Effectiveness, side effects, and cognitive outcomes of SSRIs in 22q11DS

A MULTICENTER STUDY

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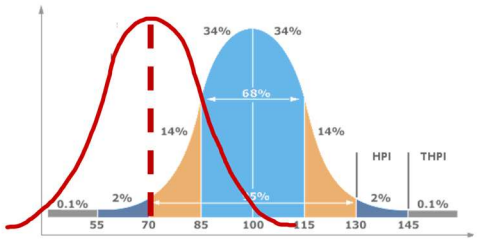
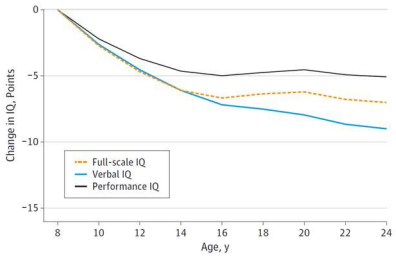
Overview of 22q11DS

Cognitive functioning (IQ)

- High interindividual variability
- Average full-scale IQ ≈ 70
- Loss of IQ points over time reflects slower pace in cognitive development





(Vorstman et al., 2015)

Mental health

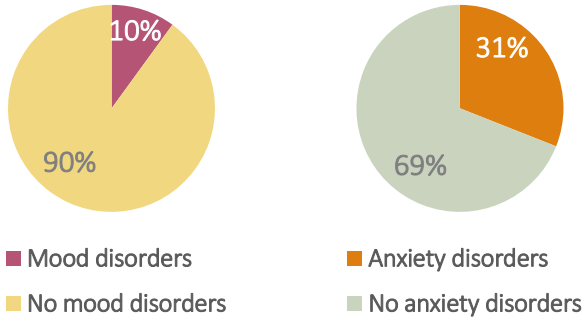
- Increased risk of difficulties related to ADHD, anxiety, depression, psychosis *(Schneider et al., 2014)*
- Treated similarly as in the general population *(Mosheva et al., 2019)*

Psychostimulants | **SSRIs** | Antipsychotics

Selective Serotonin Reuptake Inhibitors (SSRIs)

Indications

- Pharmacological treatment for mood and anxiety disorders
- Molecules: fluoxetine, sertraline, (es)citalopram



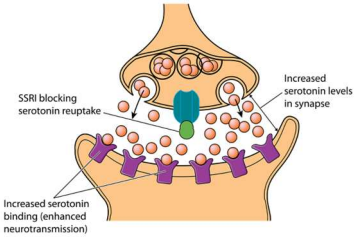
(Schneider et al., 2014)

1 What is the effectiveness and safety profile of SSRIs in 22q11DS ?

- **Case study** *(Stachon & De Souza, 2011)*: improved anxiety and perceptual disturbances in N=3
- **Retrospective study** *(Dori et al., 2017):* mild side effects and response rates similar to non-22q11DS in N=21

Selective Serotonin Reuptake Inhibitors (SSRIs)

Mechanism



- Role of serotonin in mood regulation, cognition and learning
- ↑ serotonin levels ↑ synapses in key regions for cognitive processes *(Johansen et al., 2023)*

2 What are the effects of SSRIs on cognition in 22q11DS?

- IQ increase following SSRI treatment

https://doi.org/10.1038/s41398-021-01456-x Translational Psychiatry

ARTICLE Open Access

Long-term effects of early treatment with SSRIs on cognition and brain development in individuals with 22q11.2 deletion syndrome

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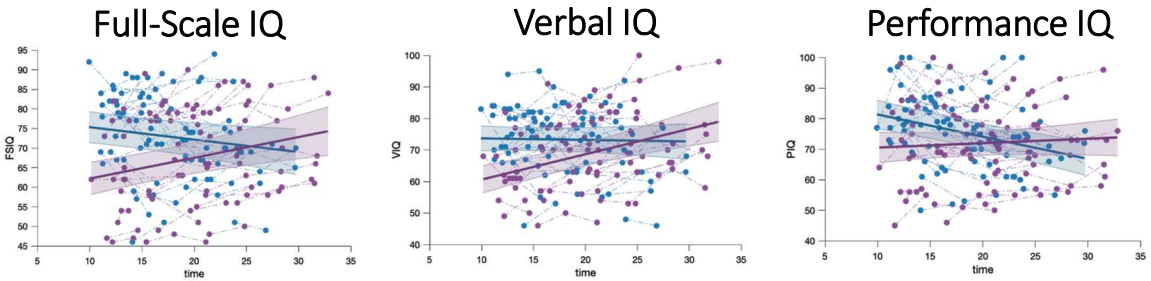
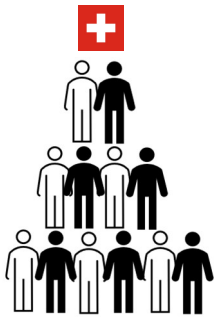
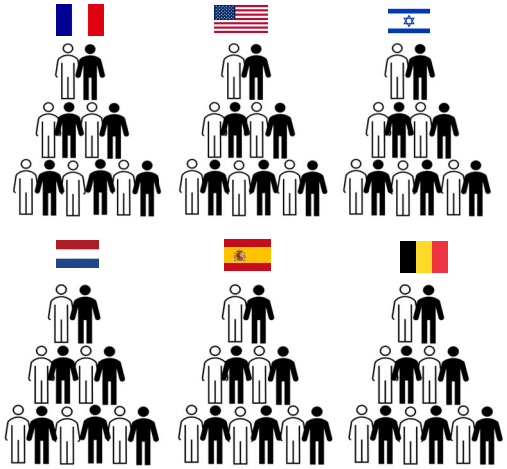




Retrospective cohort study

(Mancini et al., 2021)



Multicenter study

(Latrèche, Mancini et al., submitted)

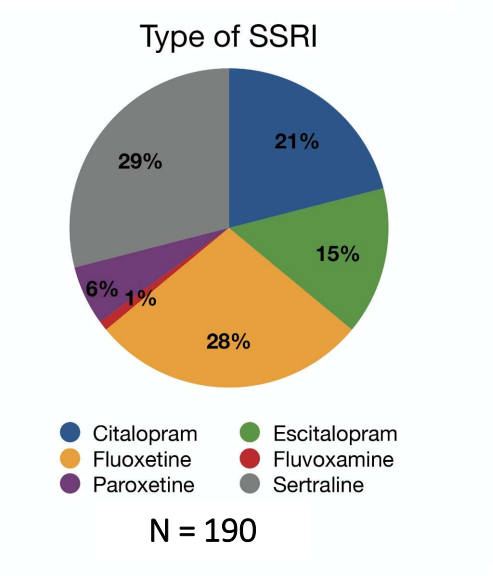
1 Effectiveness and side effects of SSRIs

Participants

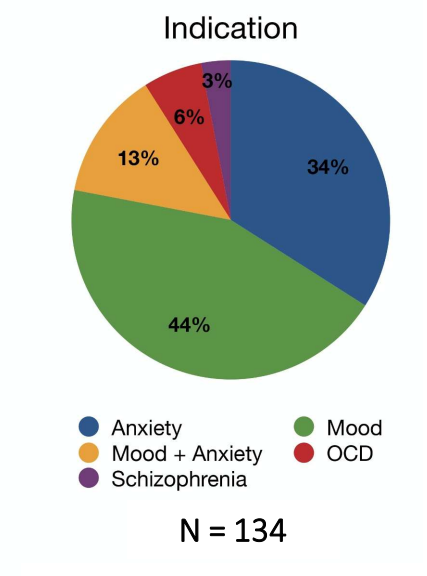
Site	N
Geneva (Prof. Eliez)	54
Paris (Prof. Chaumette)	31
Los Angeles (Prof. Bearden)	28
Tel Aviv (Prof. Gothelf)	18
Maastricht (Prof. van Amelsvoort)	18
Utrecht (Prof. Fiksinski, Prof. Velders)	12
Madrid (Prof. Arango)	11
Leuven (Prof. Swillen, Prof. Vergaelen, Prof. Vogels)	9
Noordwijk (Prof. Boot & Prof. Vingerhoets)	8
Total	190

N	190
Sex (M vs. F)	101 vs. 89
Mean age	23.8 years
Age range	6-56 years

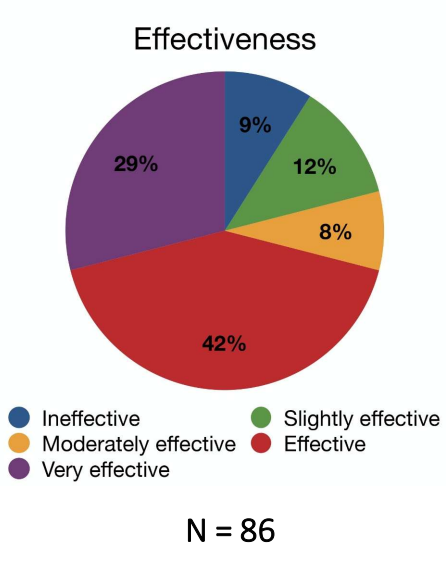
1 Effectiveness and side effects of SSRIs



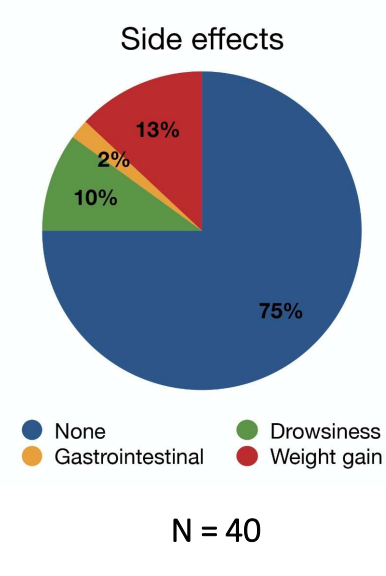
N = 190



N = 134



N = 86



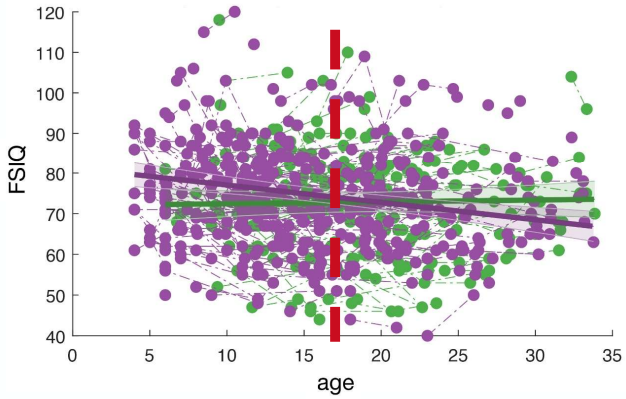
N = 40

2 Effects of SSRIs on IQ trajectories

Site	SSRI (N)	noSSRI (N)	Total N	SSRI (visits)	noSSRI (visits)	Total visits
Total	101	213	314	219	440	659

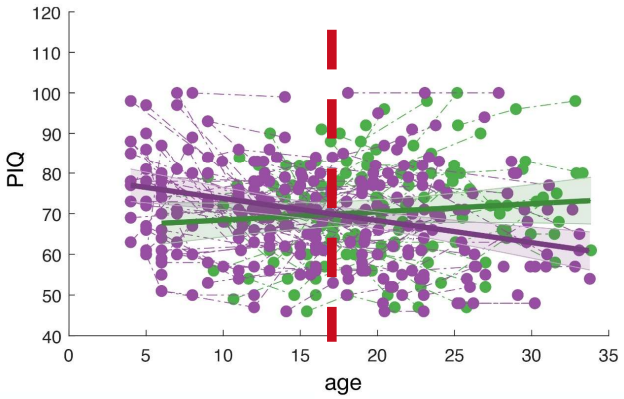
Full-scale IQ

group-effect: p=0.002 interaction: p<0.001



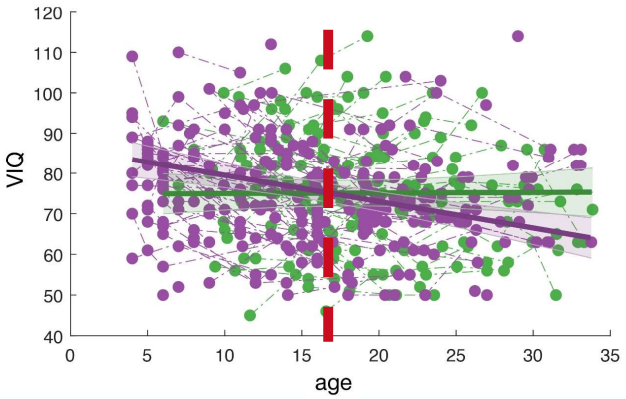
Performance IQ

group-effect: p<0.001 interaction: p<0.001



Verbal IQ

group-effect: p<0.001 interaction: p<0.001



*mean age at SSRI initiation = 17 years

SSRI vs. noSSRI

2 Effects of SSRIs on IQ trajectories

Which factors are associated with change in FSIQ ?

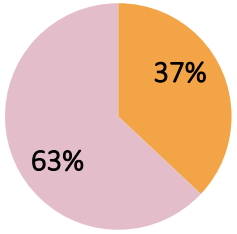
Dosage (fluoxetine equiv., mg/kg)
M = 27.90 mg (± 14)

Treatment duration
M = 49 months (± 39)

2 Effects of SSRIs on IQ trajectories

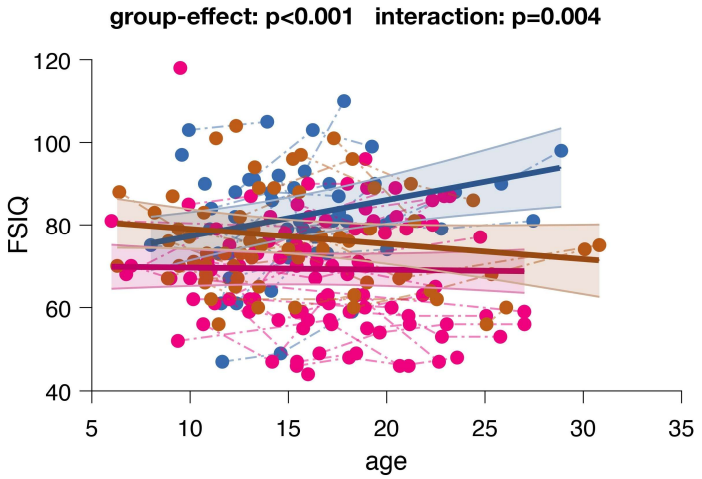
What about SSRIs + Psychostimulants ?

- High prevalence of **ADHD** in 22q11DS
- **Procognitive** effects of psychostimulants *(Spencer et al., 2015)*



(Schneider et al., 2014)

SSRI + psychostimulant (N=25)
SSRI + no psychostimulant (N=44)
Psychostimulant + no SSRI (N=38)



Conclusions

Favorable safety profile of SSRIs in individuals with 22q11DS

- Low reports of ***side effects*** and high rates of perceived ***effectiveness***

⚠ Relatively ***small*** sample sizes

Significant cognitive benefits (IQ) observed in treated individuals

- Importance of ***treatment duration*** and ***SSRI + Psychostimulants*** combination on IQ outcomes

⚠ Disentangling ***direct*** vs. ***indirect*** effects of treatment

Sustained SSRI treatment may help **preserve** cognitive functions

⚠ ***Controlled prospective studies*** are needed to confirm the findings

Thank you!

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synapsy network – Centers for neuroscience and mental health research

Swiss National Science Foundation

22q11 Europe

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GÉNÉRATION22 – VIVRE AVEC LA MICRODÉLÉTION 22q11.2

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