

The Phenotypic Expression of Neurodevelopmental CNVs

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Plan

Cognition

Background

Methods

- CNV calling, CNV selection, annotation
- Cognitive tests and educational outcomes

Results

- Cognitive tests
- Educational outcomes

Depression

Background

Methods

- Depression phenotypes

Results

- Depression
- Mediation

Background

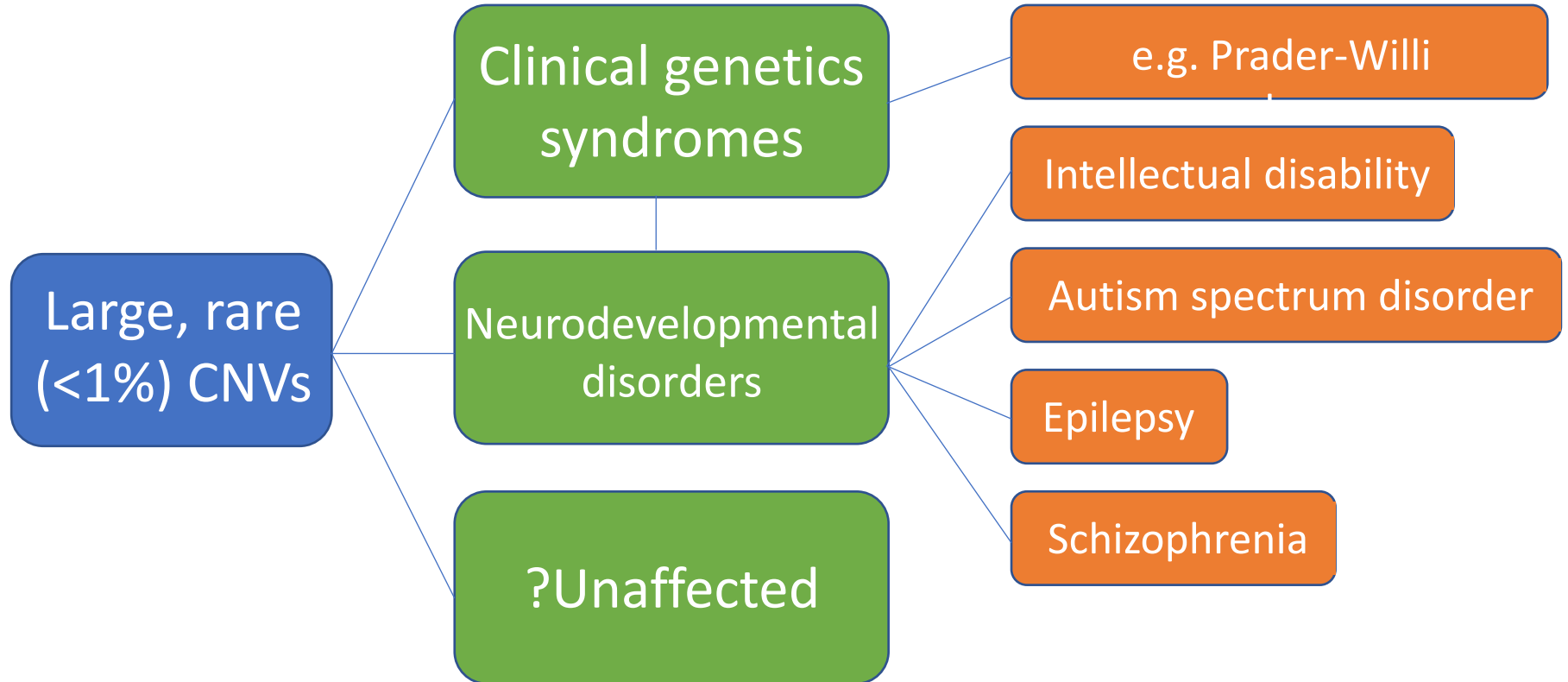


Background

Methods

Results

Discussion



Background Cognition

An aerial photograph of a vast landscape under a clear blue sky. The foreground and middle ground are dominated by rolling hills and valleys. On the left, there are large, dense coniferous forests. The central and right-hand hills are covered in a mix of green grasslands and smaller, more scattered trees. A winding river or stream is visible in the lower right quadrant, flowing through a valley. In the far distance, more hills and a body of water, possibly a lake or a wide river, can be seen under the bright sky. The overall scene is a natural, scenic view of a rural or semi-rural area.

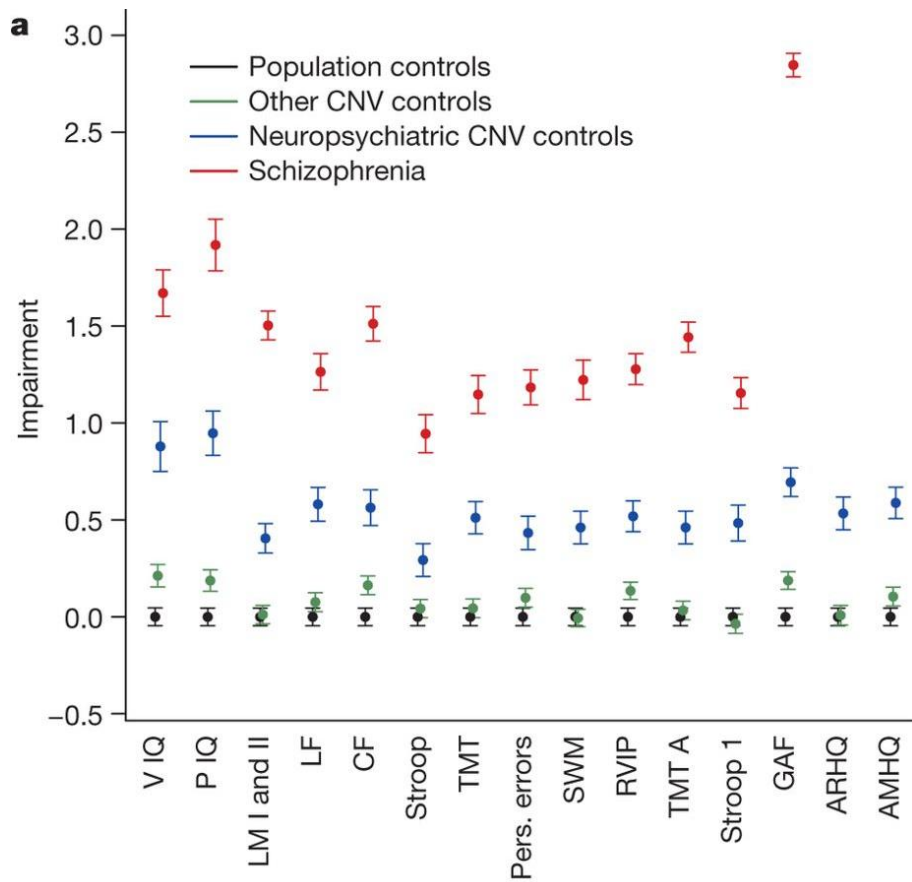
Background

144 carriers of 11 CNVs
Impaired cognitive performance
Intermediate between non-carriers and individuals with schizophrenia

Methods

Results

Discussion





56 CNV carriers

Association with educational attainment

Methods

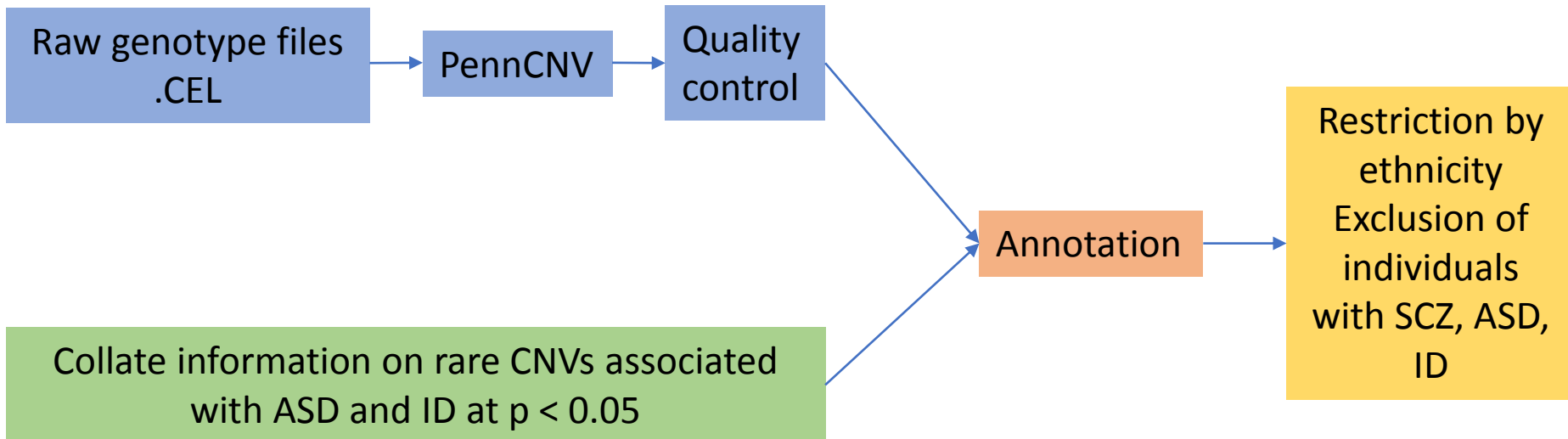


Background

Methods

Results

Discussion



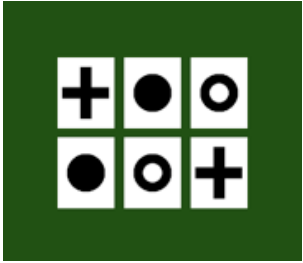
Background

Methods

Results

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Pairs Matching Test



episodic memory

Reaction Time Test

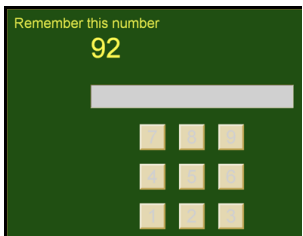


simple processing speed

Fluid Intelligence Test

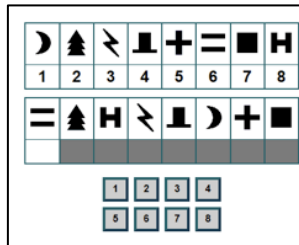
Reasoning and problem solving

Digit Span Test



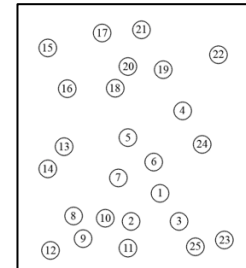
numeric working memory

Symbol Digit Substitution Test



complex processing speed

Trail Making Tests A & B

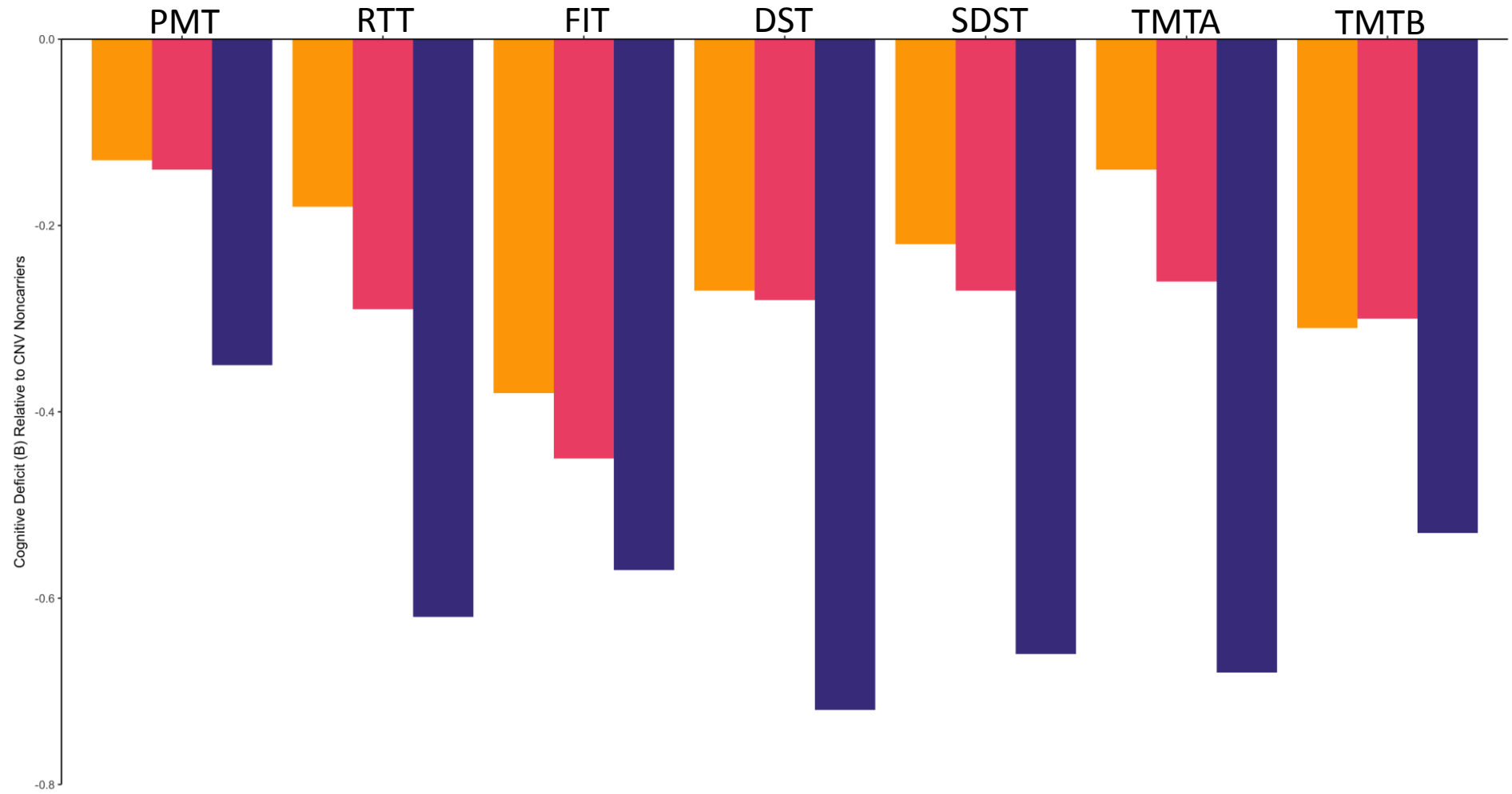


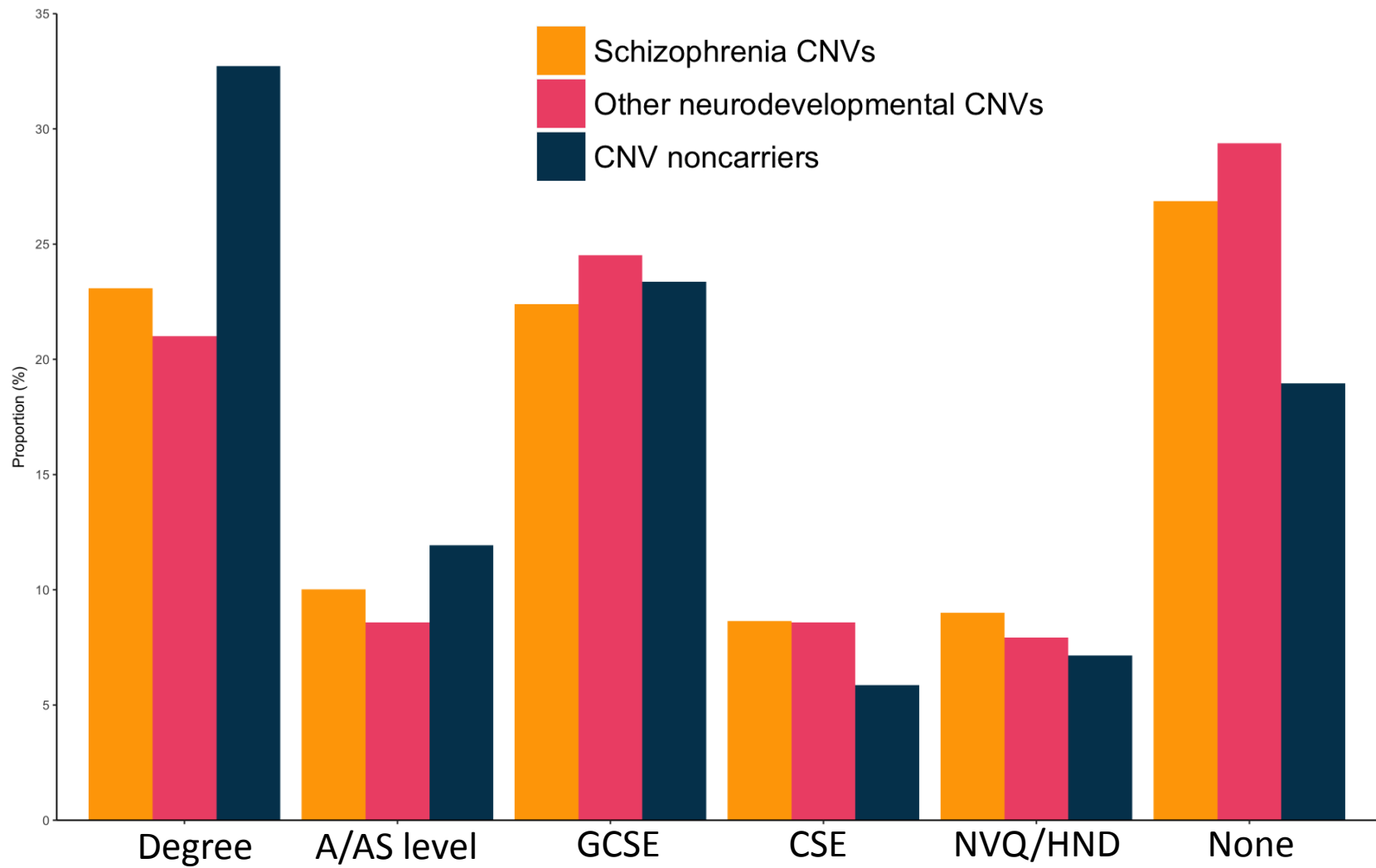
visual attention

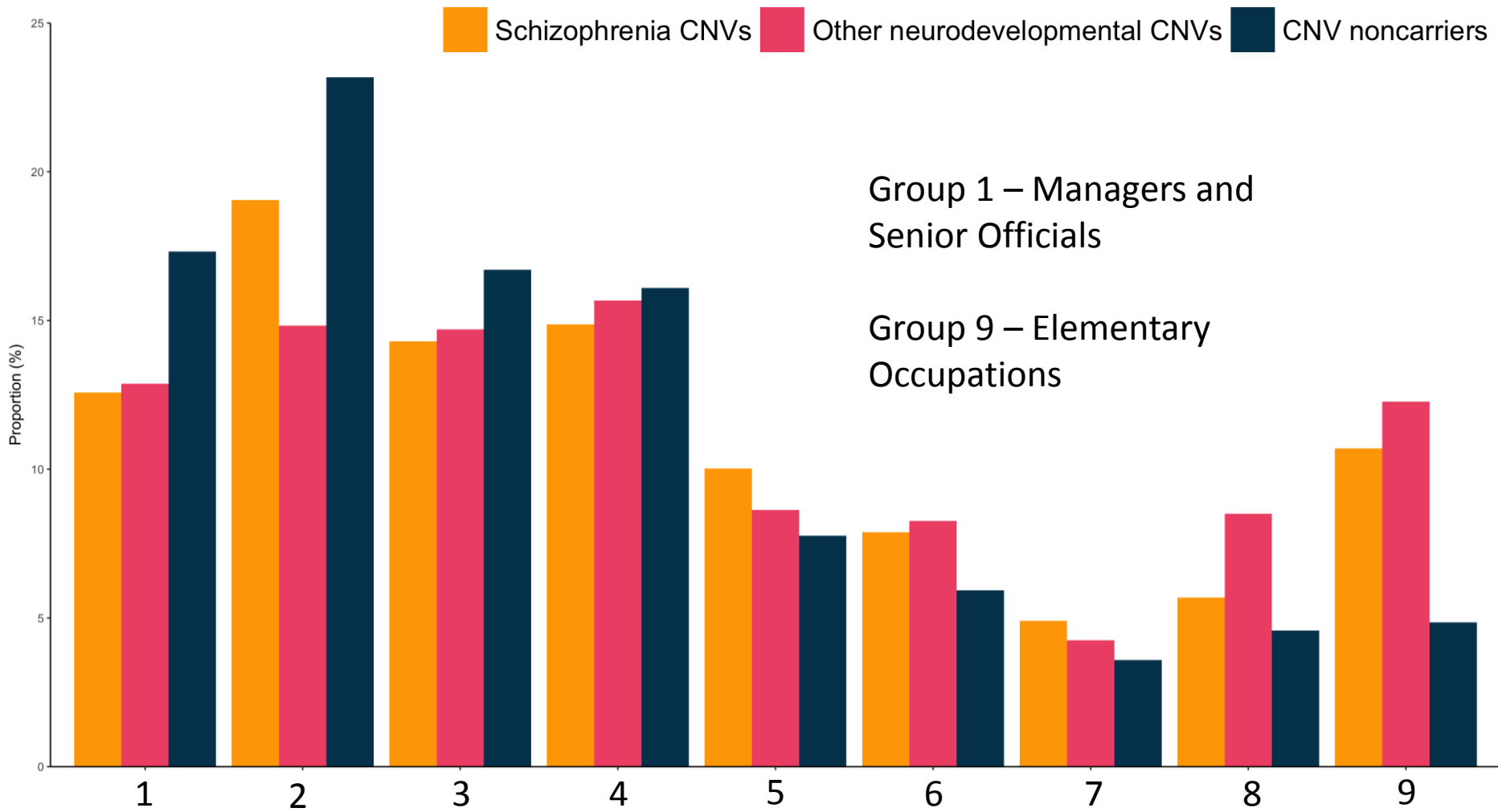
Results



Schizophrenia CNVs Other neurodevelopmental CNVs Schizophrenia







Schizophrenia CNVs Other neurodevelopmental CNVs CNV noncarriers

Group 1 – Managers and Senior Officials

Group 9 – Elementary Occupations

Depression



Background Depression

An aerial photograph of a vast landscape featuring rolling hills, dense evergreen forests, and a winding river. The terrain is a mix of green fields and brownish, possibly deforested or rocky areas. The sky is a clear, bright blue. The text 'Background Depression' is overlaid in a large, white, sans-serif font, centered in the upper half of the image.

Associations reported with depression:

- 5q35.1 dup (1,693 cases) – failed to replicate
- Burden of deletion CNVs. Re-analysis - no association (3,106 cases)

Nominally significant findings for particular phenotypic features:

- Treatment resistant depression (452 cases)
- Suicide attempts (189 cases)
- Treatment response (1,565 cases)

Glessner et al, 2010. Degenhardt et al, 2012. O'Dushlaine et al, 2014. Rucker et al, 2013.
Rucker et al, 2016. Perlis et al, 2012. Tansey et al, 2014.

Methods



Background

Methods

Results

Discussion

Depression Phenotypes

Self-reported depression

affected = 23,979

Self-reported depression,
antidepressant prescription

affected = 15,339

Hospital discharge diagnosis

affected = 11,169

Results



Background

Methods

Results

Discussion

OR (95% CI)

p

Primary analysis

Self reported depression

1.34
(1.19 – 1.49)

1.38×10^{-7}

Alternative depression phenotypes

Self reported depression,
antidepressant prescription

1.42
(1.25 – 1.62)

1.18×10^{-7}

Hospital discharge diagnosis

1.51
(1.30 – 1.75)

2.95×10^{-8}

1q21.1 dup

n	173
OR	2.17
95% CI	1.34 – 3.36
p	9.08×10^{-4}

**Prader Willi syndrome dup**

n	17
OR	8.14
95% CI	2.77 – 21.69
p	4.61×10^{-5}

**16p11.2 dup**

n	124
OR	2.65
95% CI	1.53 – 4.31
p	2.04×10^{-4}



Nominal association:

NRXN1 del

3q29 del

8p23.1 dup

16p13.11 del

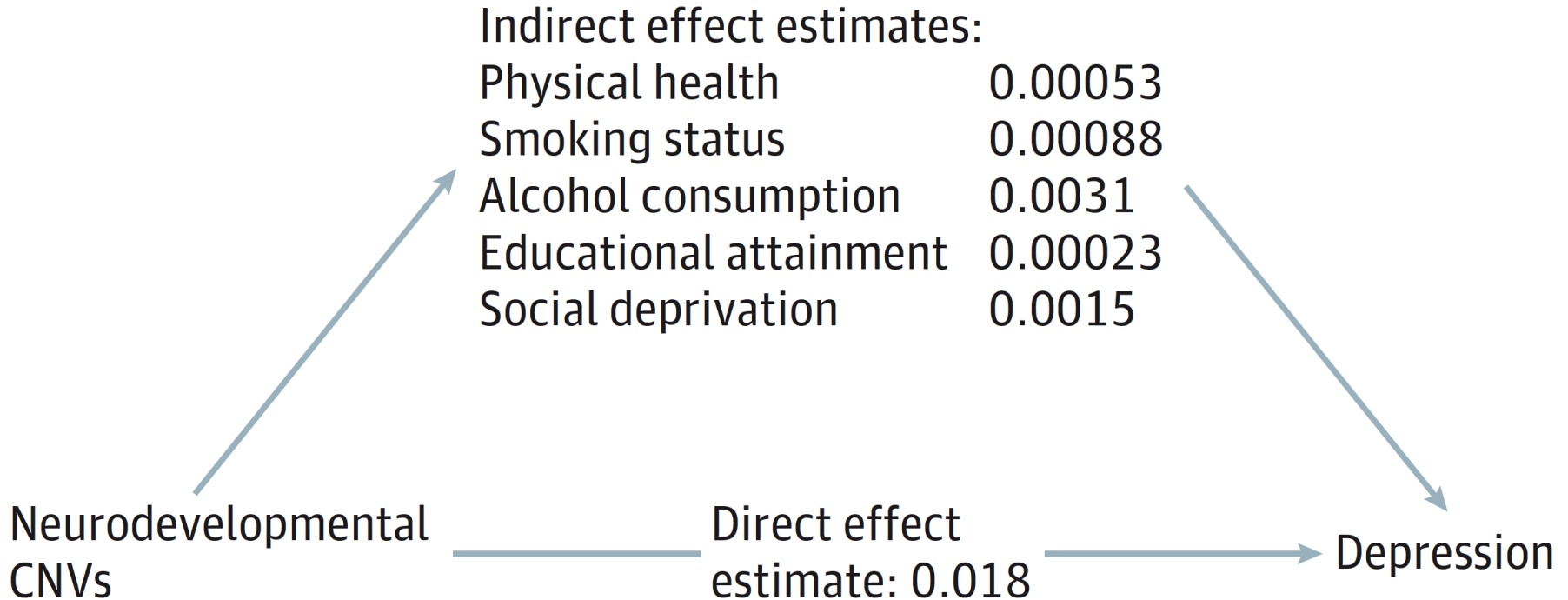
22q11.2 dup

Background

Methods

Results

Discussion



Background

Methods

Results

Discussion

Cognition

Impaired performance on
cognitive tests

Lower educational attainment

Lower occupational
attainment

Depression

Increased risk of depression

Key References from Our Group

Kendall et al, 2017. Cognitive performance among carriers of pathogenic copy number variants: analysis of 152,000 UK Biobank subjects. *Biol Psychiatry* 82(2), 103 – 110.

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References

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