

# The Danish High Risk and Resilience Study - VIA 7, VIA 11, and VIA 15

Children born to parents with schizophrenia,  
bipolar disorder and none of these disorders

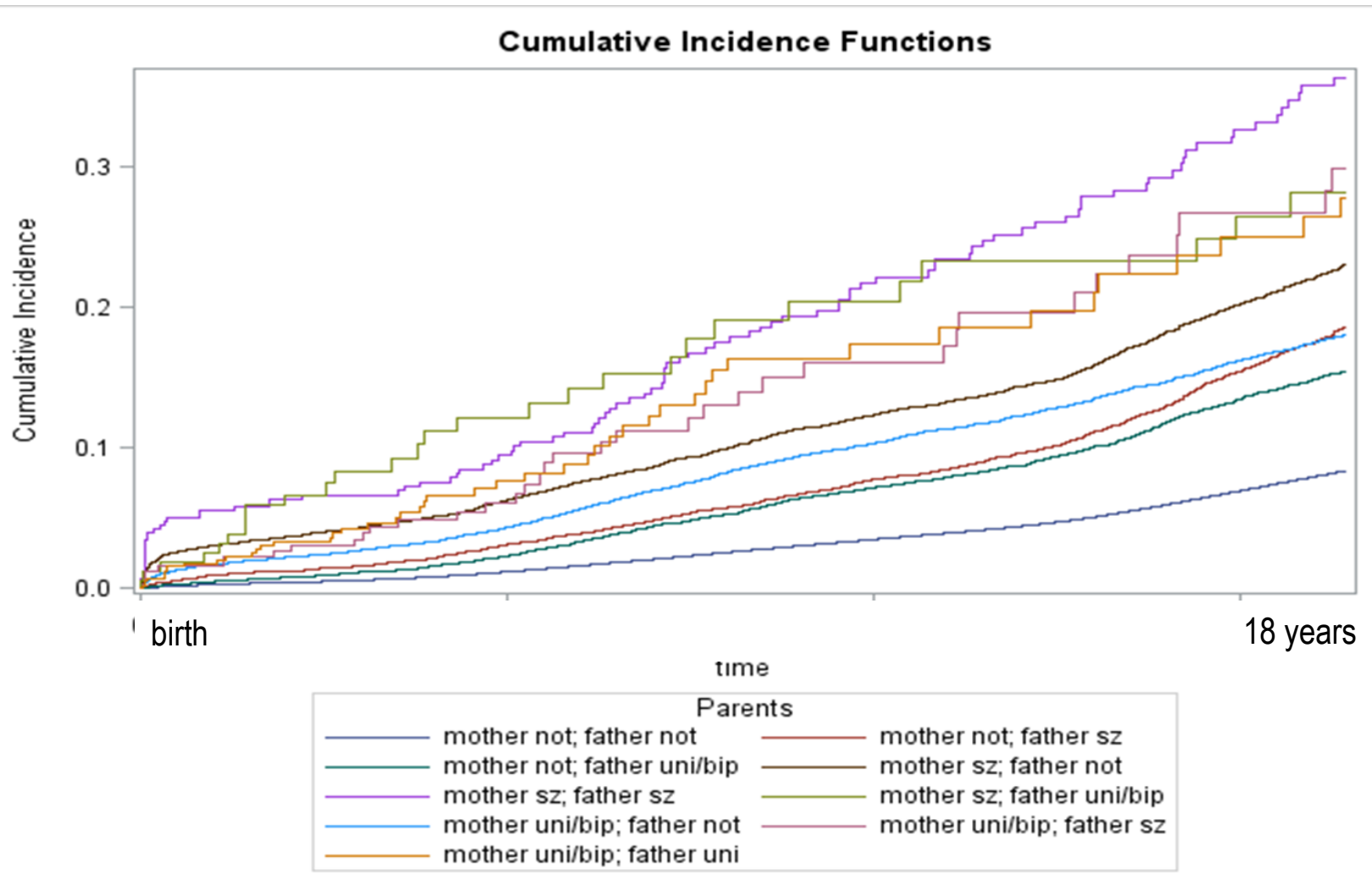
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VIA 15

- Dr Nordentoft has nothing to disclose

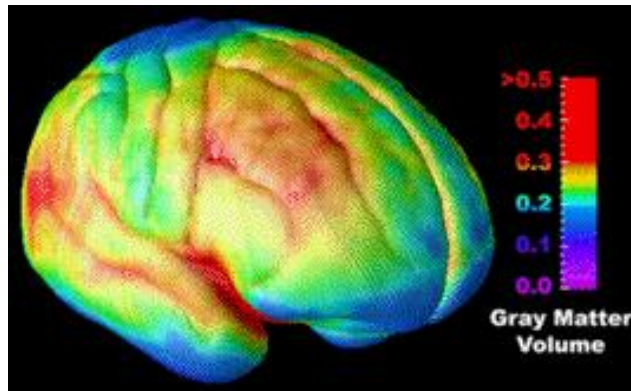
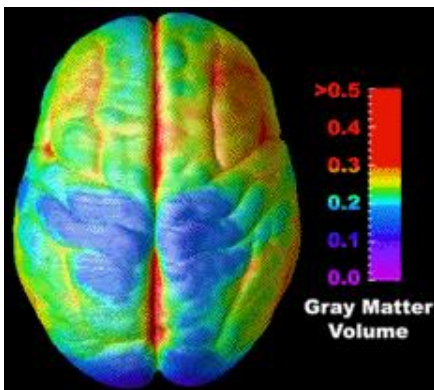
# Enriched sample: Cumulative incidences of any child psychiatric disorder, age 0-18



# Educational achievement and graduation of child according to parent's diagnoses and gender of ill parent.

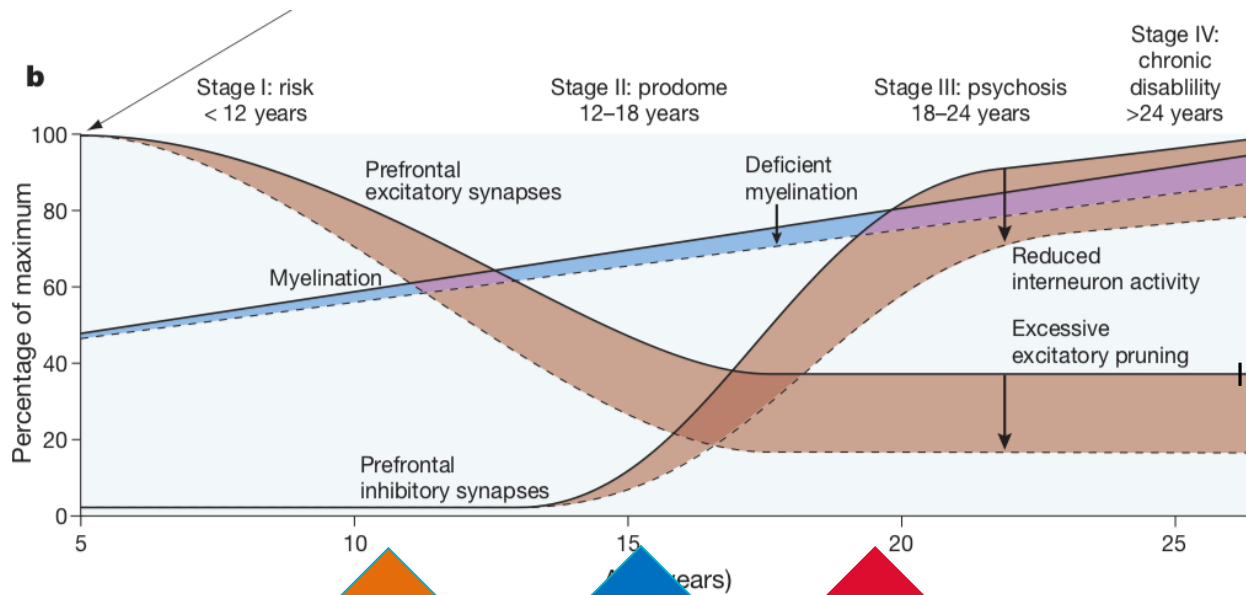
	Bipolar disorder	Bipolar disorder	Schizophrenia	Schizophrenia
	Mother	Father	Mother	Father
<b>High GPA 8 – 12</b>	OR=1.04 (0.93-1.15)	OR=1.02 (0.90-1.14)	OR=0.73 (0.64-0.84)	OR=0.71 (0.63-0.81)
<b>Medium GPA 4 – 8</b>	1 (reference)	1 (reference)	1 (reference)	1 (reference)
<b>Low GPA -3 – 4</b>	OR=1.14 (1.02- 1.28)	OR=0.95 (0.83-1.08)	OR=1.39 (1.24-1.55)	OR=1.71 (1.54-1.90)
<b>No graduation</b>	OR=1.64 (1.42-1.88)	OR=1.16 (0.97 - 1.38)	OR=2.32 (2.05-2.64)	OR=2.55 (2.24-2.86)

# Background: Patterns of brain development



age: 5 → 20

Gogtay et al., PNAS, 2004



Insel, Nature, 2010



# The Danish High Risk and Resilience Study VIA 15

## Organization



Nordentoft  
PCK, RHP  
UCPH



Mors  
MHC  
AaU



Thorup  
CAP/RHP  
UCPH



Østergaard  
CFIN  
AaU



Siebner  
DRCMR  
UCPH



Ekstrøm  
Biostat  
UCPH

- International collaborators
- 5 senior researchers
- 4 post docs
- 22 PhD-students
- Many research assistants

# Organization

The Danish High Risk and Resilience Study-VIA 19  
PI-executives: Merete Nordentoft, Ole Mors, Anne Thorup  
PI-group: PI-executives and Aja Greve and Nicoline Hemager  
Project group: PI-group and Hartwig Siebner, Leif Østergaard, Claus Ekstrøm,  
Carsten Hjorthøj

International  
advisory board  
Rudolf Uher  
Manon Hileger  
Dost Öngür

WP1: Project management.  
WP-leaders:  
Merete Nordentoft and Ole Mors

WP2: Fourth wave of clinical  
assessment in The VIA 19 study  
WP-leaders:  
Anne Thorup, Aja Greve and Nicoline  
Hemager

WP3: Brainmap, MRI, fMRI,  
EEG/MEG  
WP-leaders:  
Hartwig Siebner, Leif  
Østergaard

WP4: Physical health, sleep and  
diurnal rhythm  
WP-leaders:  
Merete Nordentoft, Kasper  
Lykkegaard

WP 5: Prediction model development  
WP leaders:  
Claus Ekstrøm and Carsten Hjorthøj

WP 6: Dissemination and Communication.  
WP-leaders:  
Anne Thorup and Merete Nordentoft

## 1) Map early disease processes of schizophrenia and bipolar disorder

Brain structure and function (MR, EEG, MEG)

Psychopathology

Cognition and motor functioning

Sleep disturbances (Polysomnography)

Substance use, self-harm, risk behavior

- High quality data on all outcomes
- Largest sample in the world
- Only representative sample in the world
- Only sample with all at the same age and repeated follow-ups
- High quality information on genetic and environment exposures

Possibilities for analyses of trajectories and causal and mediating factors for main outcomes: brain deviances, neurocognition and psychopathology

## 2) Identify possibilities for early intervention



# The Danish High Risk and Resilience Study VIA 15

The 522 children were **extracted from Danish registers.**

They constituted a **representative sample** of the total population, but non-participating parents had slightly worse prognosis e.g. higher percentage of smoking mothers. IPW didn't change results.

Falkenberg Kranz, SPPE, 2022



# The Danish High Risk and Resilience Study

## Sources of information



School teacher



Investigators observations

Information from multiple sources



Primary caregiver



The child



"Ill"/control parent



Homevisit

522 children

VIA 7

VIA 11

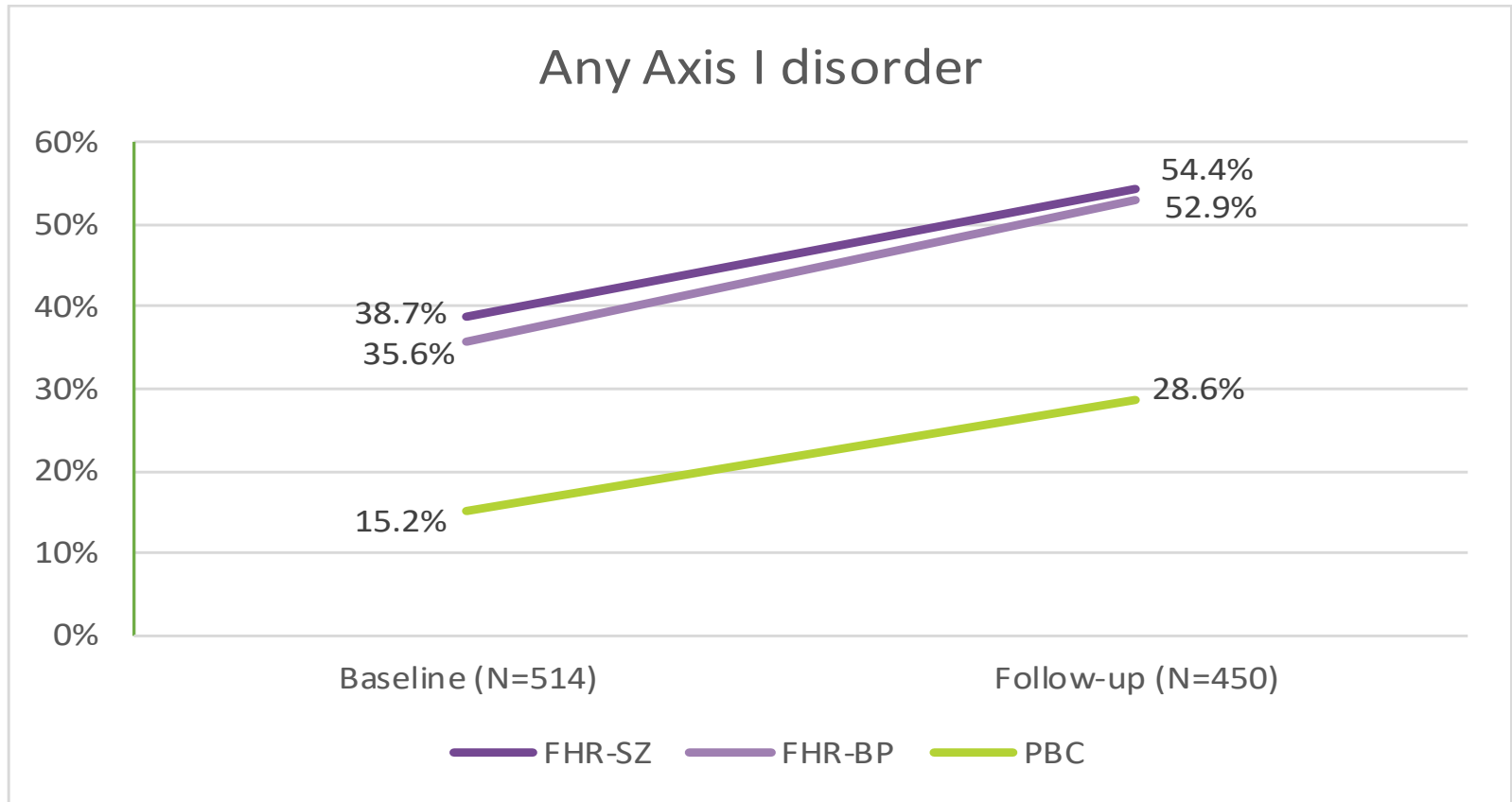
VIA 15

VIA 19

202 Familial High Risk Schizophrenia (FHR -SZ)	120 Familial High Risk Bipolar Disorder (FHR -BP)	200 Population Based Controls (PBC)
179 (88.6%) FHR -SZ	105 (87.5%) FHR -BP	181 (90.5%) PBC
XX FHR -SZ	XX FHR -BP	XX PBC
XX FHR -SZ	XX FHR -BP	XX PBC

VIA 15

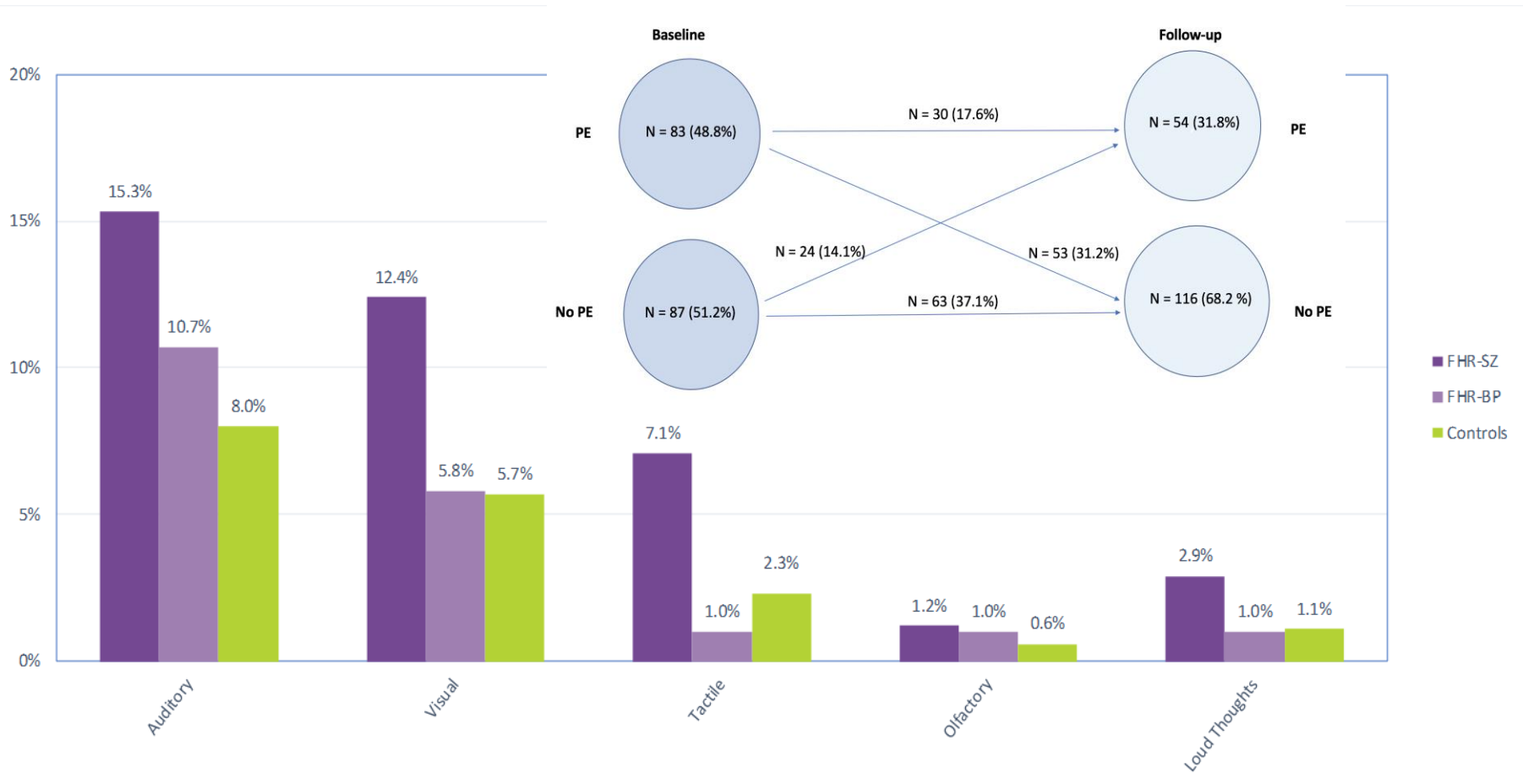
# Results from VIA 7 and VIA 11: Proportion with child psychiatric diagnosis



Ellersgaard et al, World Psychiatry 2018,  
Gregersen et al, JCCP 2022

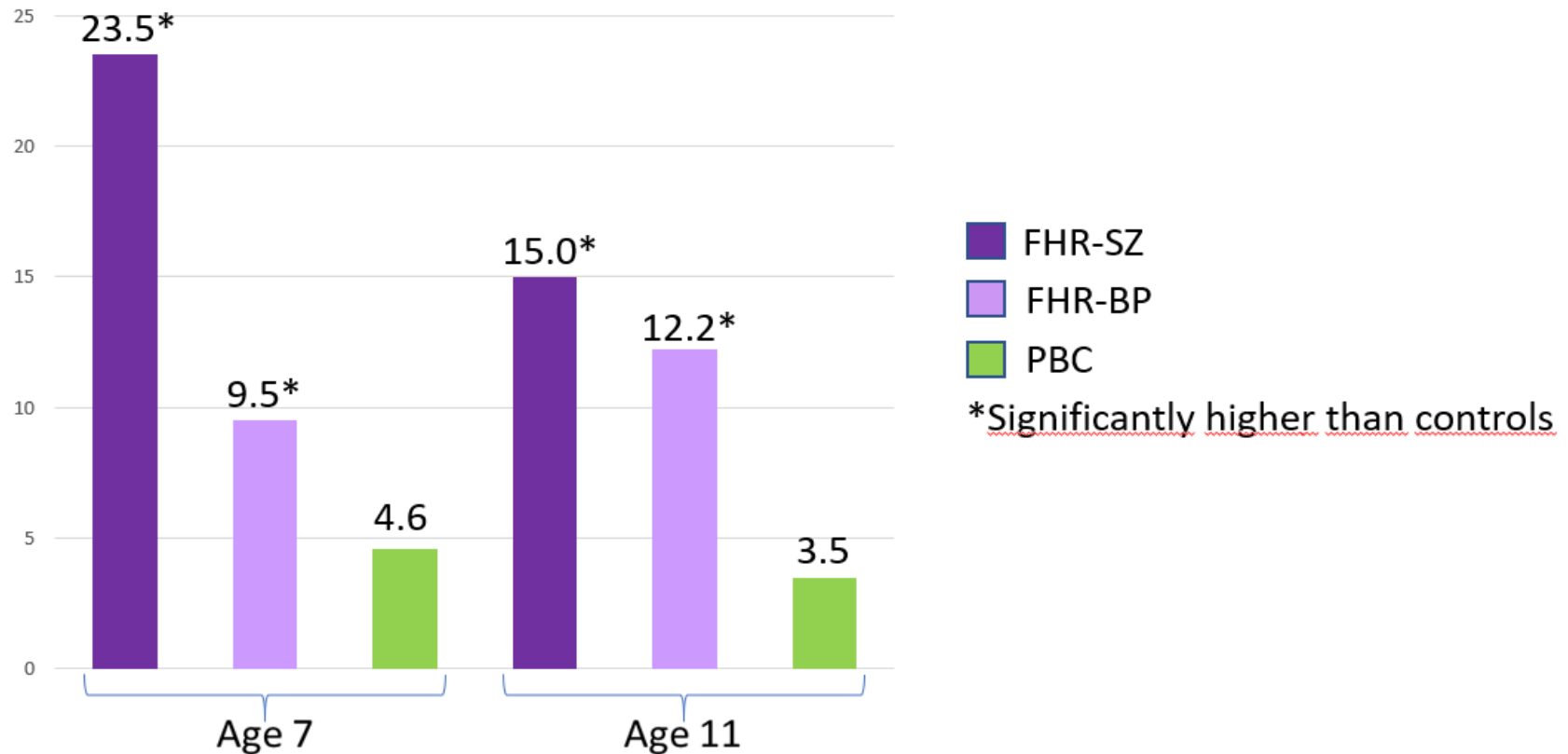
# Results from VIA 7 and VIA 11: Proportion with psychotic experiences

Figure 1a. FHR-SZ (N=170)



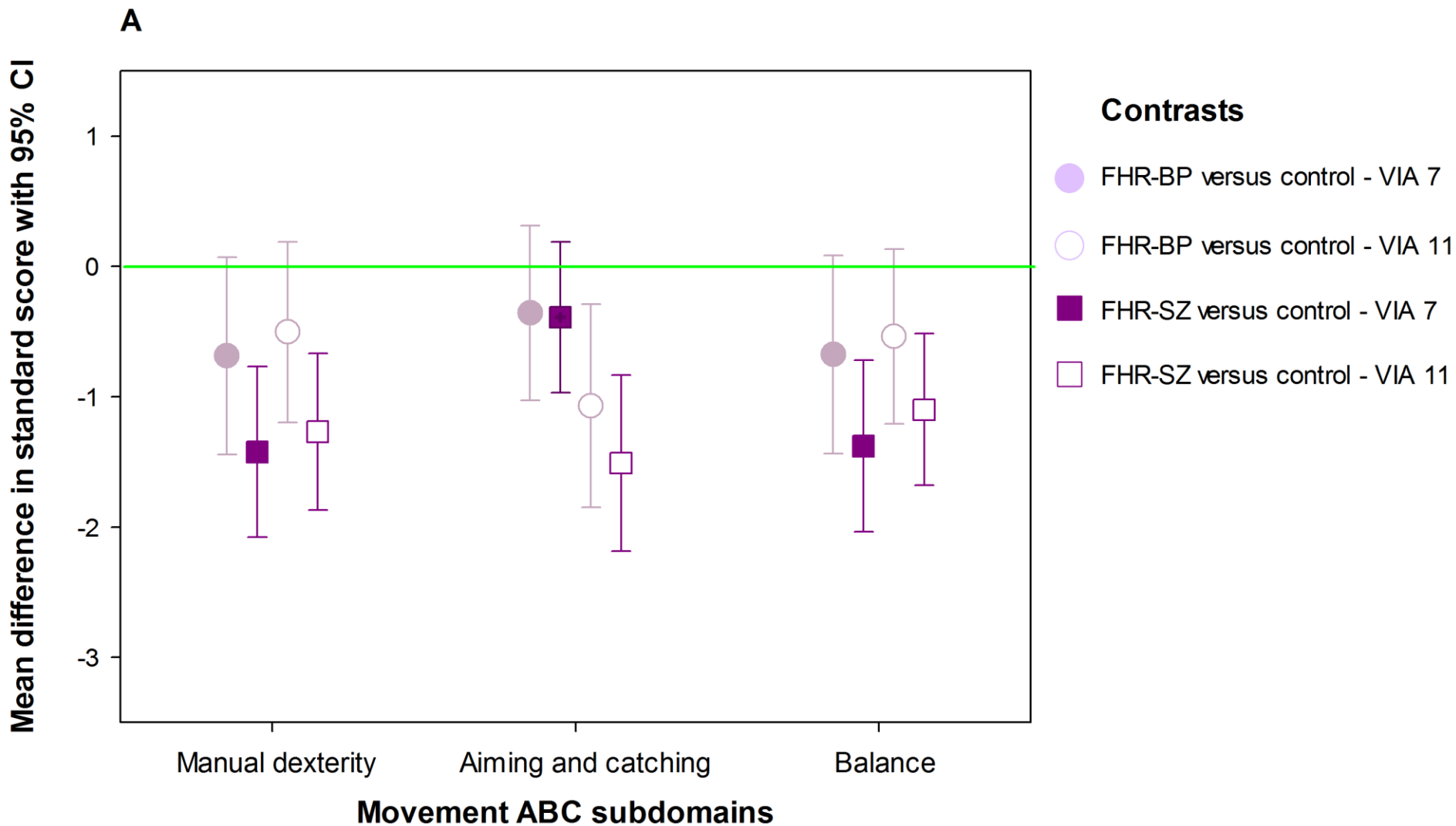
Ellersgaard et al, Sciz Res 2020,  
Gregersen, Am J Psych, 2022

# Results from VIA 7 and VIA 11: Proportion with inadequate HOME environment



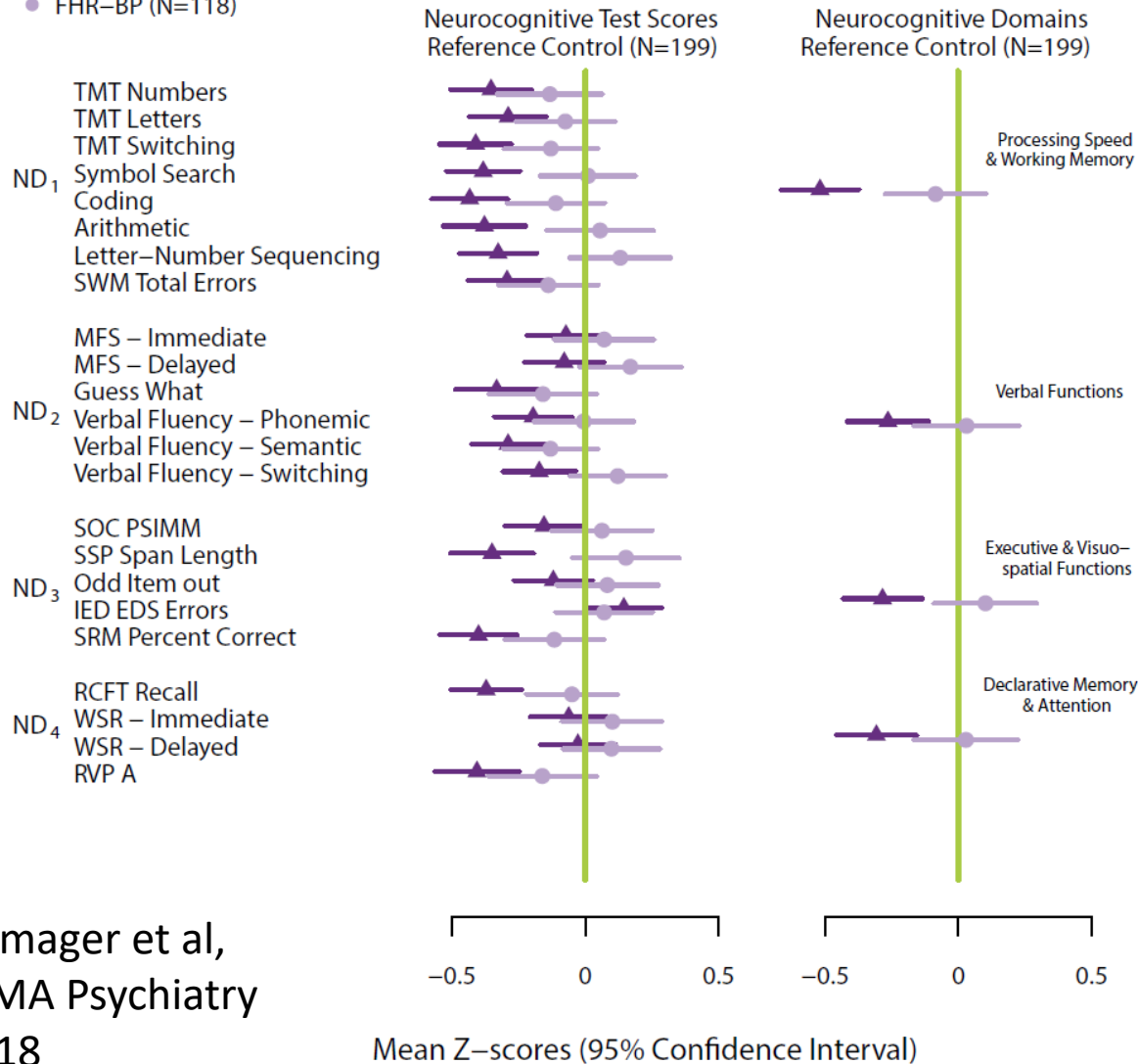
Gantriis. Acta Psych Scand 2019,  
Falkenberg Krantz, Psychological Medicine 2021

# Results from VIA 7 and VIA 11: Motor Functioning



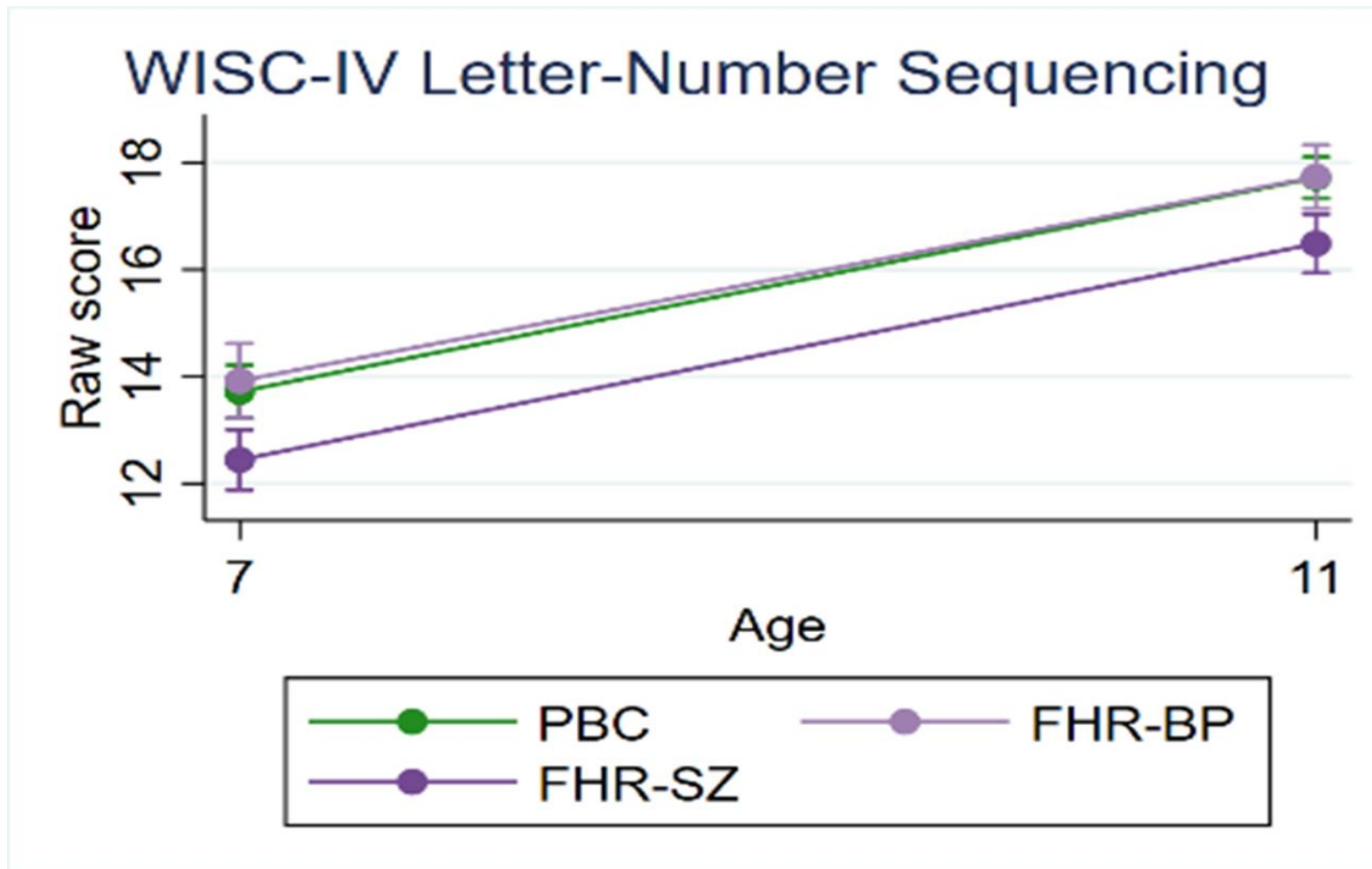
# Neurocognition – VIA 7

- ▲ FHR–SZ (N=197)
- FHR–BP (N=118)



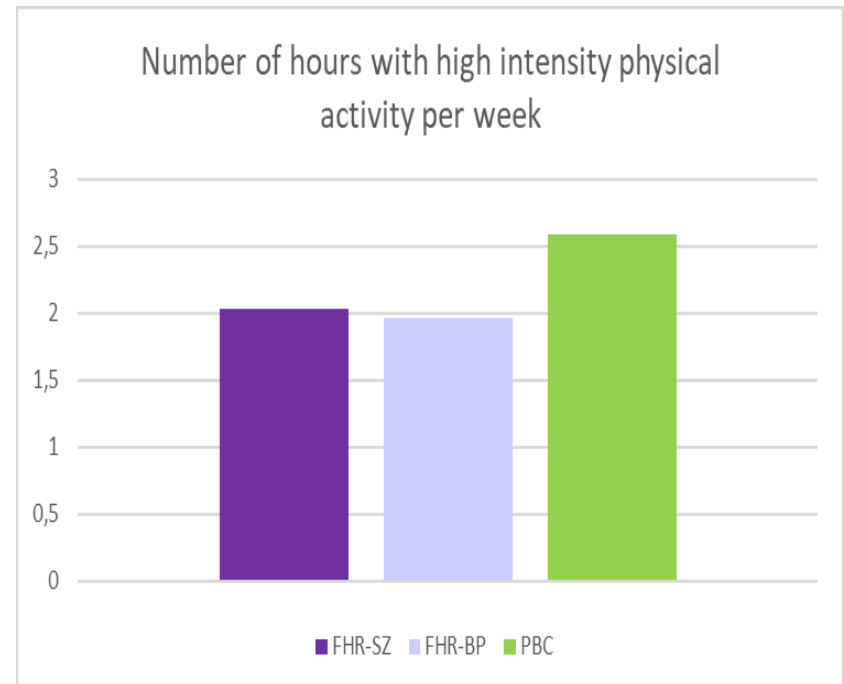
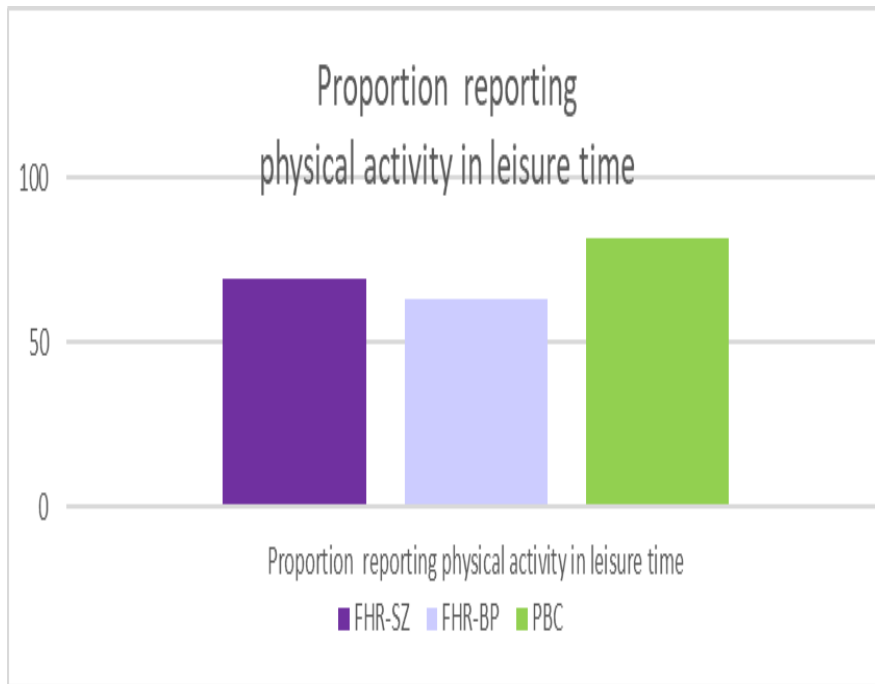


# Results from VIA 7 and VIA 11: Neurocognition



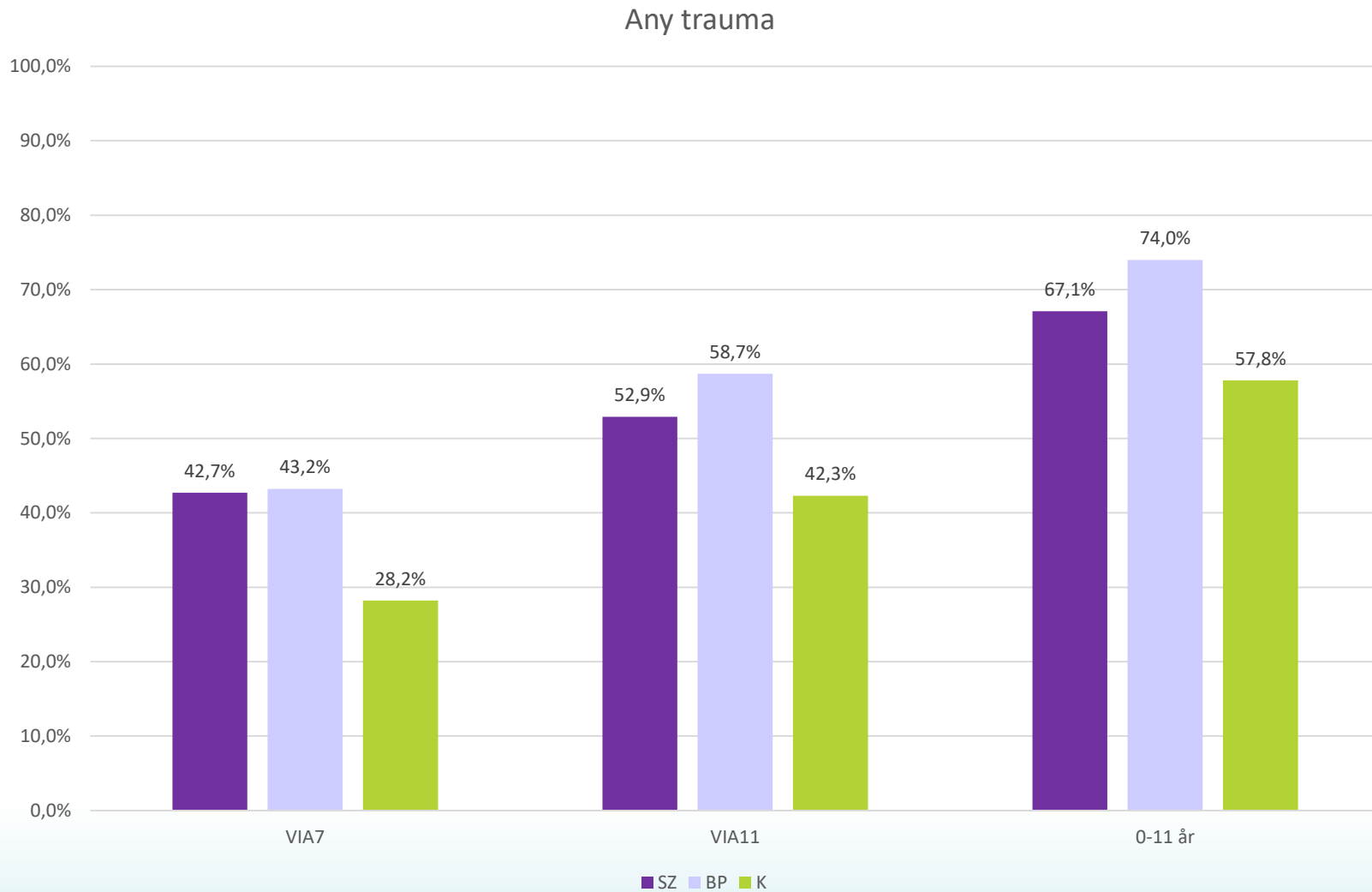
Hemager. JAMA Psych 2018  
Bruun Knudsen, JAMA Psych, 2022

# Results from VIA 11: Reporting physical activity and number of hours with high intensity physical activity

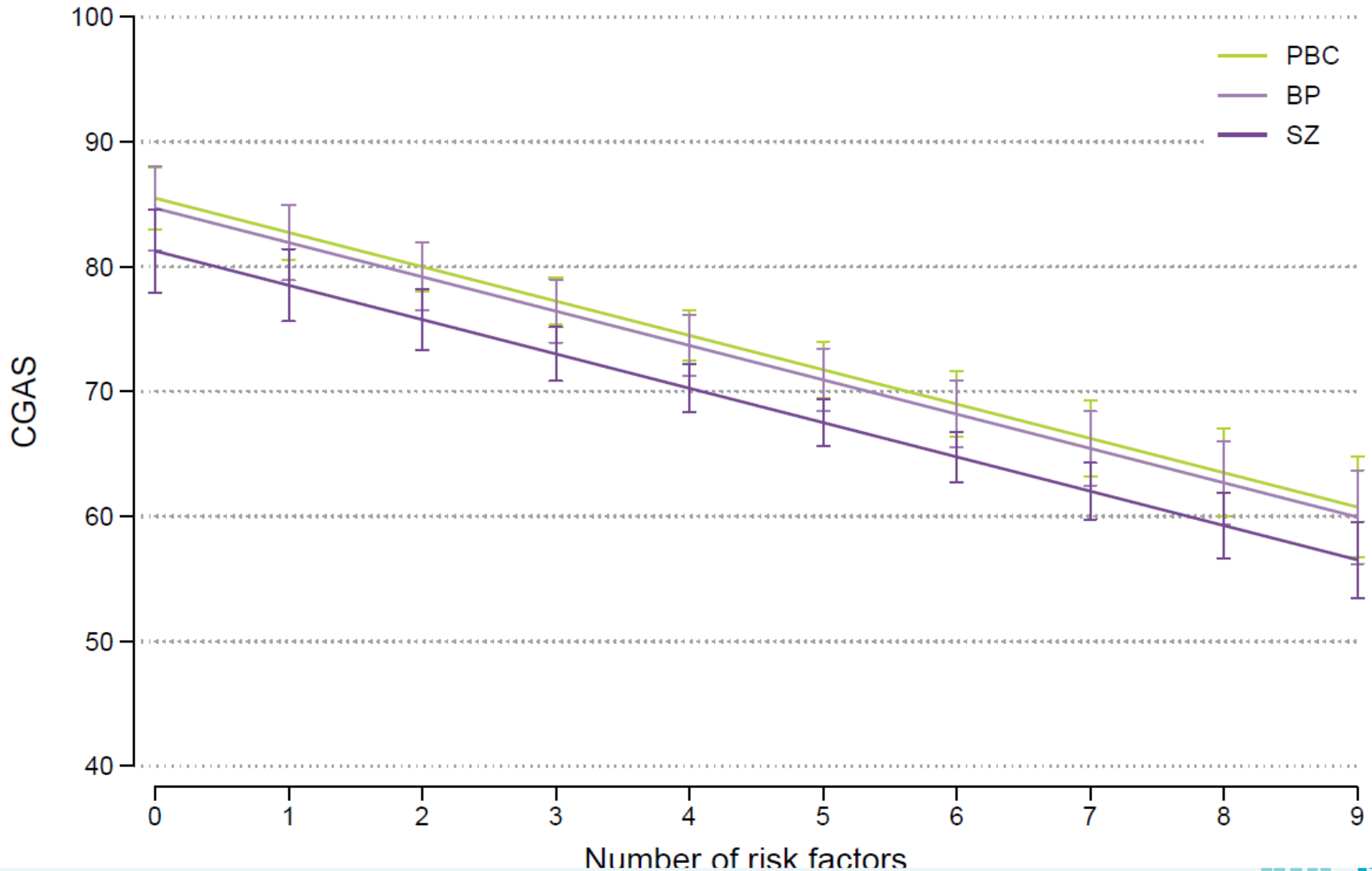


Søndergaard A. et al, Schizophrenia Bulletin Open 2021

# Proportion with any trauma, reported at age 7, 11 and lifetime

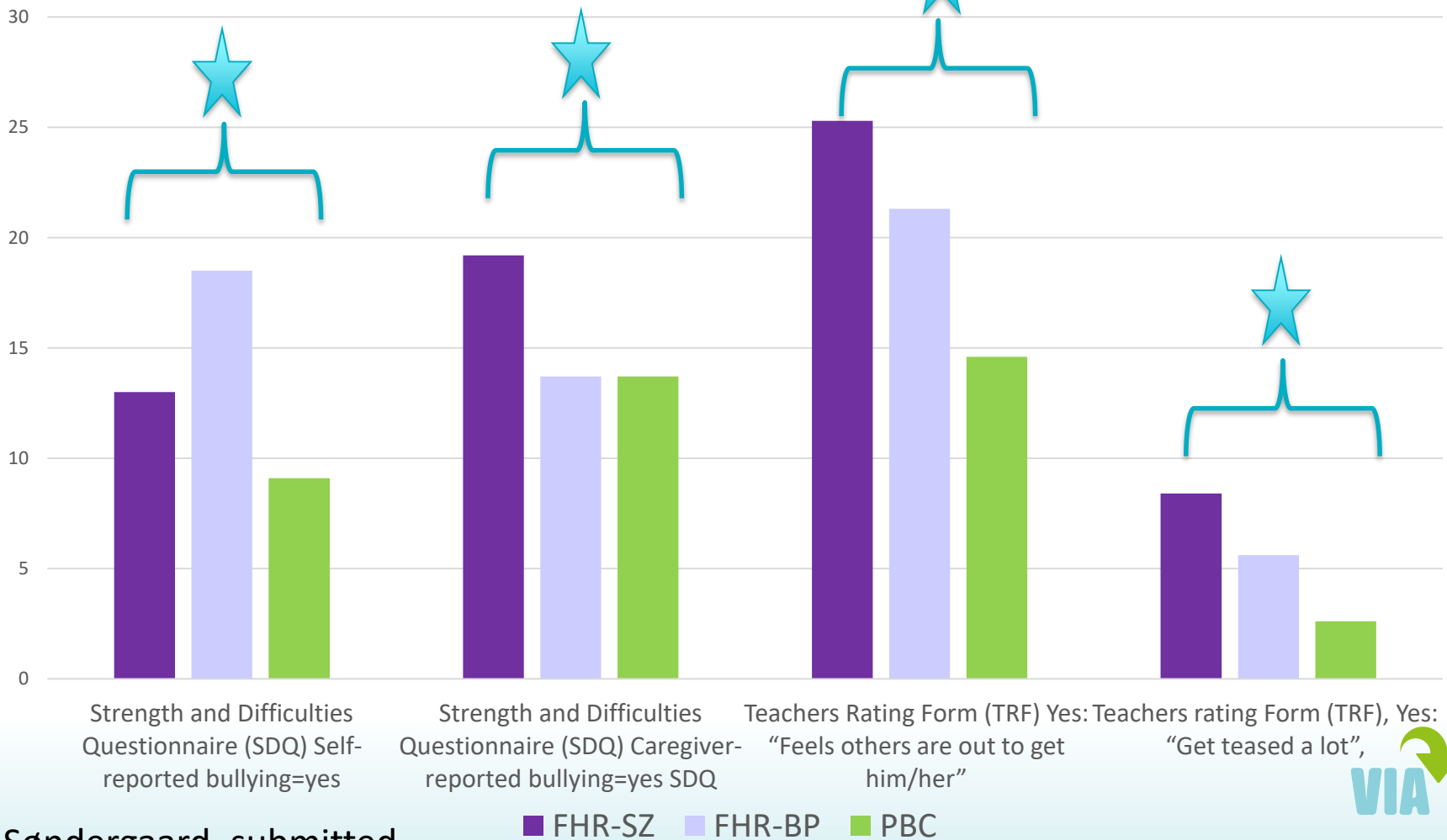


# Associations between early risk factors and functioning

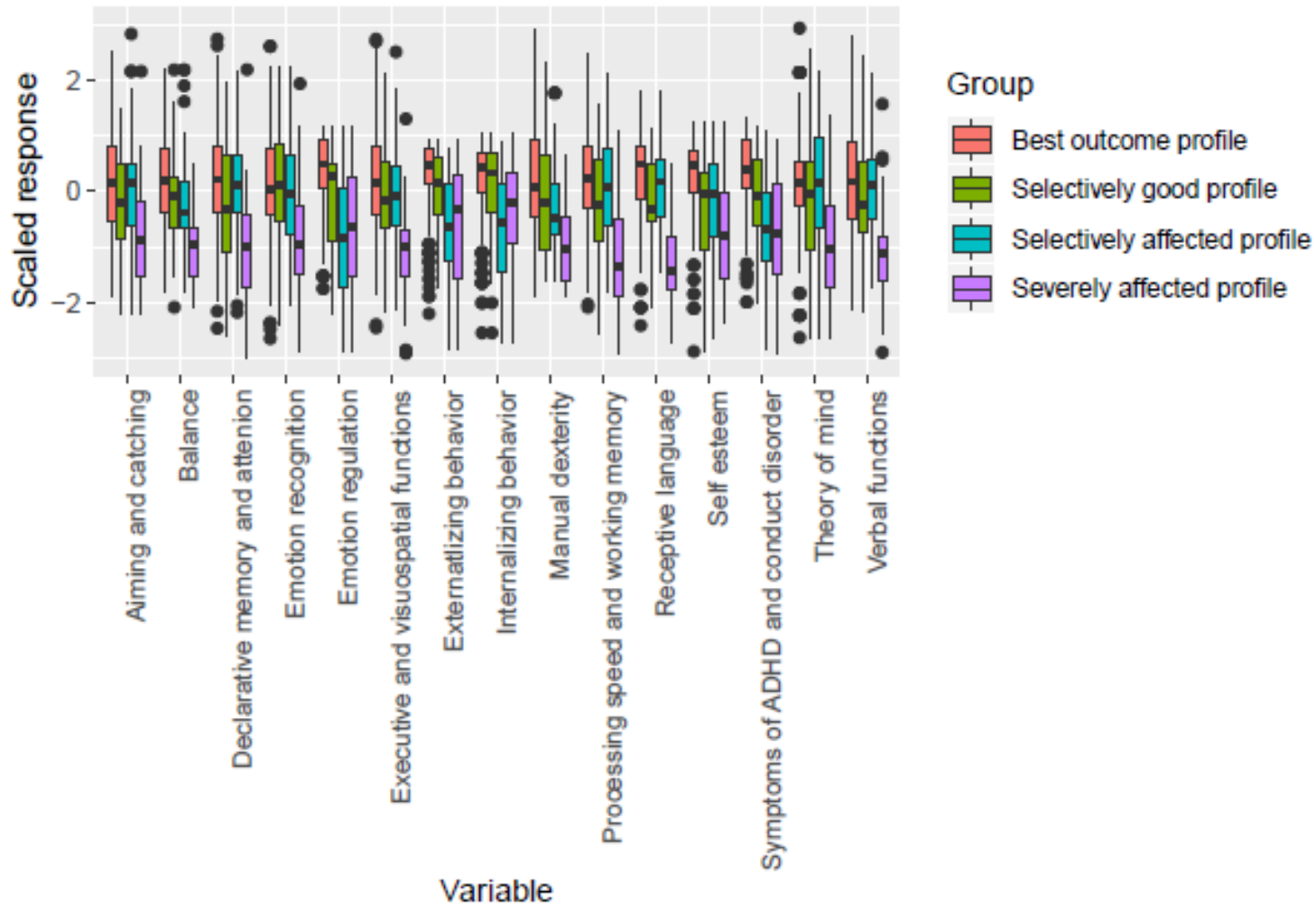


# Children's, teachers' and caregivers' reports about child being bullied, age 11

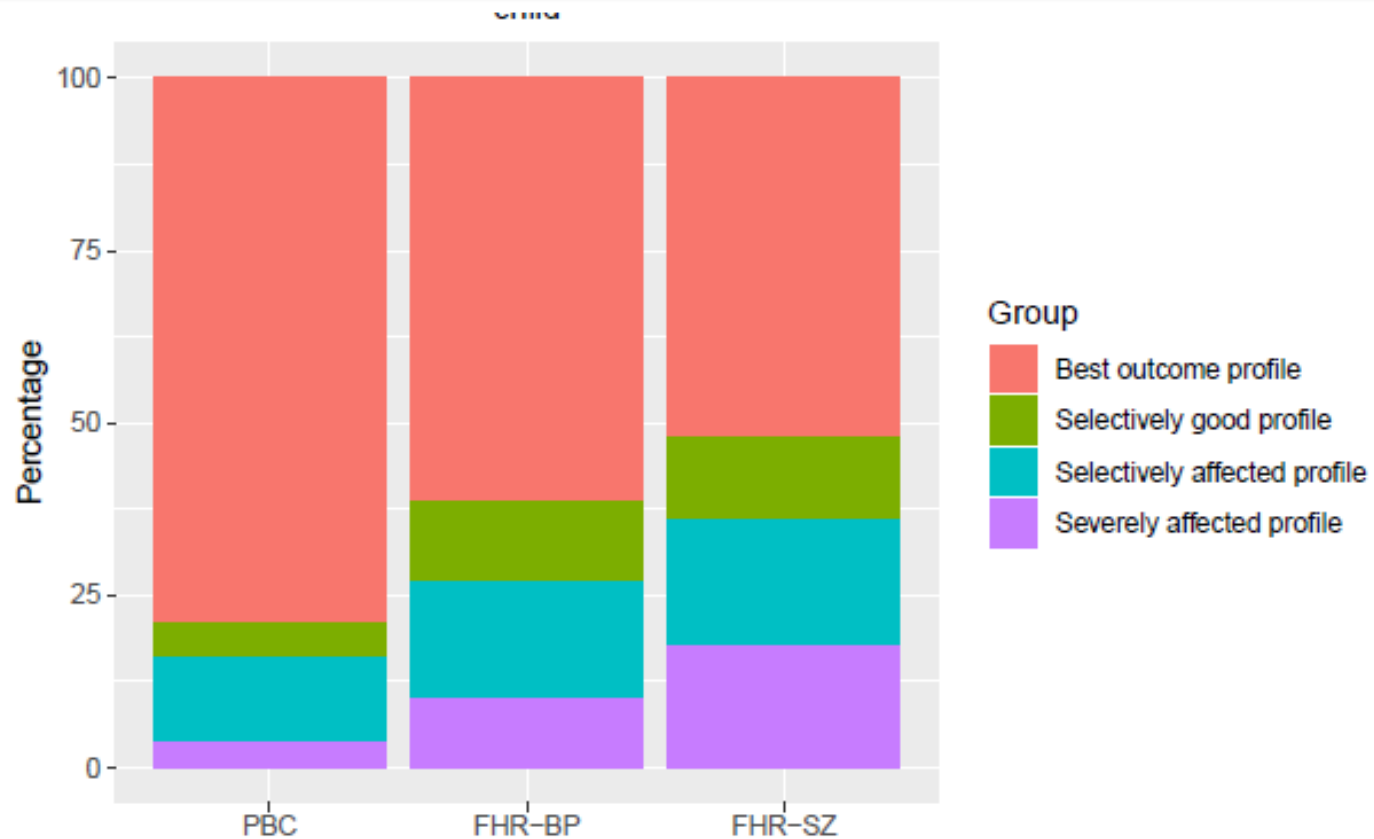
Proportion being bullied: self-report, caregivers and teachers report



# Results from VIA 7: Cross-domain cluster analysis



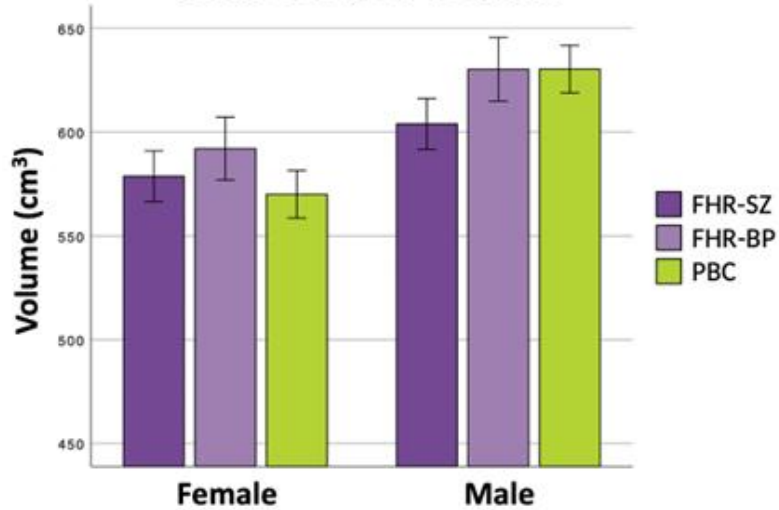
# Results from VIA 7: Cross domain impairment in high risk groups



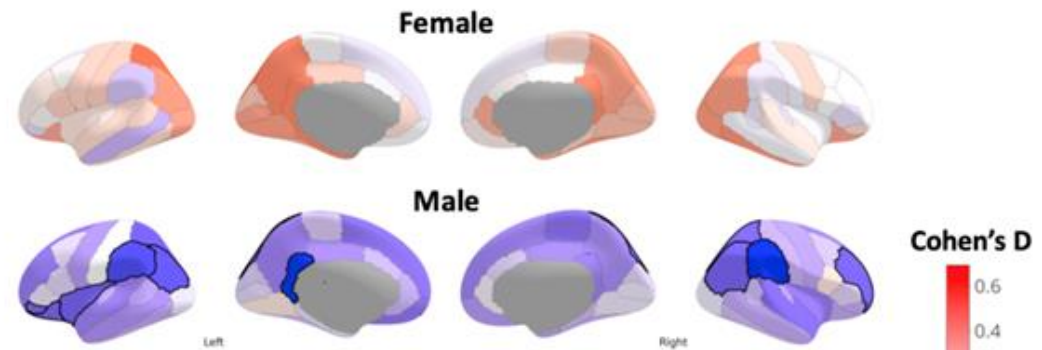
PBC : population based controls  
FHR-BP : Familial bipolar high risk  
FHR-SZ : Familial schizophrenia high risk

# BRAINMAP

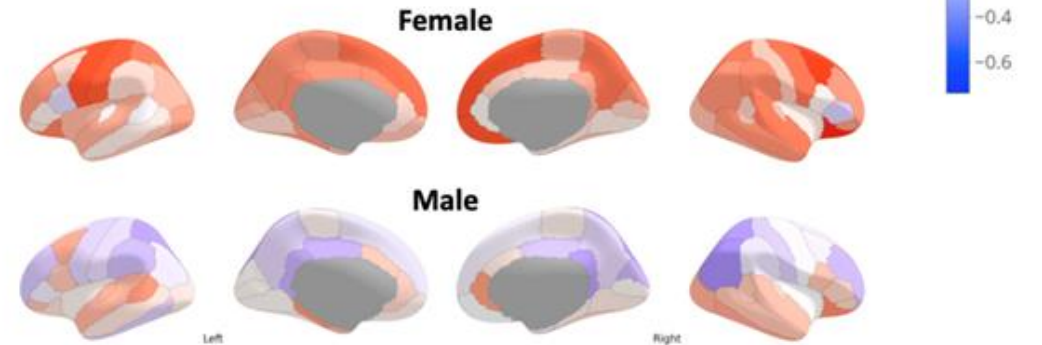
## Total Cortical Volume



## FHR-SZ vs. PBC



## FHR-BP vs. PBC





# Take home message VIA 7 and VIA 11 – so far

## -Children of parents with schizophrenia versus controls

- More likely to live in inadequate home environment
- Higher proportion have child psychiatric disorders
- More psychotic experiences
- Lower cognitive function
- Poorer understanding of language
- Poorer motor functioning
- Less high intensity physical activity
- More traumatic life events
- More likely to be bullied
- Structural brain changes at age 11
- A group of children of parents with schizophrenia have impairments in almost all domains
- This group is also living in more difficult life circumstances

# The Danish High Risk and Resilience Study: Outcomes

- More detailed knowledge about an important risk group
- Basic science: Disease processes
- Intervention: VIA Family and full scale intervention trial
- Increased awareness in relevant professional groups and planners
- Focus on high risk families: the whole family is affected
- Extreme visibility nationally and internationally: Many keynote lectures and presentation for NGO's
- High risk children are included as an important target group in 10 year plan for psychiatry
- Nine completed PhDs, another 11 to follow
- To be continued: VIA 19 and trials testing family based interventions

# Researchers in VIA 7 and VIA 11

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William Baaré, PhD

Torben Lund, PhD

Leif Østergaard, Prof, PhD

Vibeke Bliksted, PhD.

Carsten Hjorthøj. Ass Prof, PhD

Claus Thorn Ekstrøm, Prof, PhD

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Nicoline Hemager, PhD

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SENS Motion

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Dost Öner Prof PhD