.ly/3v2lSxY
Technical tutorial: https://rpubs.com/MichelNivard/565885
GitHub repo for paper: https://github.com/PerlineDemange/non-cognitive
The Paper: https://rdcu.be/cddNY




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The goal of this GWAS

- What affects educational success?

  Cognitive skills: Intelligence, IQ

  genetic correlation with EA: 0.70

- What else?

  motivation
  curiosity
  social skills
  etc.

  } Non-cognitive skills

Wouldn’t it be nice…

- … to have a GWAS of non-cognitive skills?

Unravelling the biology of non-cognitive skills

Investigating what are the important non-cognitive skills

Identify mechanisms behind the correlation between EA and other behavioural and health traits.

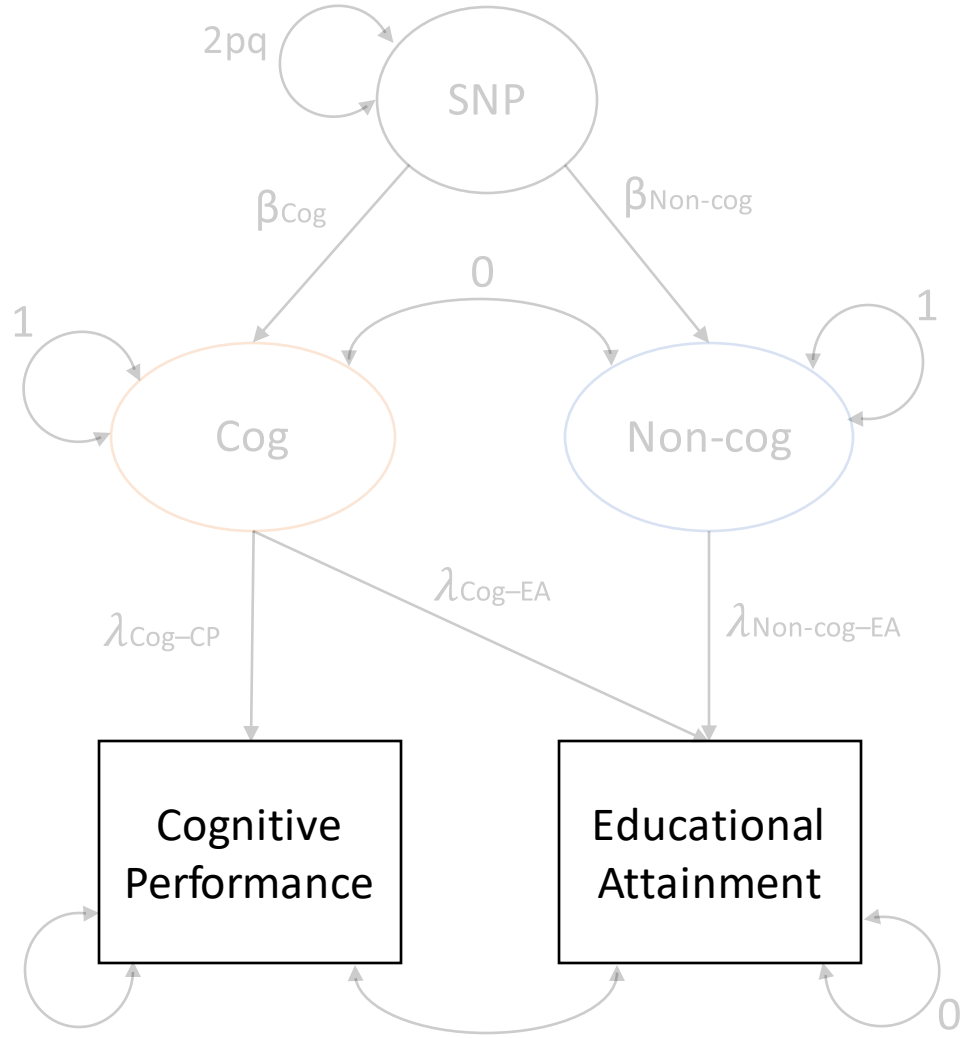
But…

- What is our phenotype?
  - Considerable heterogeneity in association with education
  - Poor test-retest reliability of measures
  - Low heritability

- Do we have enough power?
  - Few consistent measures in large cohorts

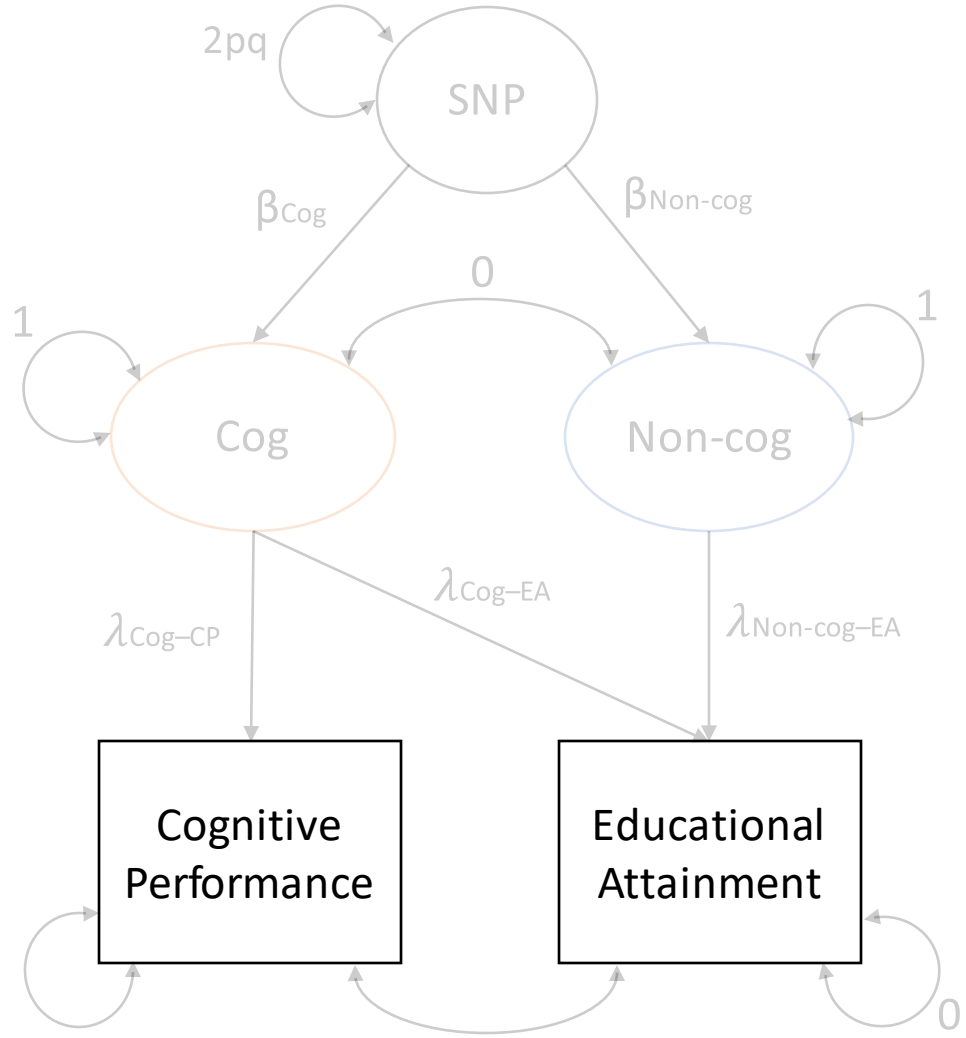
Smithers et al., 2018
Morris et al., 2018

The Solution in GenomicSEM



EA3 Lee et al. 2018 summary statistics

The Model & Syntax in GenomicSEM

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Model <-    'C =~ NA*EA + start(0.4)*CP
            NC =~ NA*EA
            C ~ SNP
            NC ~ SNP

            NC ~~ 1*NC
            C  ~~ 1*C
            C  ~~ 0*NC
            CP ~~ 0*EA
            CP ~~ 0*CP
            EA ~~ 0*EA
            SNP ~~ SNP '
```

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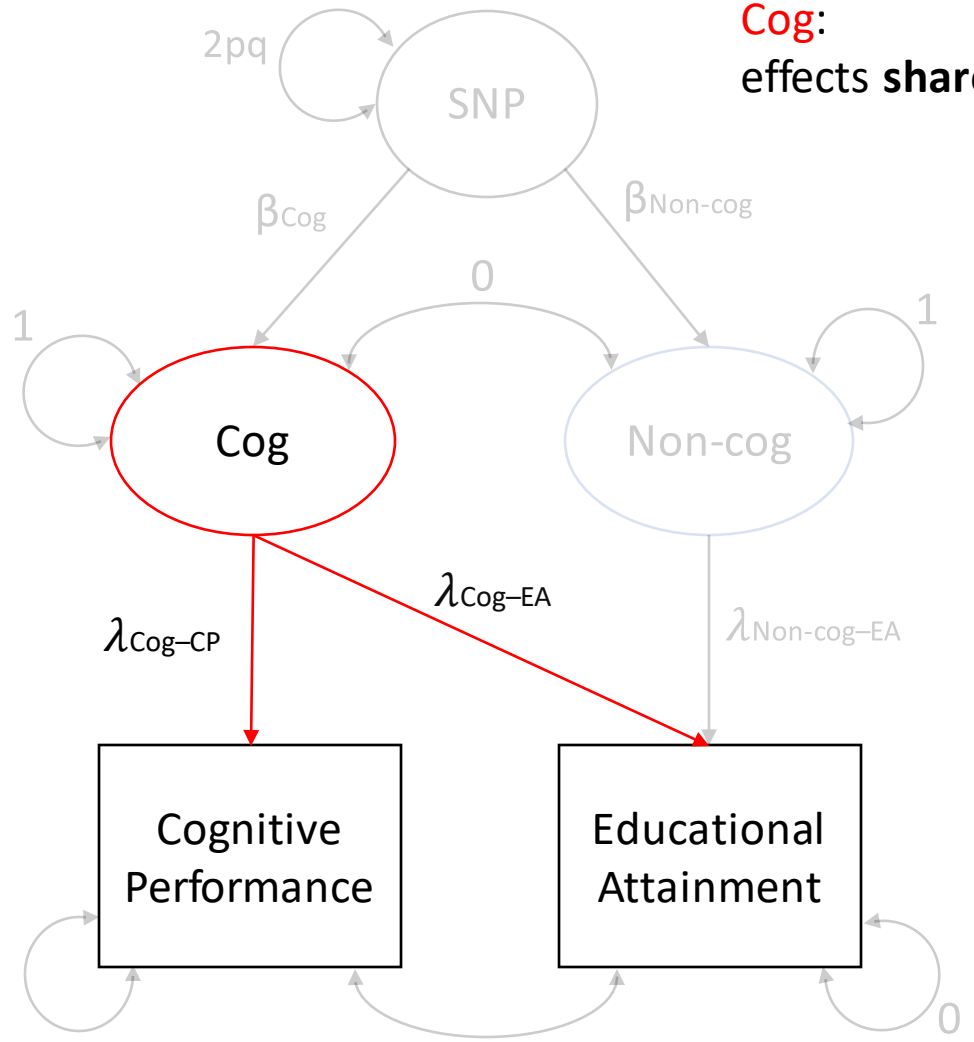

Cog:
effects **shared** between EA and CP

```
Model <-    'C =~ NA*EA + start(0.4)*CP
             NC =~ NA*EA
             C ~ SNP
             NC ~ SNP

             NC ~~ 1*NC
             C  ~~ 1*C
             C  ~~ 0*NC
             CP ~~ 0*EA
             CP ~~ 0*CP
             EA ~~ 0*EA
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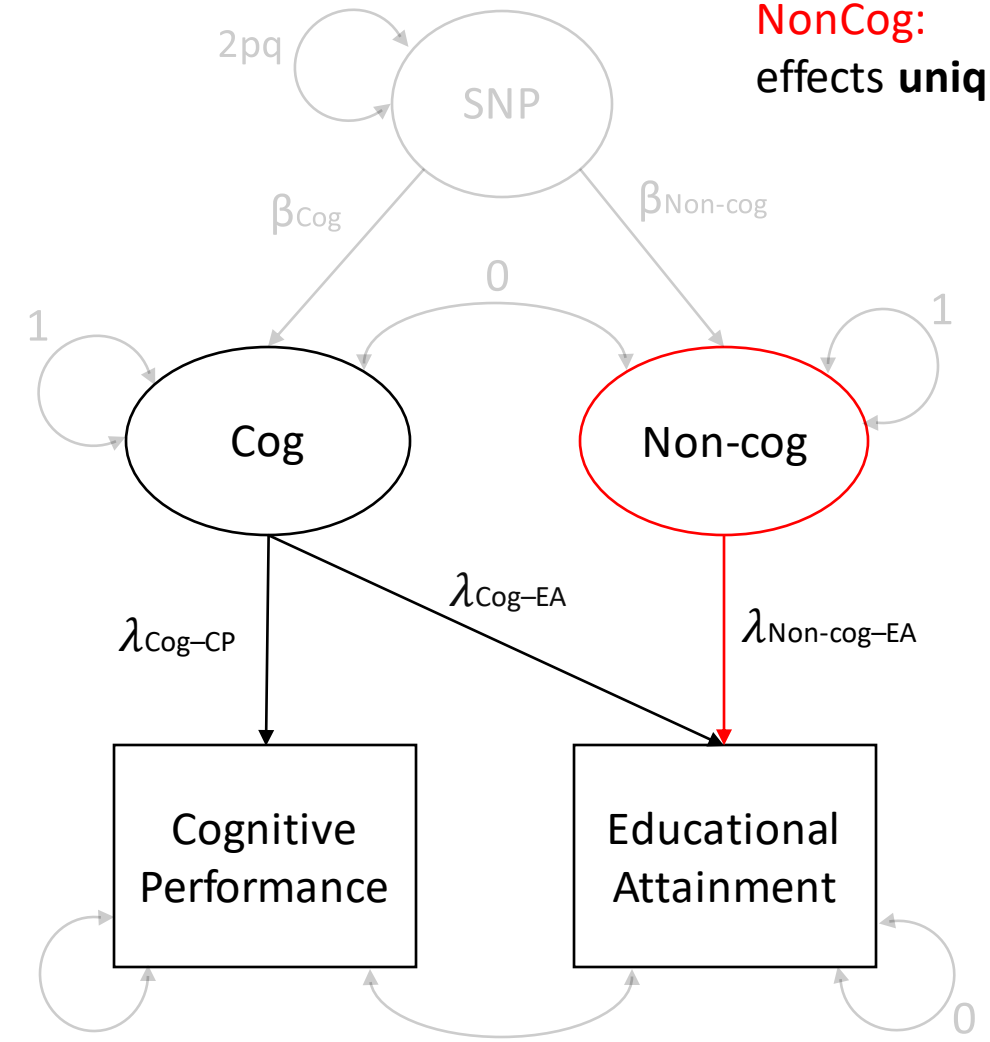

NonCog:
effects **unique** to EA after accounting for Cog

```
Model <-    'C =~ NA*EA + start(0.4)*CP
            NC =~ NA*EA
            C ~ SNP
            NC ~ SNP

            NC ~~ 1*NC
            C  ~~ 1*C
            C  ~~ 0*NC
            CP ~~ 0*EA
            CP ~~ 0*CP
            EA ~~ 0*EA
            SNP ~~ SNP '
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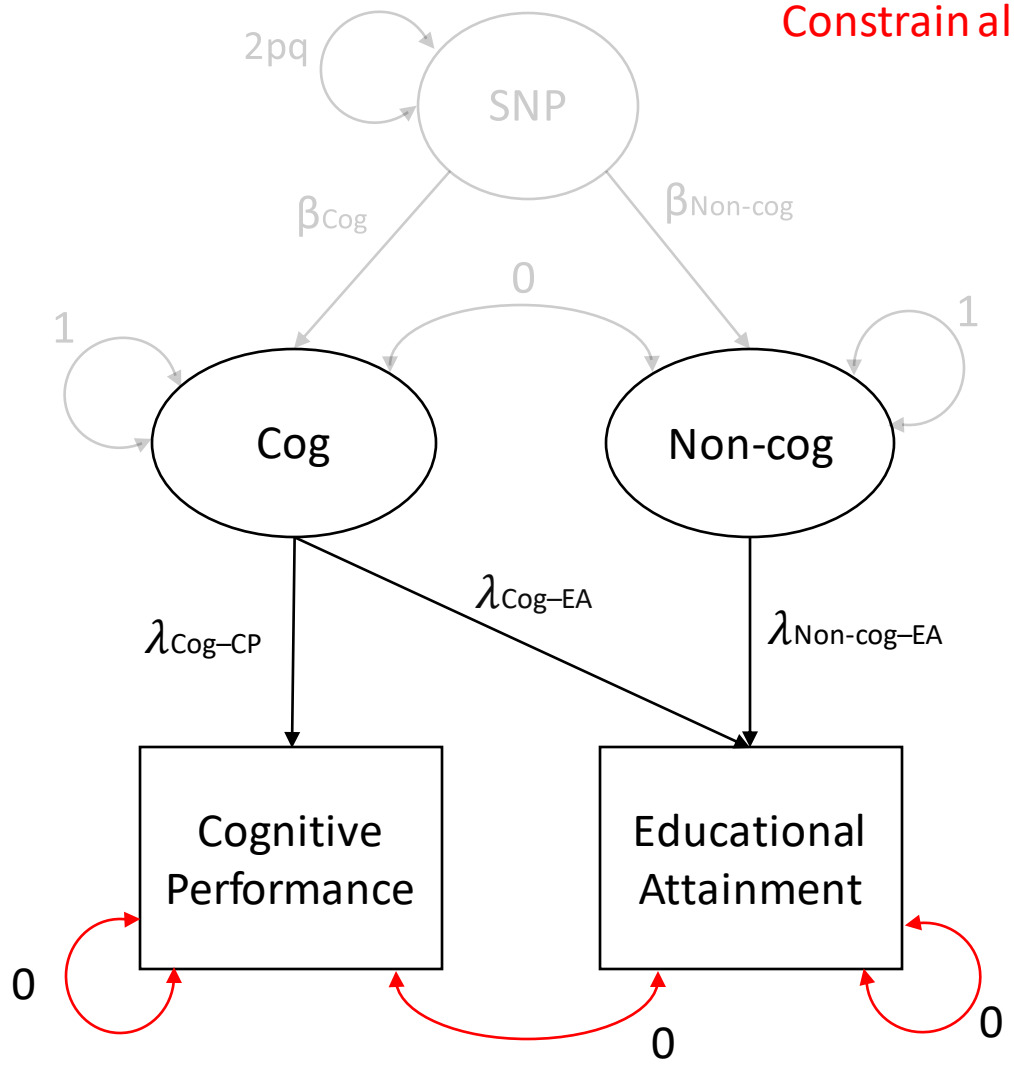

Constrain all other variance in EA and CP

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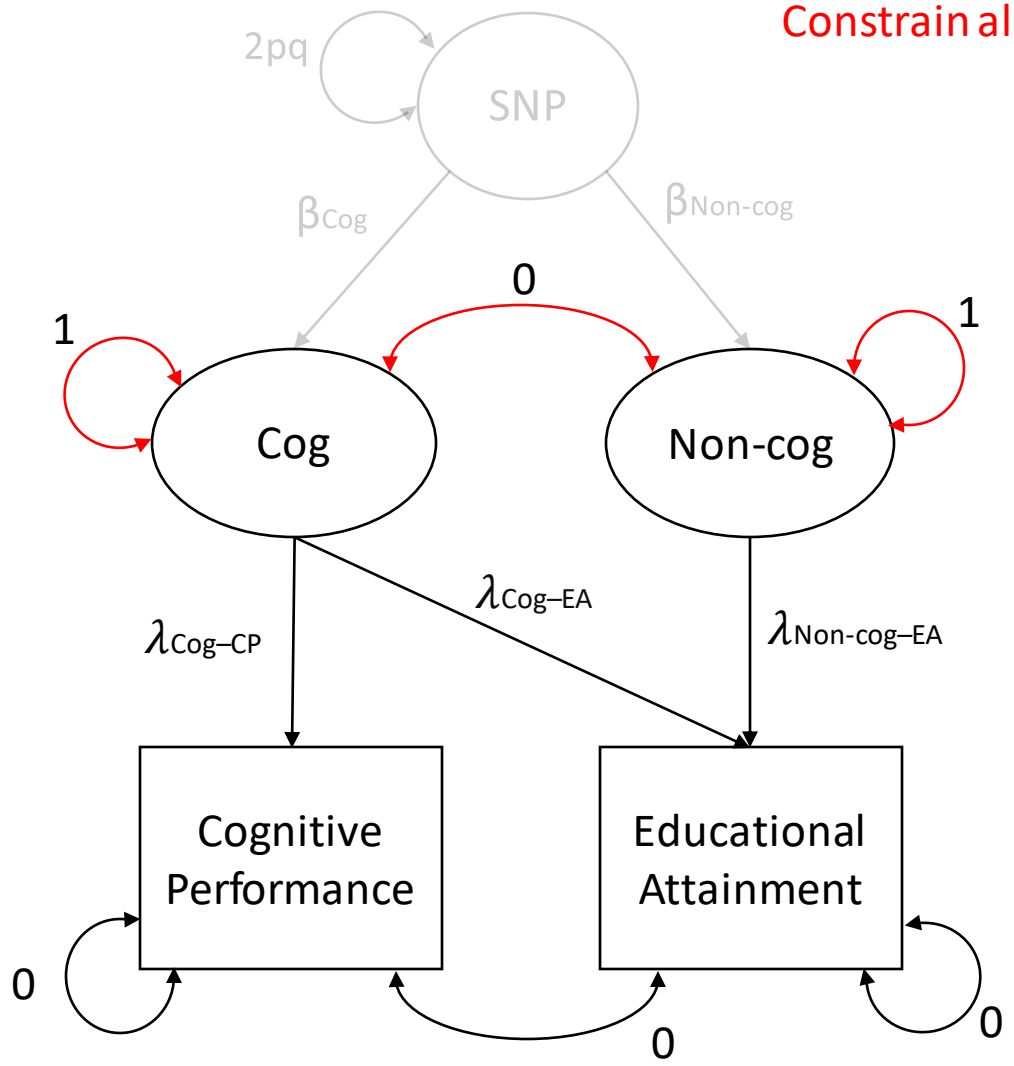
            CP ~~ 0*EA
            CP ~~ 0*CP
            EA ~~ 0*EA
            SNP ~~ SNP '
```

The Model & Syntax in GenomicSEM



Constrain all other variance in Cog and NonCog

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Model <-    'C =~ NA*EA + start(0.4)*CP
            NC =~ NA*EA
            C ~ SNP
            NC ~ SNP

            NC ~~ 1*NC
            C  ~~ 1*C
            C  ~~ 0*NC
            CP ~~ 0*EA
            CP ~~ 0*CP
            EA ~~ 0*EA
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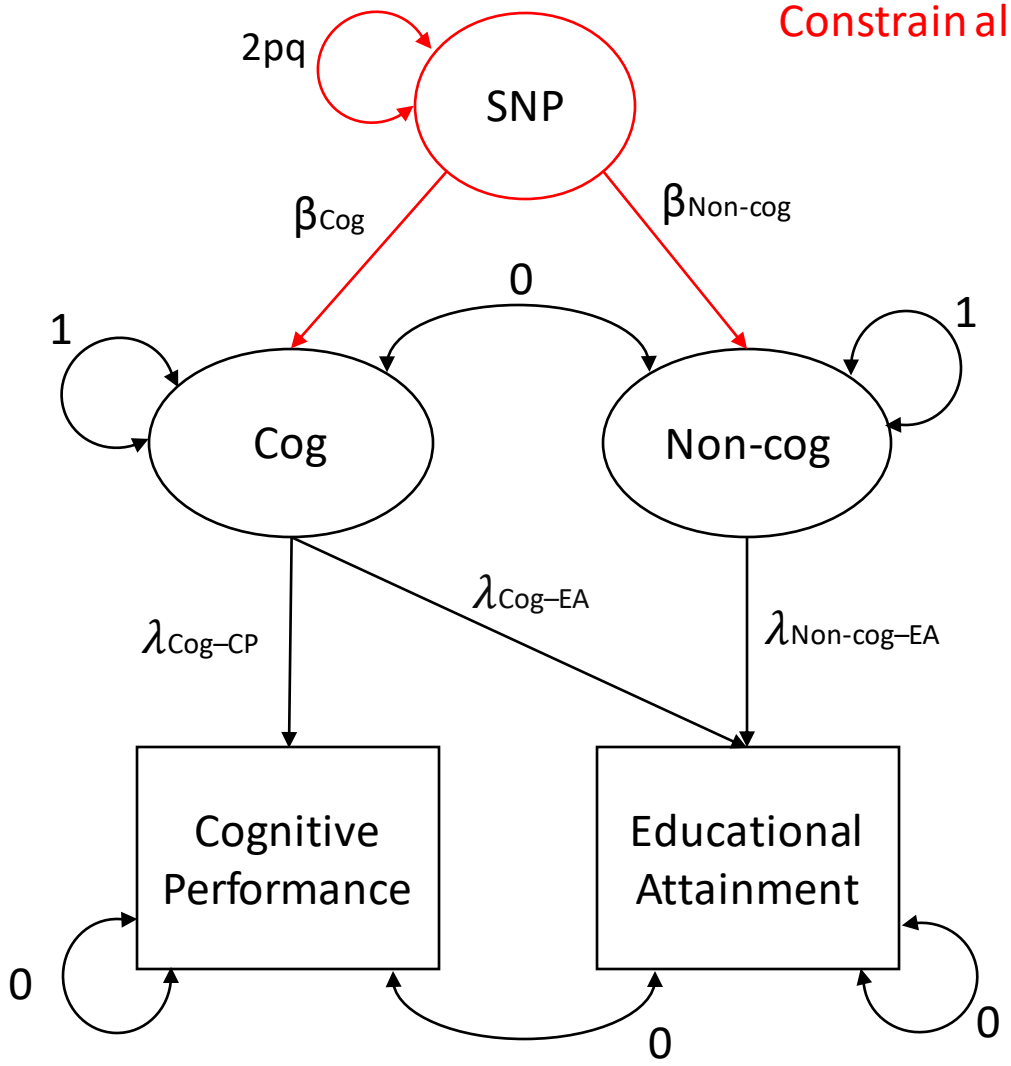
The Model & Syntax in GenomicSEM



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            C  ~~ 0*NC
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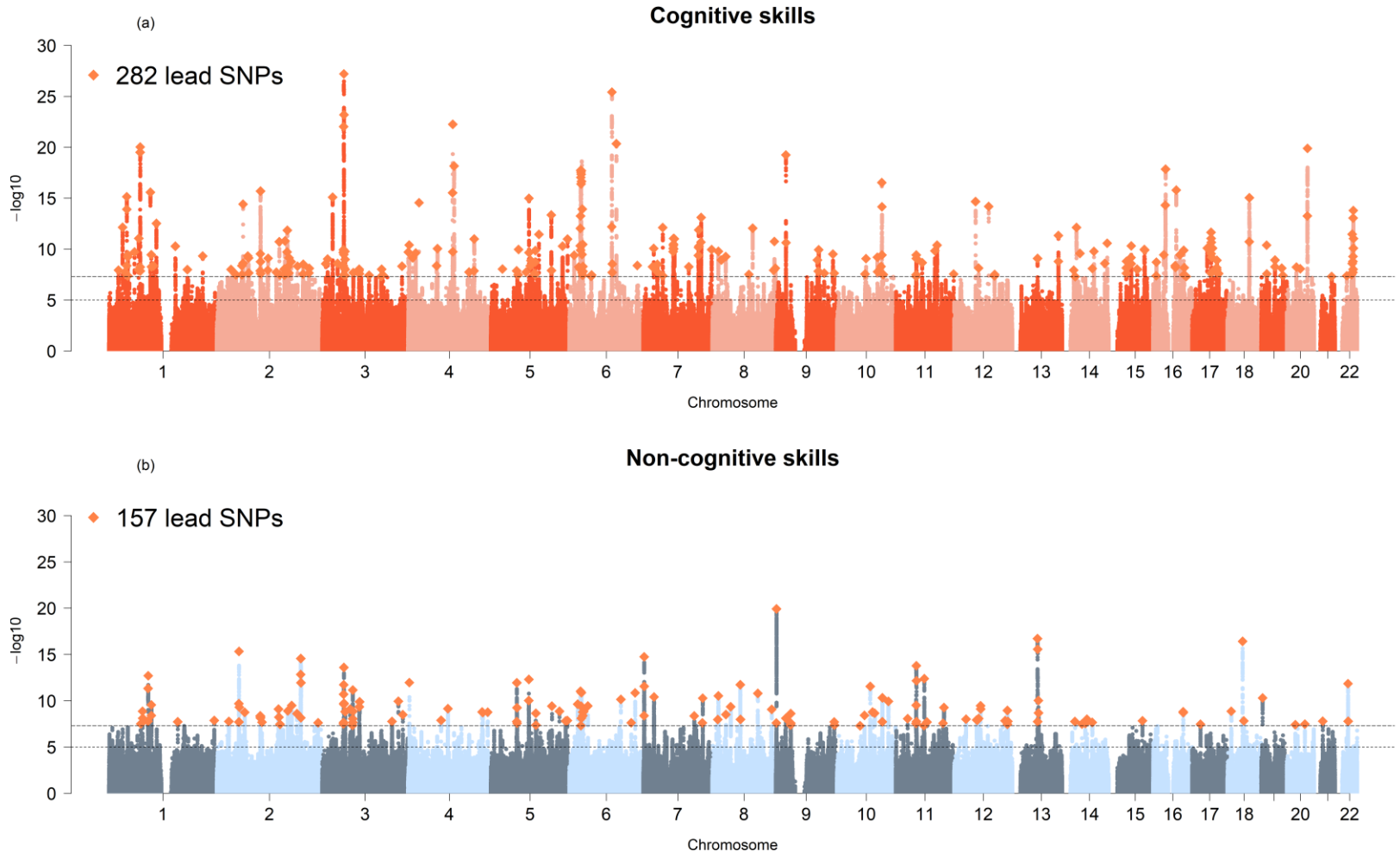
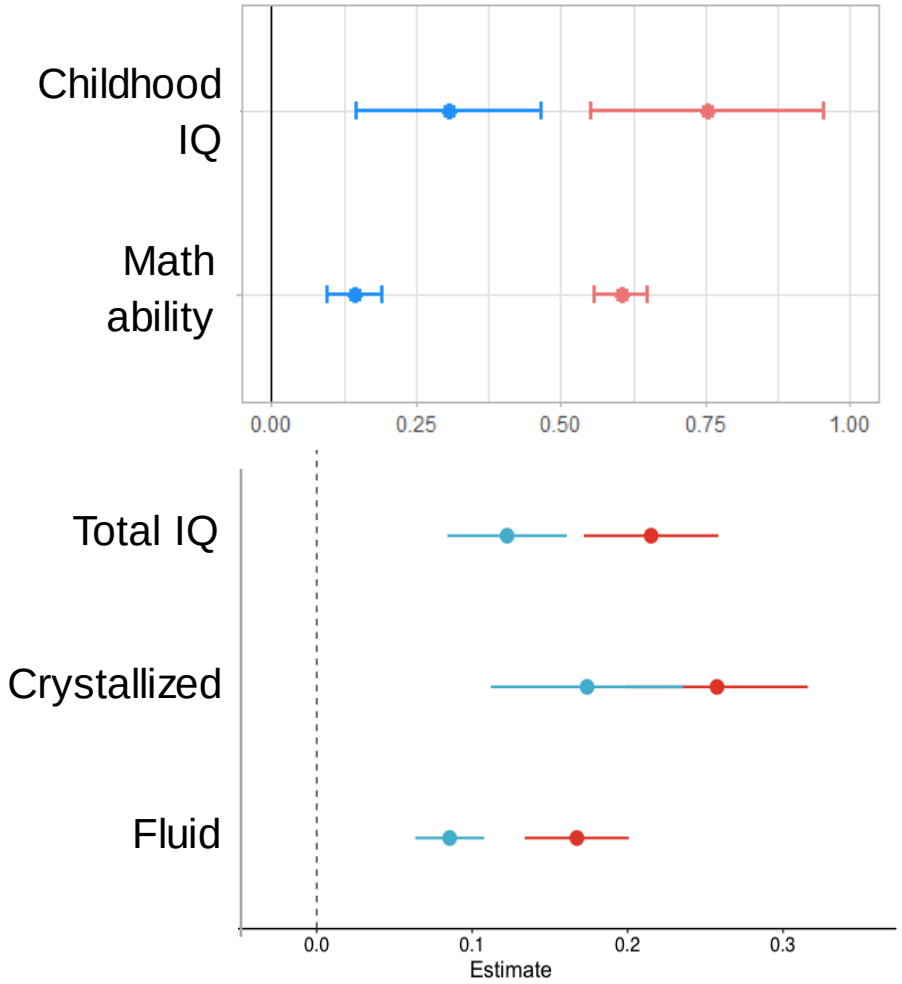
The Results:


(a)
Cognitive skills
282 lead SNPs
−log10
Chromosome
(b)
Non-cognitive skills
157 lead SNPs
−log10
Chromosome

Did it work?

Genetic correlations



Polygenic score predictions

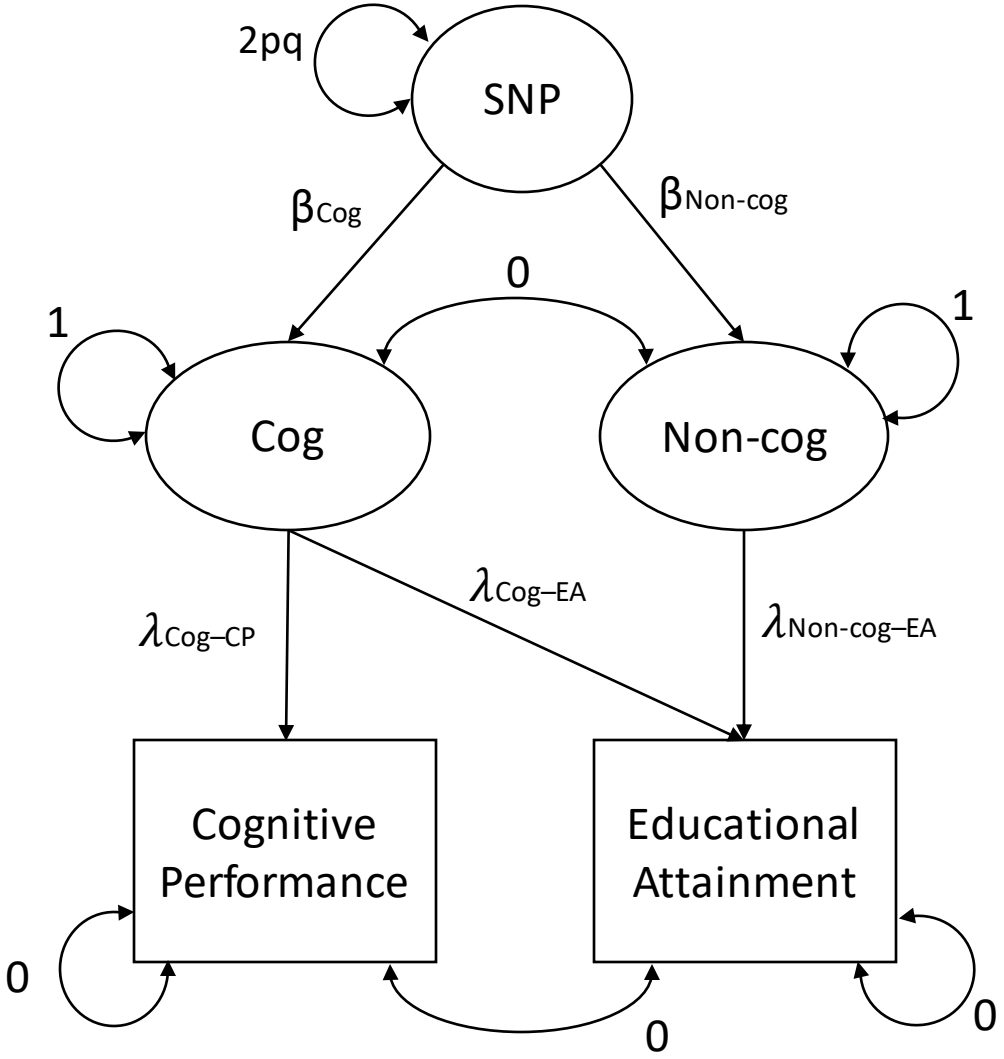
Meta-analysis across 4 cohorts:

Dunedin, ERisk, Texas Twins, NTR

Non-cognitive Cognitive

0

What about the assumptions we made?



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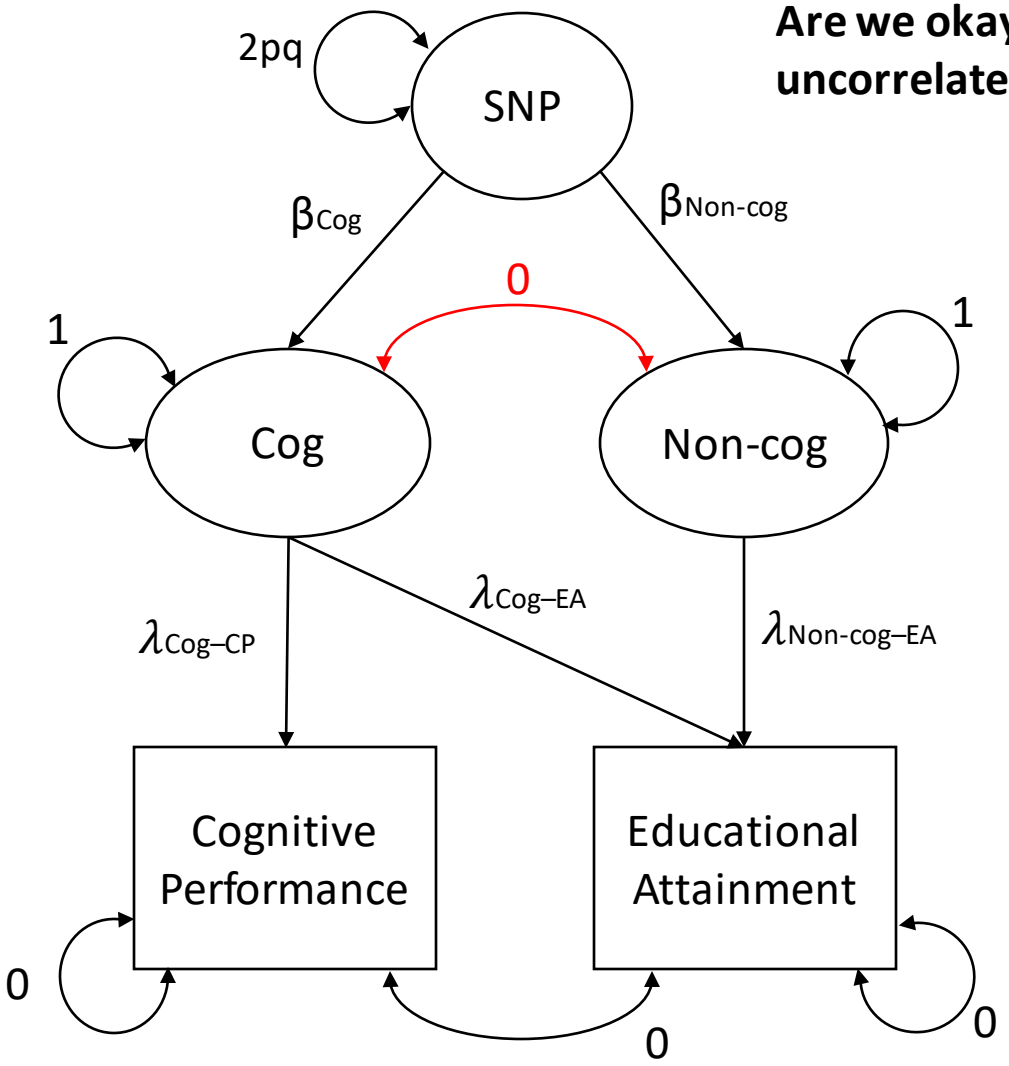

Are we okay with assuming Cog and NonCog are uncorrelated?

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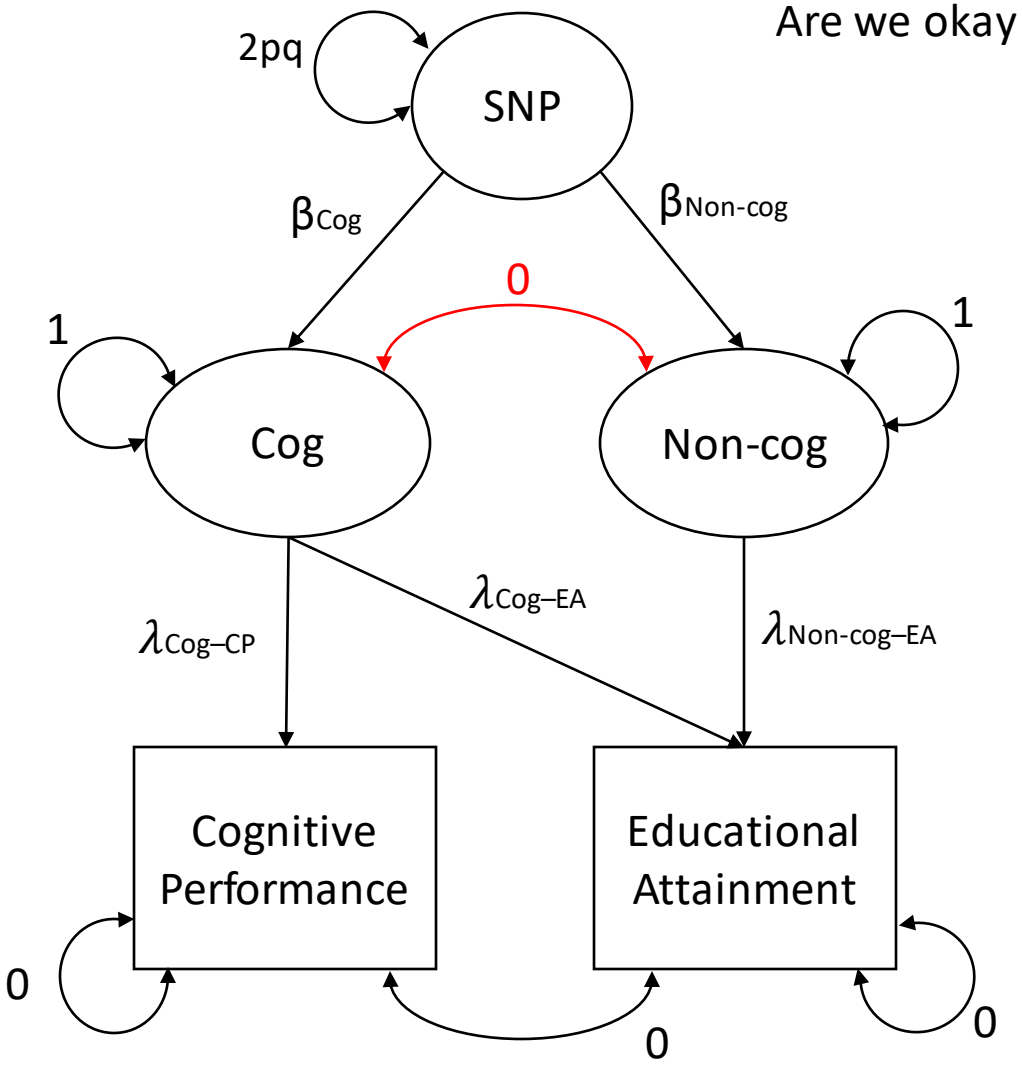

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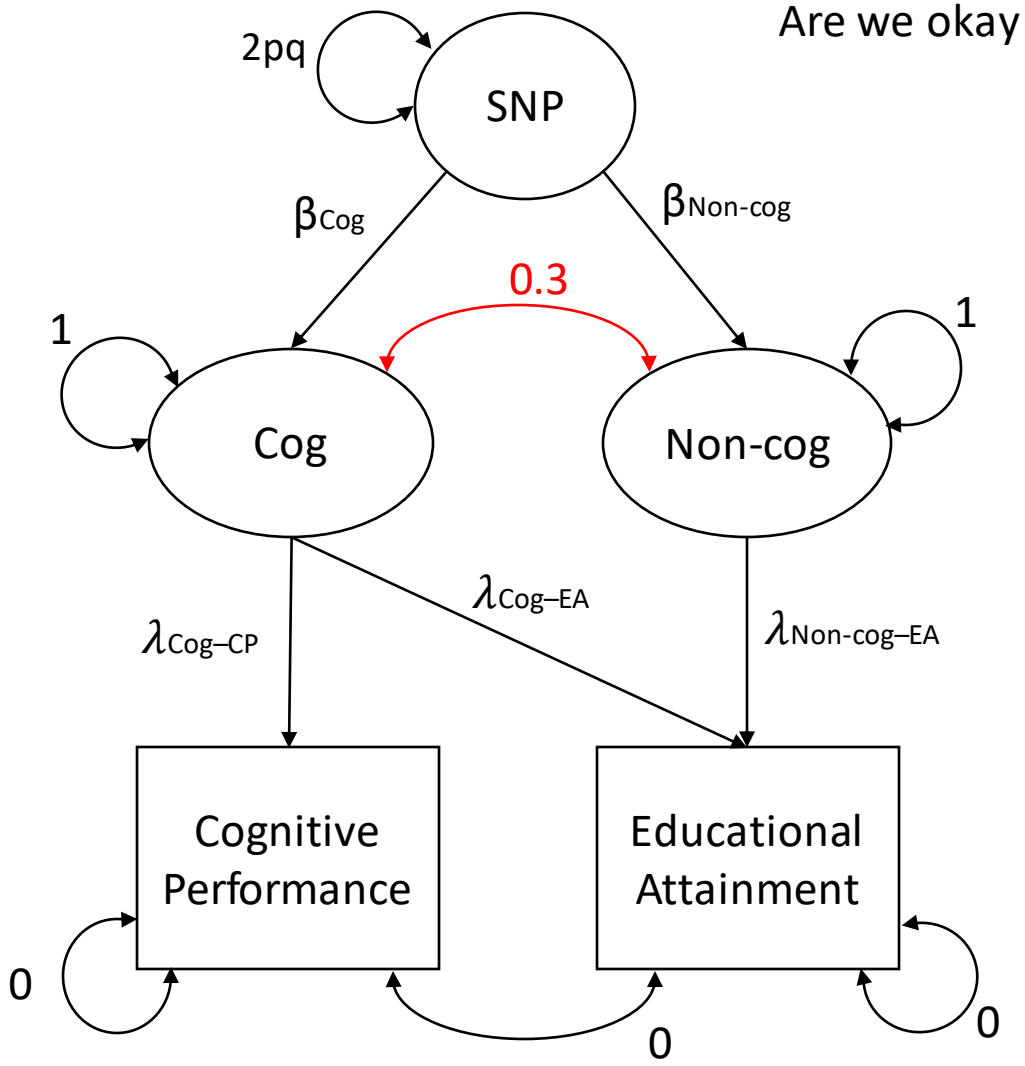

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            NC ~~ 1*NC
            C  ~~ 1*C
            C  ~~ 0.3*NC
            CP ~~ 0*EA
            CP ~~ 0*CP
            EA ~~ 0*EA
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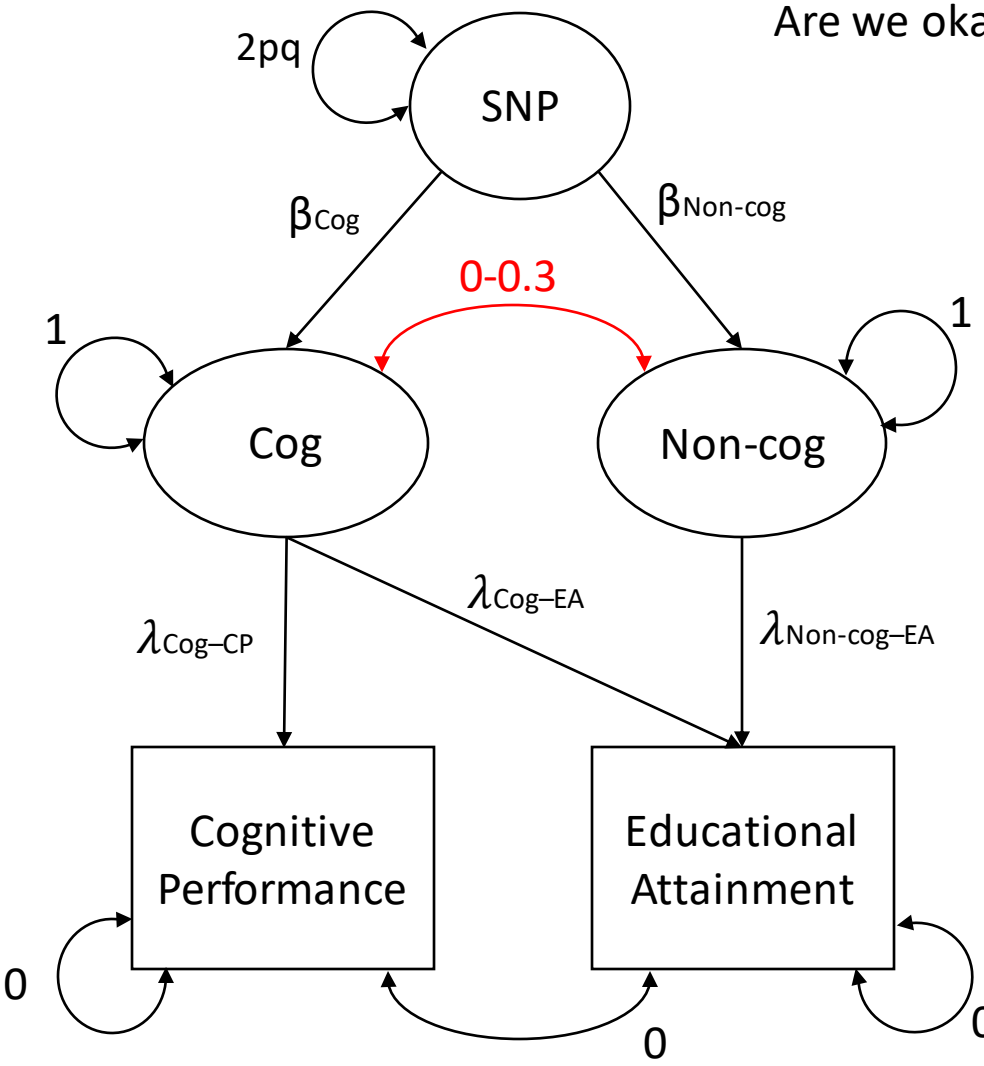

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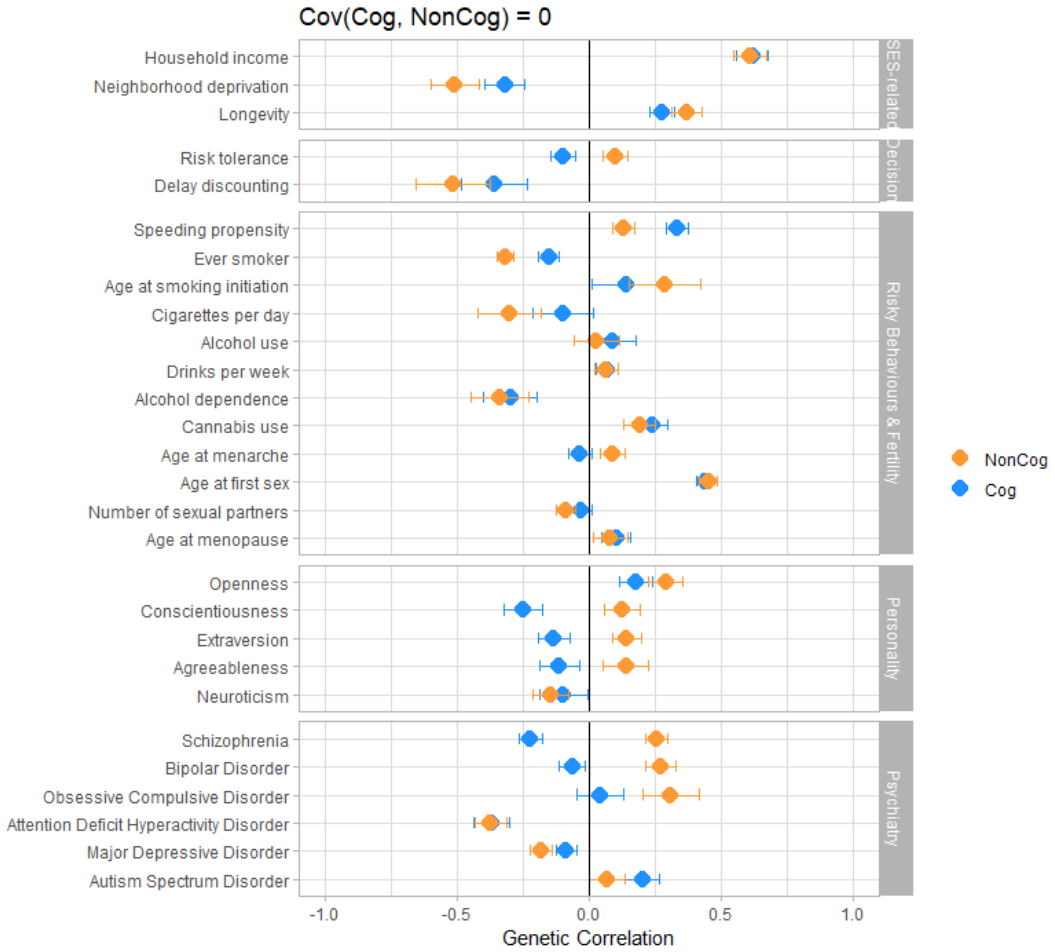

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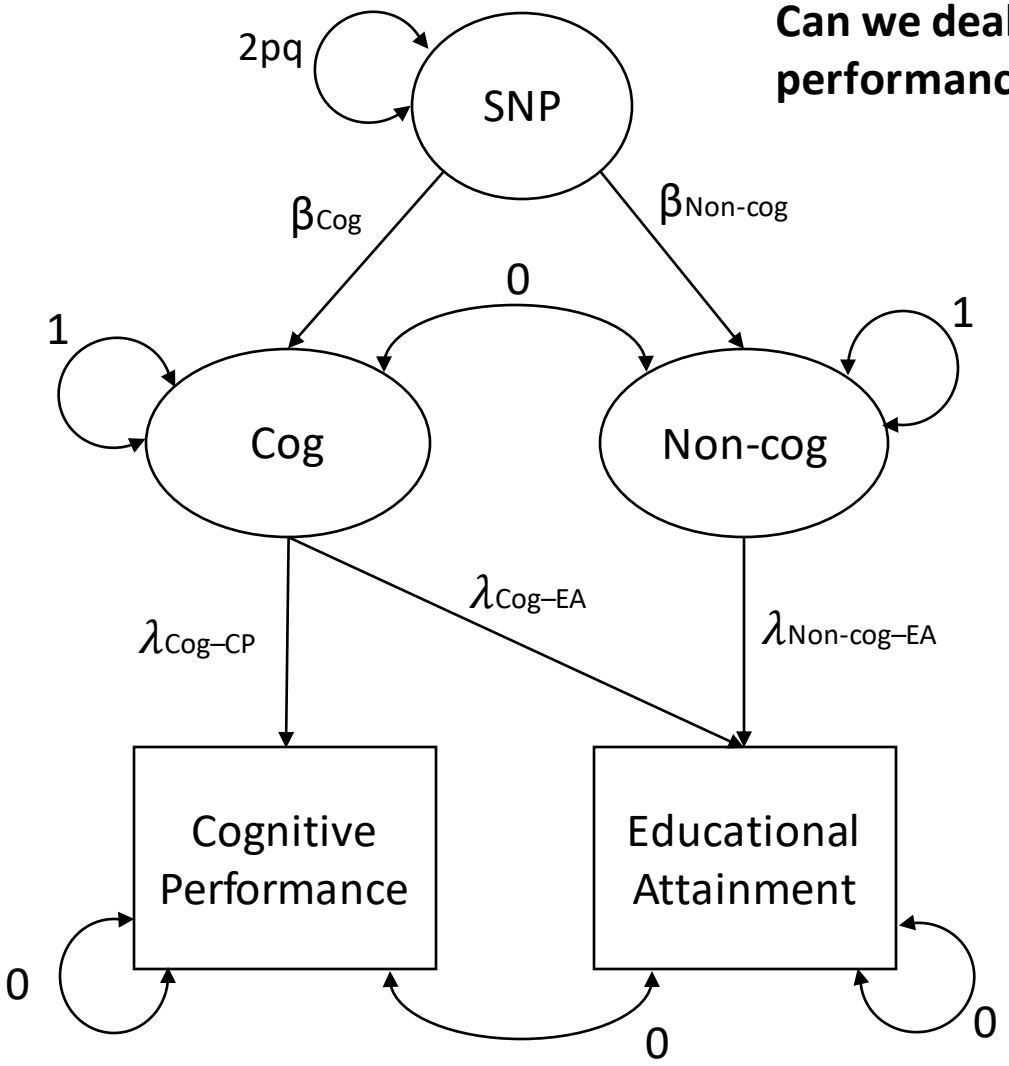

Can we deal with evidence that education improves cognitive performance?

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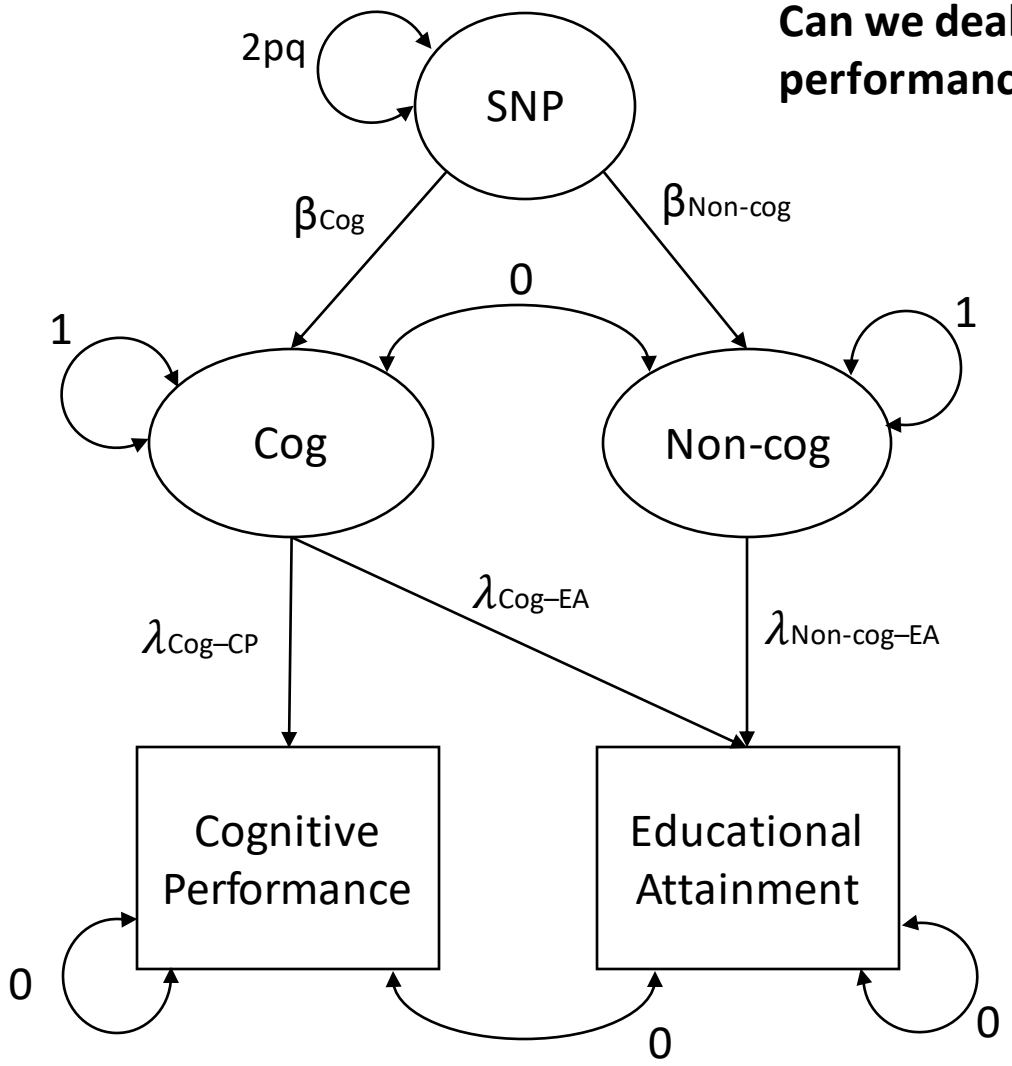

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Meta-Analysis > Psychol Sci. 2018 Aug;29(8):1358-1369. doi: 10.1177/0956797618774253. Epub 2018 Jun 18.

How Much Does Education Improve Intelligence? A Meta-Analysis

Stuart J Ritchie [1 2], Elliot M Tucker-Drob [3 4]

Affiliations + expand

PMID: 29911926 PMCID: PMC6088505 DOI: 10.1177/0956797618774253

Free PMC article

Abstract

Intelligence test scores and educational duration are positively correlated. This correlation could be interpreted in two ways: Students with greater propensity for intelligence go on to complete more education, or a longer education increases intelligence. We meta-analyzed three categories of quasiexperimental studies of educational effects on intelligence: those estimating education-intelligence associations after controlling for earlier intelligence, those using compulsory schooling policy changes as instrumental variables, and those using regression-discontinuity designs on school-entry age cutoffs. Across 142 effect sizes from 42 data sets involving over 600,000 participants, we found consistent evidence for beneficial effects of education on cognitive abilities of approximately 1 to 5 IQ points for an additional year of education. Moderator analyses indicated that the effects persisted across the life span and were present on all broad categories of cognitive ability studied. Education appears to be the most consistent, robust, and durable method yet to be identified for raising intelligence.

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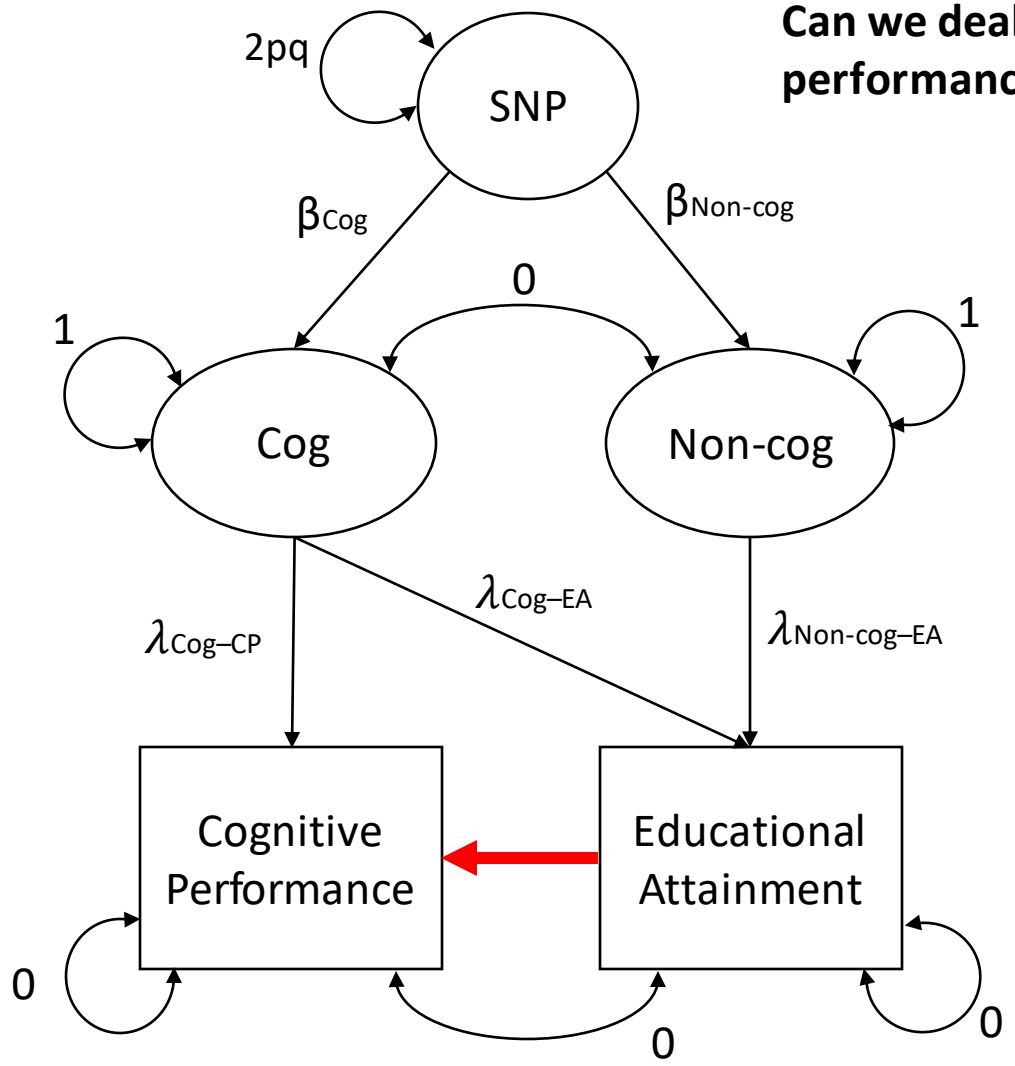

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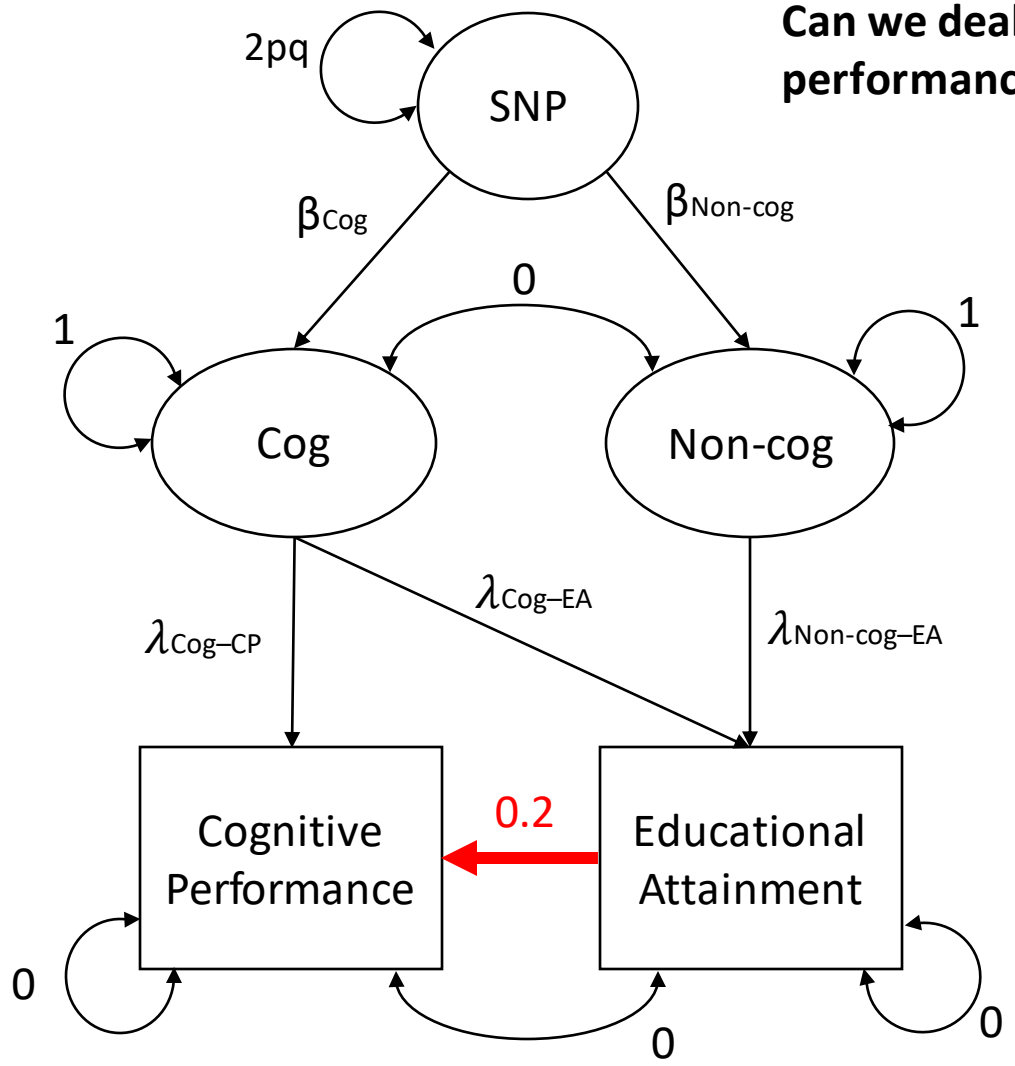

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            CP ~~ 0*CP
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            CP ~ 0.2*EA'
```

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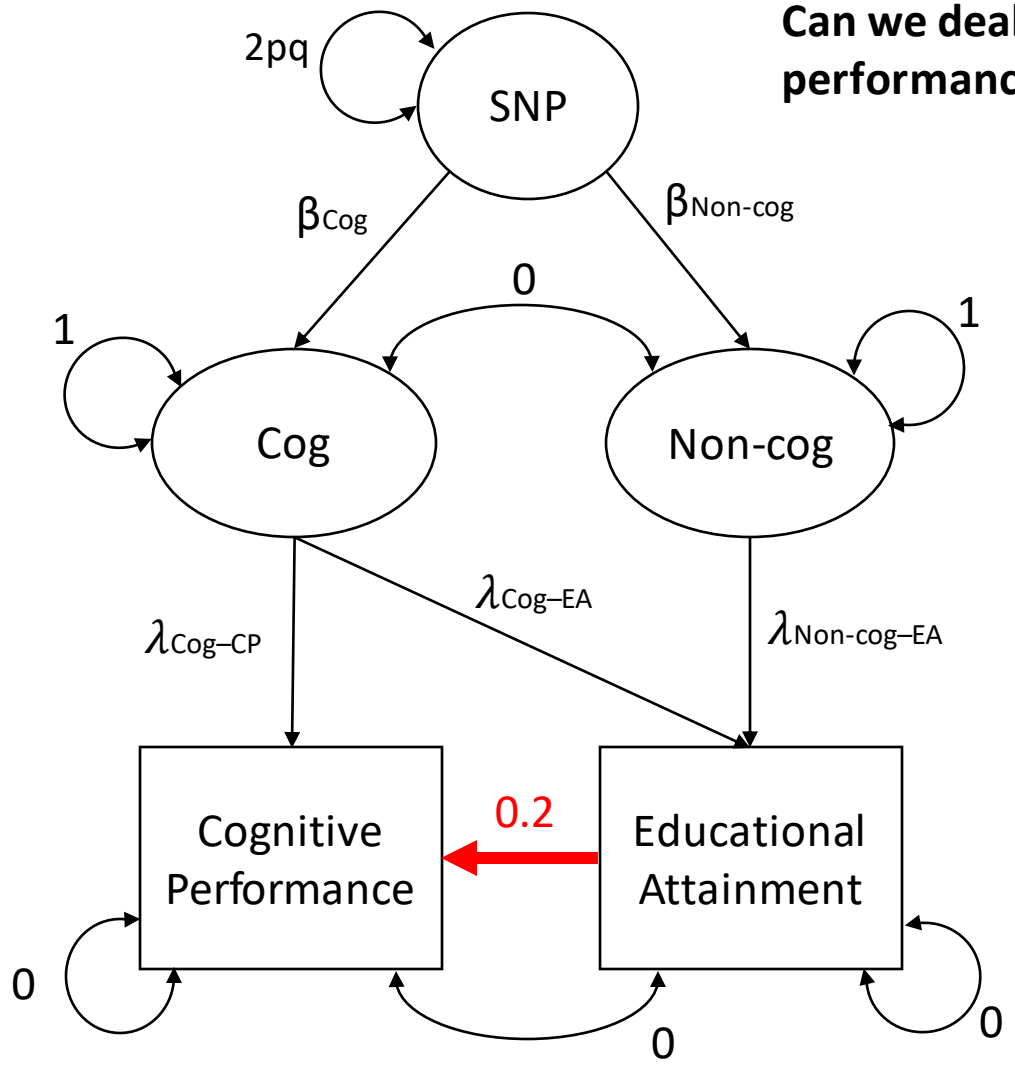

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