

Clinical characteristics of autistic youth in the SPARK cohort with a co-occurring schizophrenia diagnosis

Amandeep Jutla, MD

Postdoctoral Fellow

NIMH T32 Fellowship in Translational Child Psychiatry Research

Division of Child & Adolescent Psychiatry

Columbia University

New York State Psychiatric Institute



Department of Psychiatry
Division of Child and Adolescent Psychiatry

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Autism and schizophrenia

ASD

Typically
diagnosed in
childhood

Stable course

SCZ

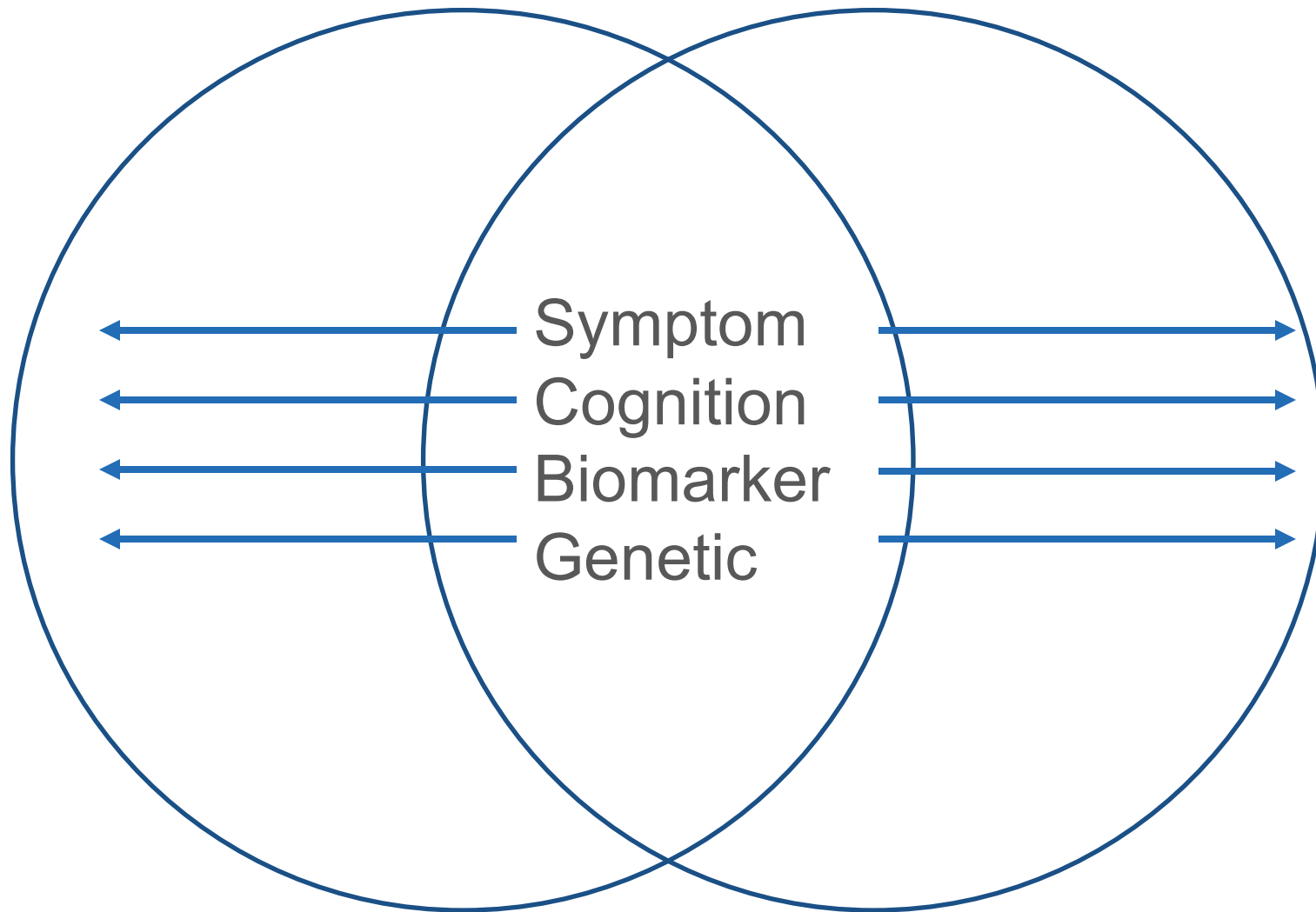
Typically
diagnosed in
**adolescence or
early adulthood**

Deteriorating
course

ASD

Levels of overlap

SCZ



ASD

Symptom

SCZ

Deficits in social-emotional reciprocity

Deficits in nonverbal communication

Difficulty developing or maintaining relationships

ASD

Cognition

SCZ

Sensory processing deficits

Executive function impairment

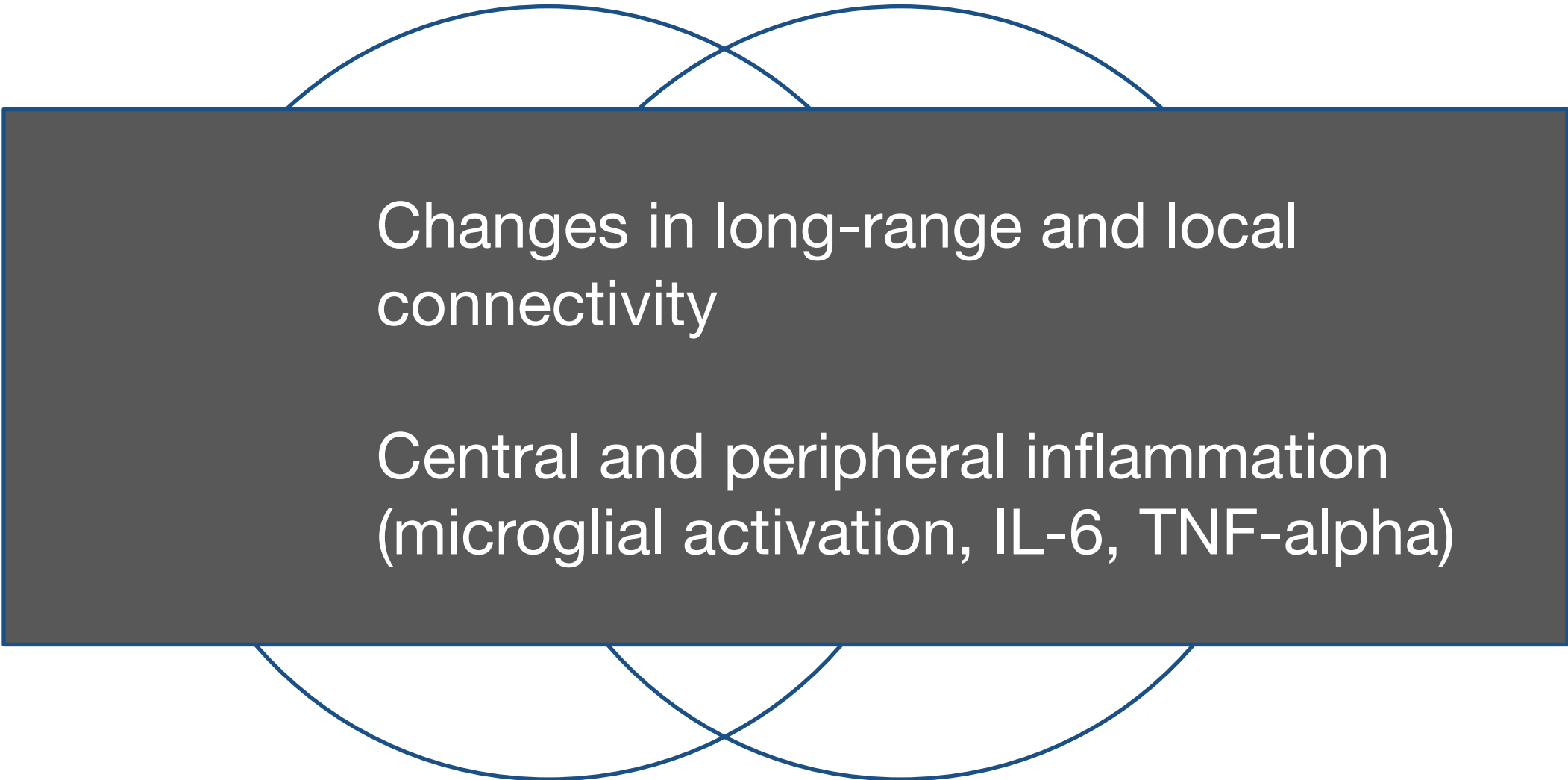
Processing speed impairment

Language impairment

ASD

Biomarkers

SCZ



Changes in long-range and local connectivity

Central and peripheral inflammation
(microglial activation, IL-6, TNF-alpha)

ASD

Genetics

SCZ

CNVs: 16p11.2, 22q11.2, q121.1,
7q11.23, 17q12, 15q13.3, 2p16.3,
16p21.32

CACNA1C, GRIN2B

- Schizophrenia in the general population:
 - 1% prevalence
- Schizophrenia risk in people **with ASD** by adulthood:
 - 3.55x odds**
 - 4% prevalence**

Zheng, Zheng & Zou, 2018
Lai et al, 2019

Rationale for this study

- The clinical profile of schizophrenia or emerging schizophrenia among children and adolescents with ASD is not well-understood, which has public health implications

Foss-Feig et al, 2019

Jutla et al, 2020a

Jutla et al, 2021

- Simons Powering Autism Research for Knowledge (SPARK) cohort:
 - ASD cohort of unprecedented size
 - Recruitment is ongoing

The SPARK Consortium, 2018

- As of 4/24/2020 (data release 4):
 - 77,017 children and adolescents with an ASD diagnosis
- Within a large subset ($n = 73,435$) of ASD youth in SPARK, we wanted to look at the extent to which several variables, selected *a priori*, statistically predicted a schizophrenia diagnosis

Characteristics of ASD youth from SPARK (n = 73,435)

Schizophrenia diagnosis

Mean age at autism diagnosis

Mean age at study enrollment

OCD diagnosis

Tic disorder diagnosis

Intellectual disability

Seizures

History of premature birth

History of serious infection during pregnancy

Language: nonverbal

Language: single words

Language: short sentences

Language: longer sentences

Characteristics of ASD youth from SPARK (n = 73,435)

Schizophrenia diagnosis	333 (0.45%)
Mean age at autism diagnosis	4.47 ± 3.10 years
Mean age at study enrollment	9.83 ± 6.06 years
OCD diagnosis	2,906 (3.96%)
Tic disorder diagnosis	1,096 (1.49%)
Intellectual disability	14,330 (19.51%)
Seizures	2,007 (2.73%)
History of premature birth	4,708 (6.41%)
History of serious infection during pregnancy	106 (0.14%)
Language: nonverbal	10,511 (14.31%)
Language: single words	10,475 (14.26%)
Language: short sentences	12,507 (17.03%)
Language: longer sentences	39,942 (54.39%)

Statistically significant predictors of schizophrenia diagnosis among youth enrolled in SPARK

Predictor	OR	95% CI	<i>p</i>
<i>Positive predictors</i>			
OCD diagnosis	6.68	5.06 – 8.75	5.1×10^{-42}
Tic disorder diagnosis	4.23	2.94 – 5.98	1.7×10^{-15}
Intellectual disability	1.75	1.36 – 2.24	1.2×10^{-5}
Age at autism diagnosis	1.34 per 2 SD increase	1.11 – 1.61	0.0021
<i>Negative predictors</i>			
Male sex	0.50	0.40 – 0.63	2.7×10^{-9}
Nonverbal language level	0.41	0.23 – 0.68	9.1×10^{-4}

Interpreting these findings

OCD and tic disorder diagnoses as strong positive predictors

- Consistent with increasing evidence of genetic convergence among OCD, schizophrenia and ASD
- Also potentially consistent with the clinical challenge of separating intense rituals, intense special interests, and frank delusions from one another

Jutla et al, 2020b

Older age at diagnosis as positive predictor and male sex as negative predictor

- Interesting, unexpected findings that warrant further study – we may be better able to understand this in the context of genetic data

Future directions

- Genetic data from SPARK
- Collecting new data to characterize psychotic symptoms more granularly

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Amandeep.Jutla@nyspi.columbia.edu