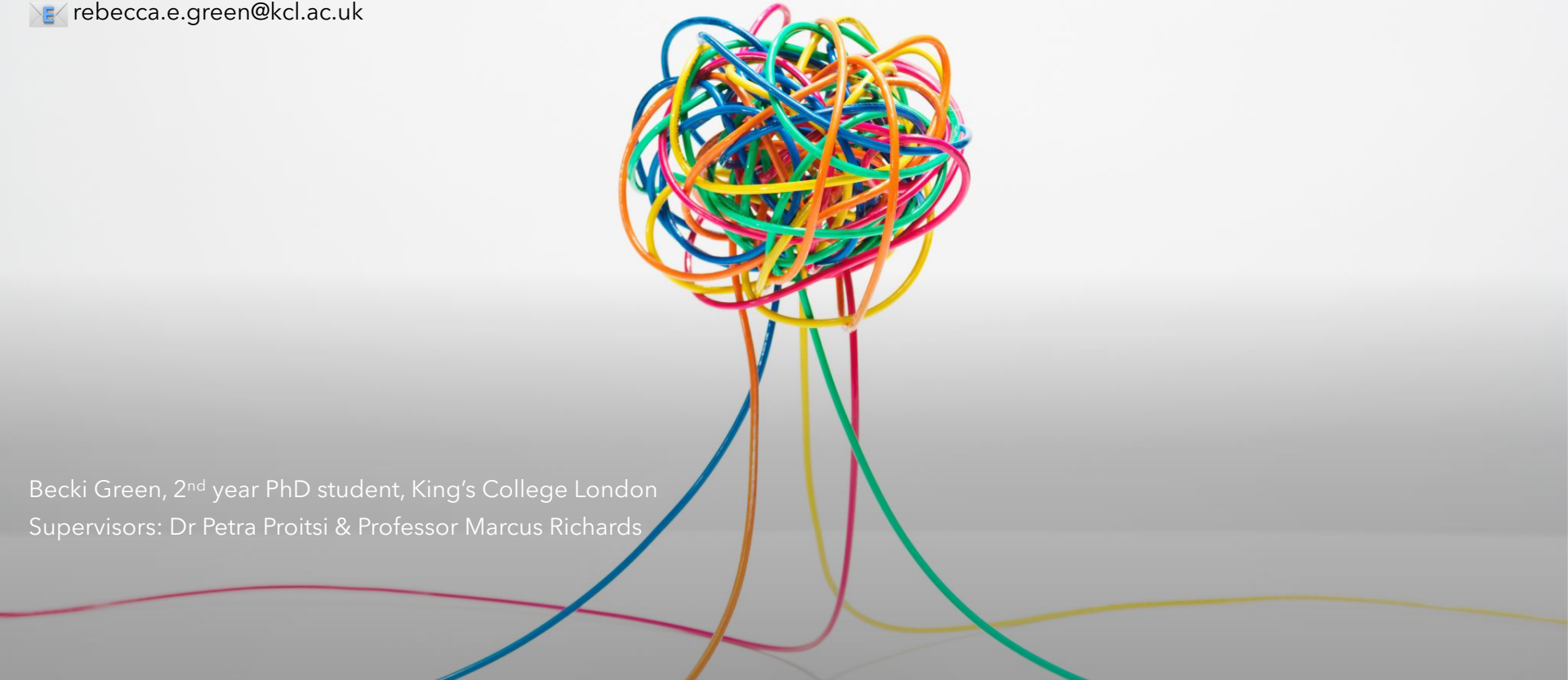
INVESTIGATING THE USE OF METABOLITES AS MARKERS OF EARLY COGNITIVE CHANGES RELEVANT TO DEMENTIA: A LIFE COURSE PERSPECTIVE

becki_e_green

rebecca.e.green@kcl.ac.uk



Becki Green, 2nd year PhD student, King's College London

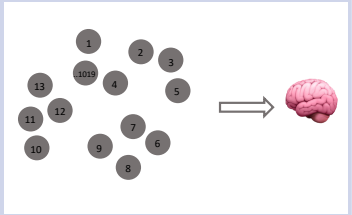
Supervisors: Dr Petra Proitsi & Professor Marcus Richards

BACKGROUND

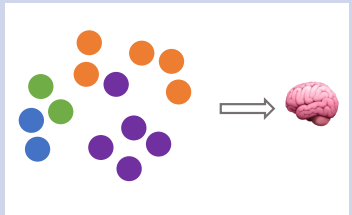
- Metabolites = intermediates and products of biological events
- **Modifiable, accessible, holistic**
- Relevant, but..
- Small studies, life course factors?

MRC 1946 British Birth Cohort Study (n=1740)

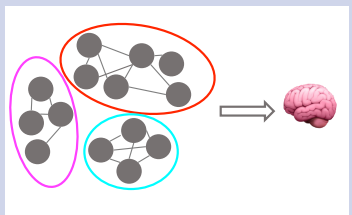
1) Identify single metabolites associated with cognitive outcomes at baseline and 5-9 years later



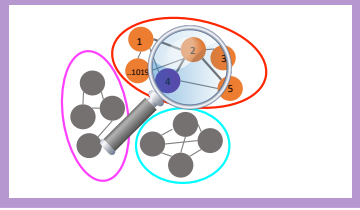
2) Identify pathways associated with cognitive outcomes at baseline and 5-9 years later



3) Identify modules associated with cognitive outcomes at baseline and 5-9 years later



4) Integrate results to reveal key drivers and pathways



→
Life course factors

kg/m²

(Age 15)

SES

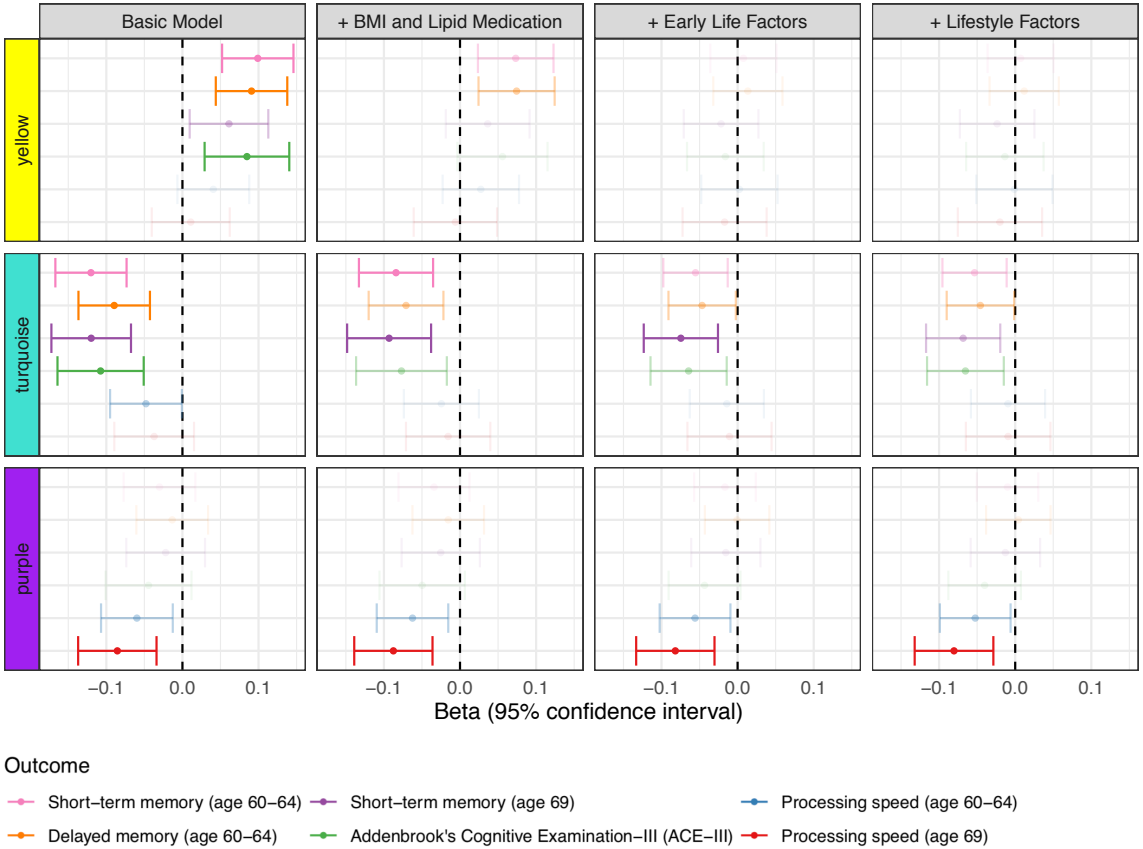
KEY RESULTS

- 155 metabolites, 10 pathways, 5 modules
- 35 key drivers for further study
- Distinct life course patterns…

Fully explained relationships: yellow (sphingolipids)

Partially independent relationships: cyan (vitamin A and C metabolites), turquoise (methionine metabolism and modified amino acids + nucleotides).

Independent relationships: purple (medium and long-chain acylcarnitines)



CONCLUSIONS

- Largest metabolomics study to date on cognitive function and decline
- Used a comprehensive design, illuminating metabolites and pathways for further study
- Life course approach revealed relationships we may otherwise have missed
- *Do metabolites mediate associations between life course factors and cognitive outcomes?*
- *Do these metabolites lie in the causal pathway?*

THANK YOU!

I would be very grateful for any questions or feedback and would love to hear from you via email or over twitter!

becki_e_green

rebecca.e.green@kcl.ac.uk

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