

# FROM GENES TO BIOLOGY-INFORMED COGNITIVE TESTING: MAPPING THE GENETIC ARCHITECTURES OF COGNITIVE FUNCTIONING

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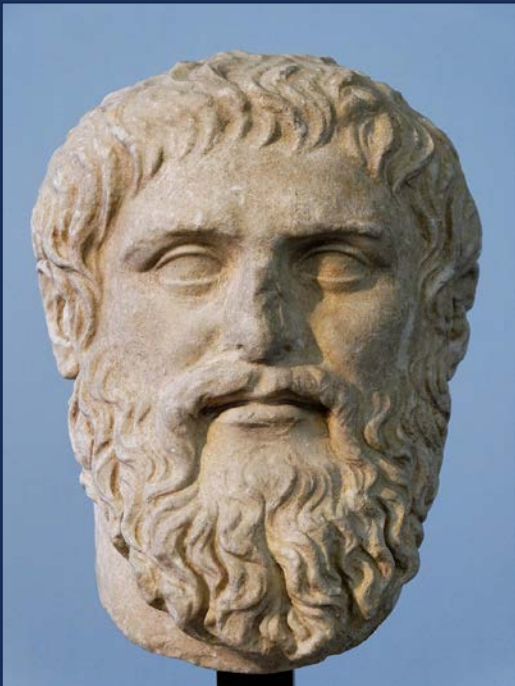
# THE NATURE OF INTELLIGENCE

INTELLIGENCE AND THE ASSESSMENT OF COGNITIVE PROCESSES



# EARLY IDEAS ABOUT THE NATURE OF INTELLIGENCE

**PLATO**  
427 BC – 347 BC



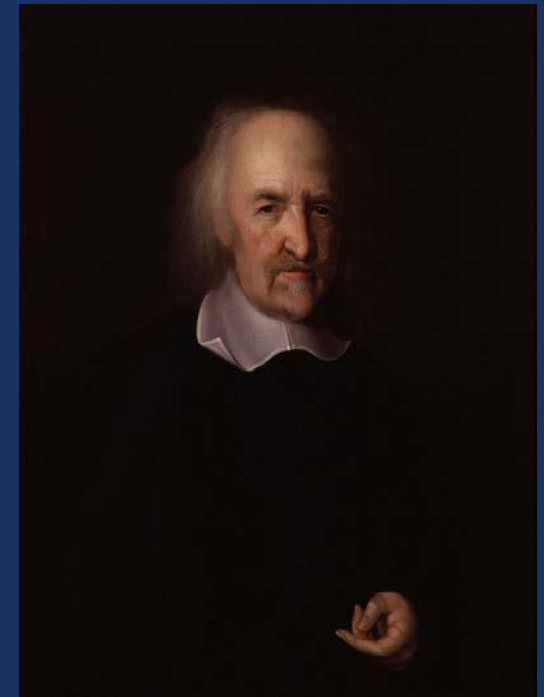
The love of learning –  
and the love of truth

**ST. AUGUSTINE**  
354 – 430



Superior intelligence might lead  
people away from God

**THOMAS HOBBS**  
1588 - 1679



Superior intelligence is the ability to see  
similarities between different things, and  
differences between similar things (*Leviathan*)

# ORIGINS OF MODERN UNDERSTANDING OF INTELLIGENCE

Charles Spearman



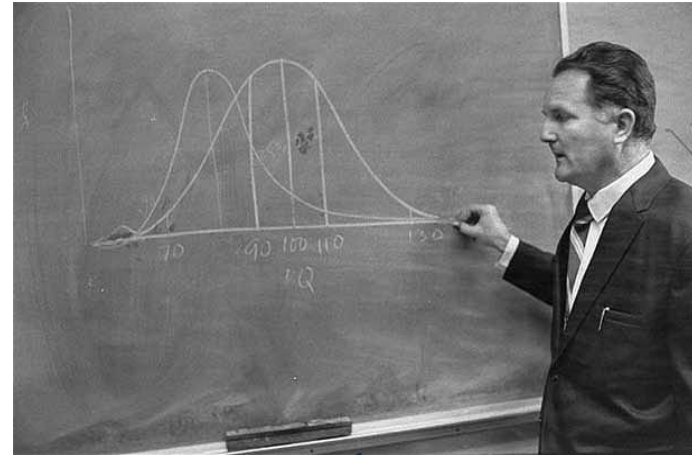
Alfred Binet  
1857 - 1911



Louis Thurstone  
1887 - 1955



Arthur Jensen  
1923 - 2012



Hans Eysenck  
1916 - 1997



*g*, general intelligence

Mental energy

Mental speed

Multiplicity of higher mental processes

# HOW WE DEFINE INTELLIGENCE TODAY?



## intelligence

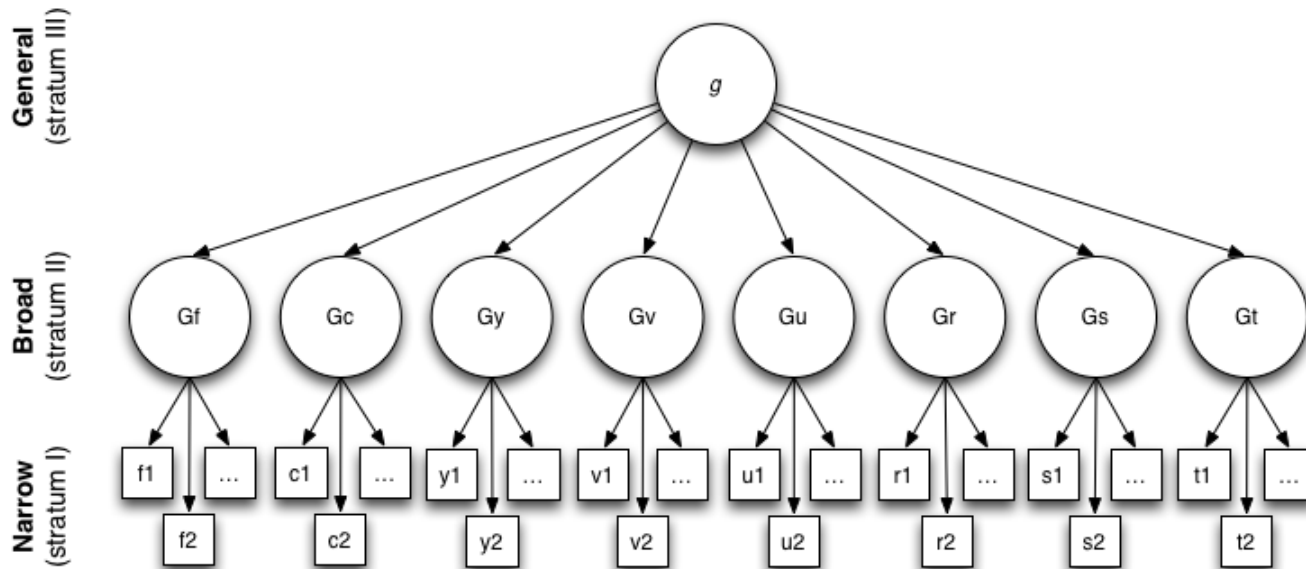
n. the ability to derive information, learn from experience, adapt to the environment, understand, and correctly utilize thought and reason.

## cognition

n.

1. all forms of knowing and awareness, such as perceiving, conceiving, remembering, reasoning, judging, imagining, and problem solving. Along with affect and conation, it is one of the three traditionally identified components of mind.
2. an individual percept, idea, memory, or the like.

# THE CATTELL-HORN-CARROLL (CHC) THEORY



- Performance on a test as a function of multiple domain-general and domain-specific abilities
- Widely accepted as the most comprehensive and empirically supported theory of cognitive abilities, informing a substantial body of research
- Kovacs and Conway (2019) have proposed Process Overlap Theory (POT) which describes overall performance on a test as a function of multiple domain-general and domain-specific abilities

All cognitive theories and measurement instruments have been developed without taking biological bases of cognitive behaviour into consideration!



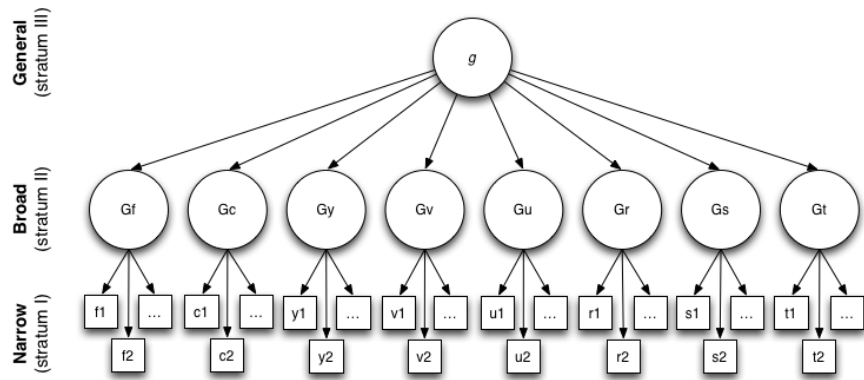
# SETTING THE STAGE: ARE SPECIFIC COGNITIVE ABILITIES GENETICALLY SEPARABLE FROM G?

WHAT DO WE KNOW ABOUT GENETIC ARCHITECTURE OF COGNITION



# WHAT DO WE KNOW ABOUT GENETICS OF COGNITION?

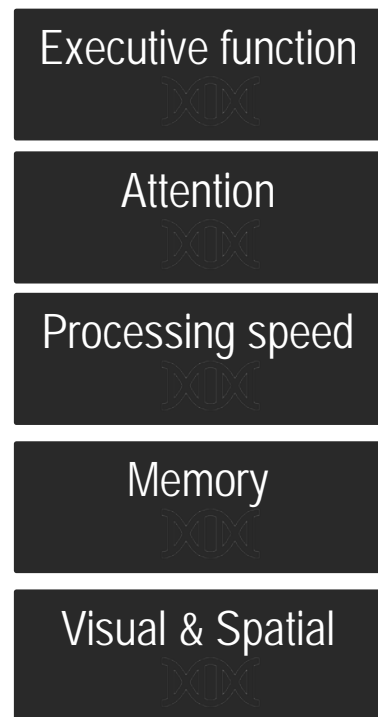
## ■ General intelligence, $g$



- Arrived at by factor analysis of results of multiple tests
- Claims a general component to intelligence, supplemented by specific components
- Over 1,000 genetic variants identified across 12 studies at  $p < 5 \times 10^{-8}$

## • Limited translation due to lack of specificity

## ■ Specific cognitive abilities

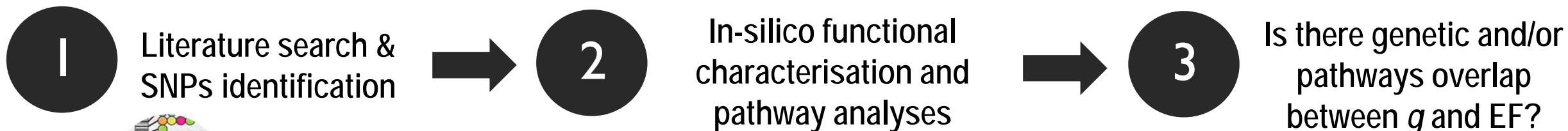


- **Limited understanding of genetics of specific cognitive abilities**
- **Not clear whether specific cognitive abilities are genetically separable from  $g$**

## • Are specific cognitive abilities, such as EF, genetically separable from $g$ ?



# IS EF GENETICALLY SEPARABLE FROM G?



GWAS Catalog  
The NHGRI-EBI Catalog of published genome-wide association studies

SNPnexus

## Studies of interest:

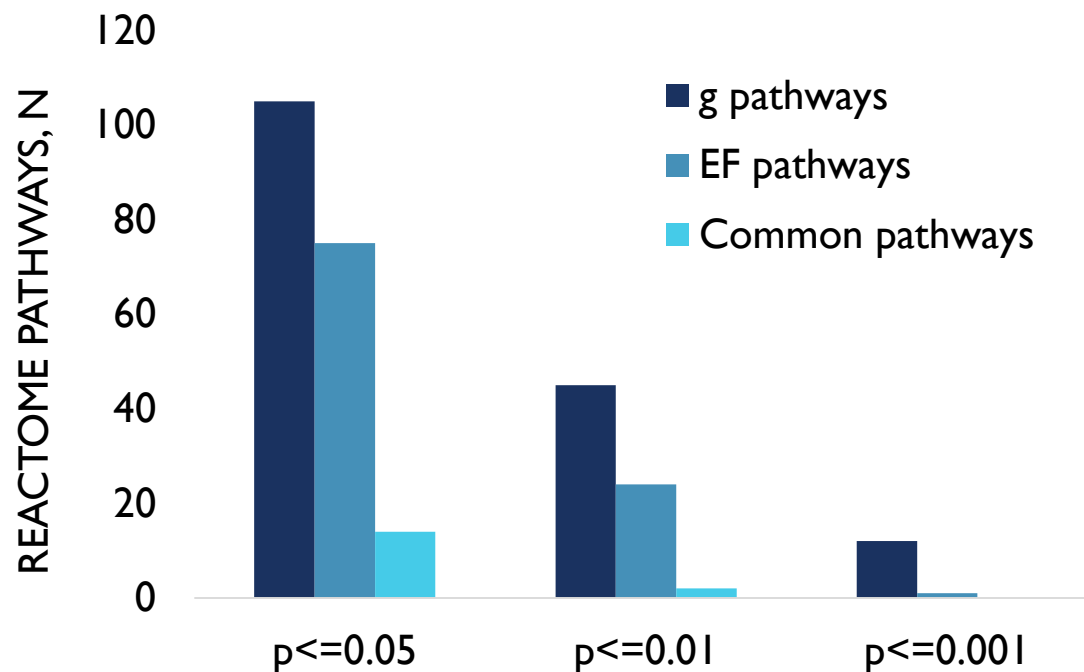
- 12 studies on general intelligence, g
- 5 studies on executive function

## Index SNPs:

- 1,372 g SNPs at  $p < 5 \times 10^{-6}$
- 300 EF SNP  $p < 5 \times 10^{-6}$

## Proxy SNPs (LD, $R^2 > 0.8$ ):

- 37,547 g SNPs
- 8,493 EF SNPs



## RESULTS

- Minimal LD-based genetic overlap between g & EF (4.6%)
- Small pathway overlap between g & EF (7.8%)

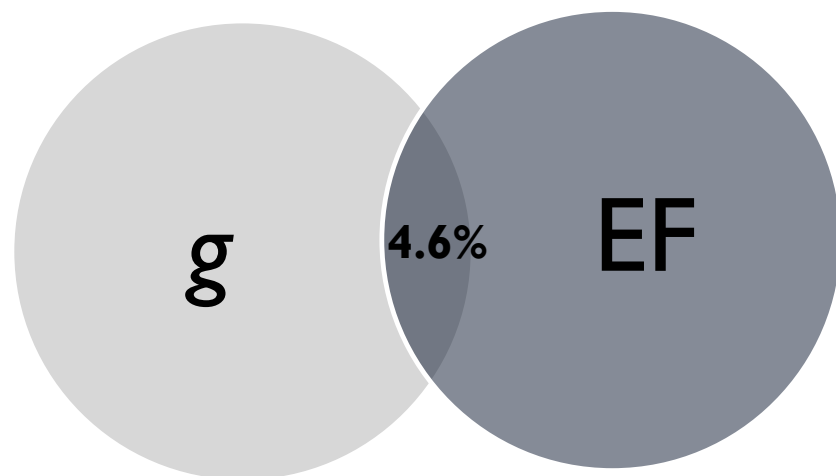
## CONCLUSION

EF appear to be separable from g at the molecular level

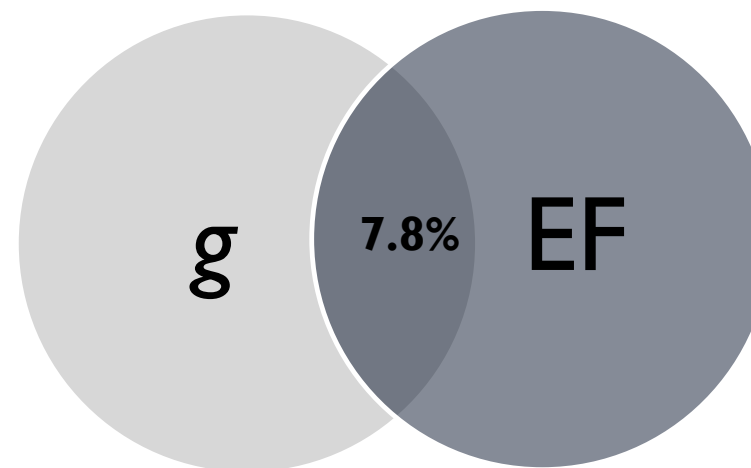
# YES, EF APPEAR TO BE GENETICALLY SEPARABLE FROM G



Genetic overlap



Molecular pathways overlap



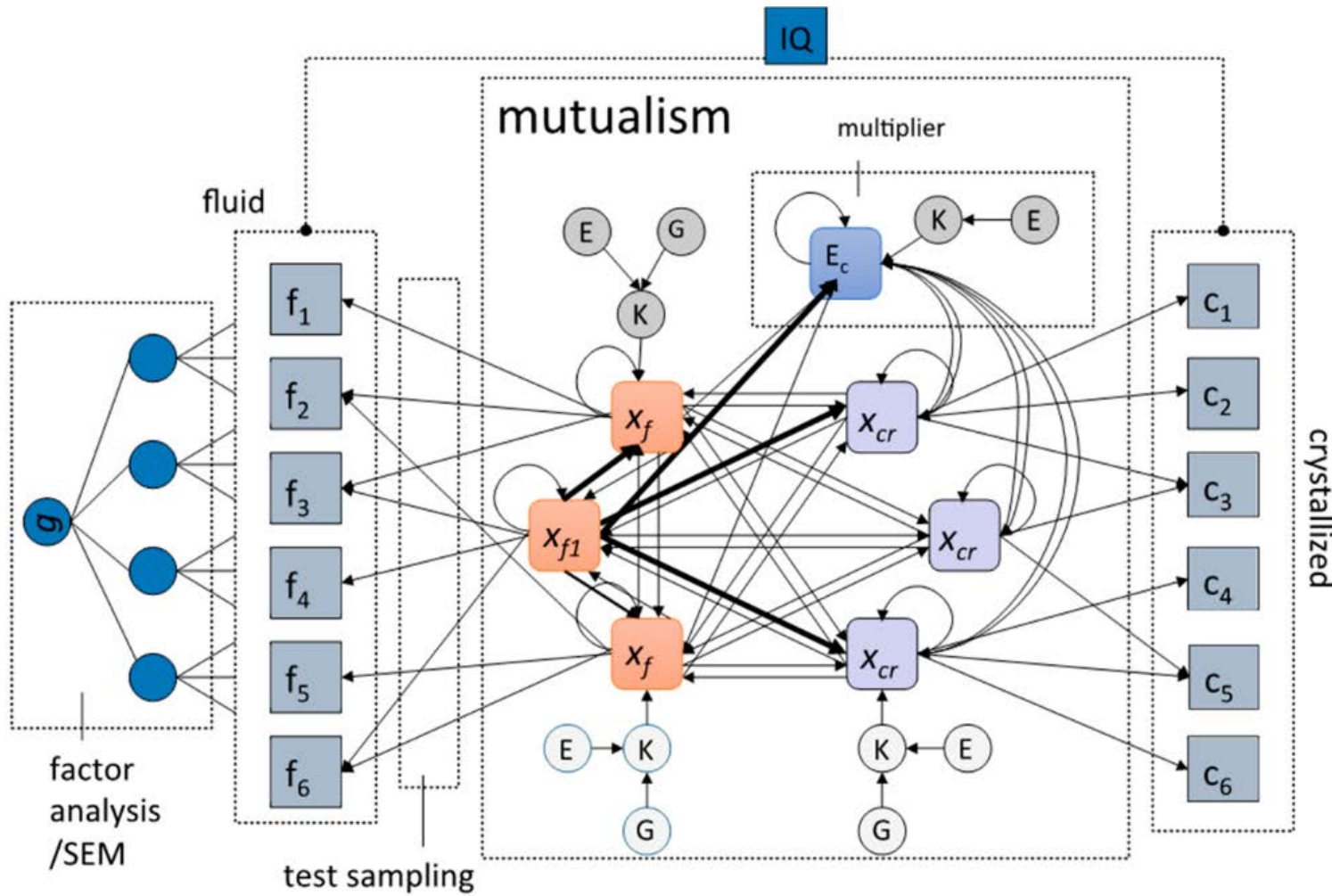
**EF & g showing minimal overlap at genetic variant and biological pathways levels, suggesting that EF is genetically separable from g**



# A NOVEL FRAMEWORK FOR DERIVING BIOLOGY- INFORMED STRUCTURE OF COGNITION

A NETWORK-BASED APPROACH





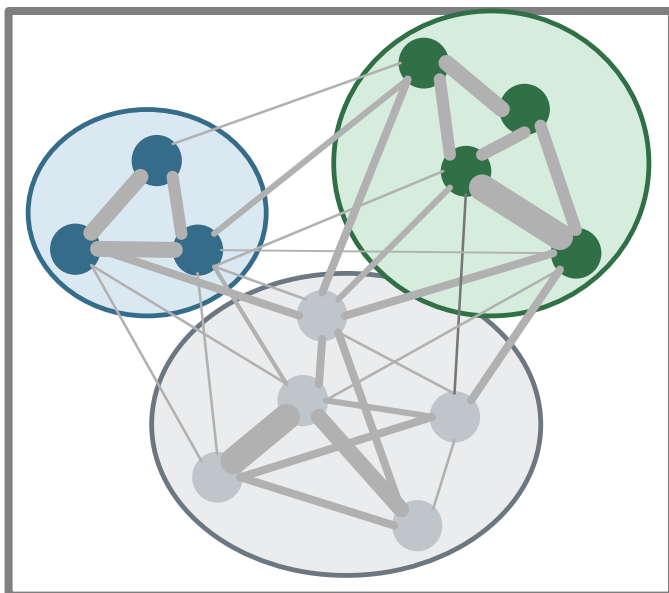
# A UNIFIED MODEL OF GENERAL INTELLIGENCE

Figure from (Van Der Maas, Kan et al. 2017)

# A NOVEL NETWORK-BASED FRAMEWORK

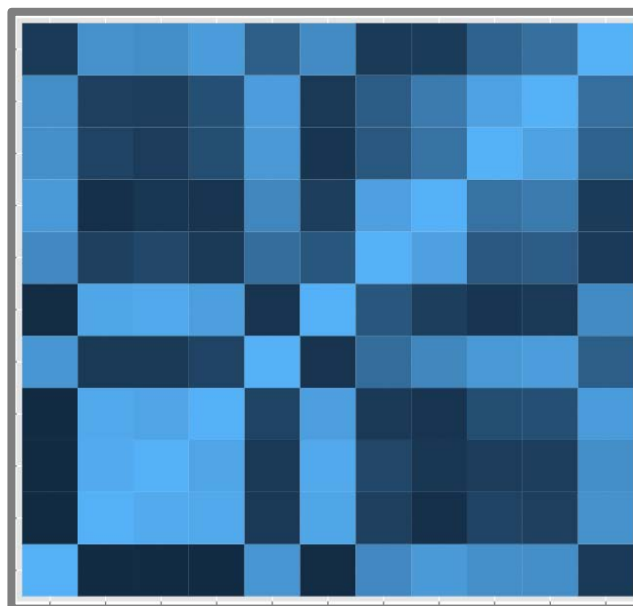


**Network modeling of cognitive behaviour**



**Genetic markers of basic units of cognitive behaviour**

Genetic markers (SNPs)



Sub-components of cognition



**Biology-informed assessments**



- **Biology-informed structure of cognitive functioning**



- **Better understanding of molecular mechanisms involved**



- **Biology-informed cognitive assessment battery**

# ACKNOWLEDGEMENTS

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