Autism and Psychosis

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TALK OUTLINE

- Case Examples
- History of ASD and Psychosis
  - Diagnostic criteria and DSM
  - Childhood onset schizophrenia
  - Psychosis prodrome
- Research Findings
  - Clinical overlap
  - Genetics and neurobiology
- Clinical Implications
  - Differential Diagnosis
  - Treatment Implications

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DIFFERENTIAL DIAGNOSIS: CASE EXAMPLE 1

"Josh": 14yo M

- Family history of both autism and schizophrenia
- History of language delay and delayed echolalia, current formal speech and atypical intonation on exam
- Limited range of facial expressions, gestures on exam
- No friendships, difficulties with reciprocal interactions
- History of restricted interests (trains, certain videos), also at present (history, weapons)

Now also presenting with:

- Visual hallucinations (shadows of aliens)
- Paranoid ideation (being poisoned, being video taped)
- Disorganized thinking, particularly in high affect situations

DIFFERENTIAL DIAGNOSIS: CASE EXAMPLE 2

"Kyle": 17yo M

- History of early language delays, but no stereotyped language or echolalia on exam
- Difficulties with conversation
- Social skills deficits, social withdrawal
  - Worsening beginning in 4th grade
- Sensory sensitivities (irritated by noises and smells)

Now presenting with:

- Decline in self-care
- Paranoia about people staring at him, foods being poisoned
- History of visual hallucinations at age 16
- Frequent violent, graphic nightmares
- Increasing agitation and irritability

DIFFERENTIAL DIAGNOSIS: QUESTIONS

- Per DSM: Is it one OR the other?
- But… might it be both?
  - Can ASD and Schizophrenia be comorbid?
  - Can schizophrenia masquerade as ASD in early childhood?
  - Might symptom patterns that are called "autism" actually be caused by another underlying problem?
  - Does ASD make one more susceptible to a psychotic process?

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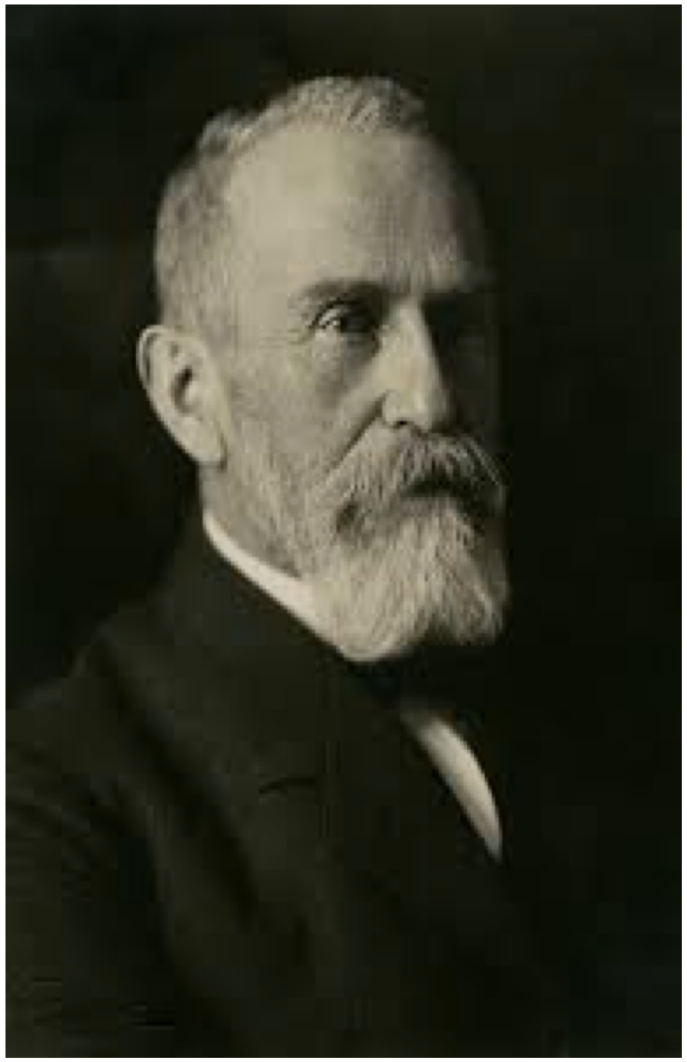
EUGEN BLUELER

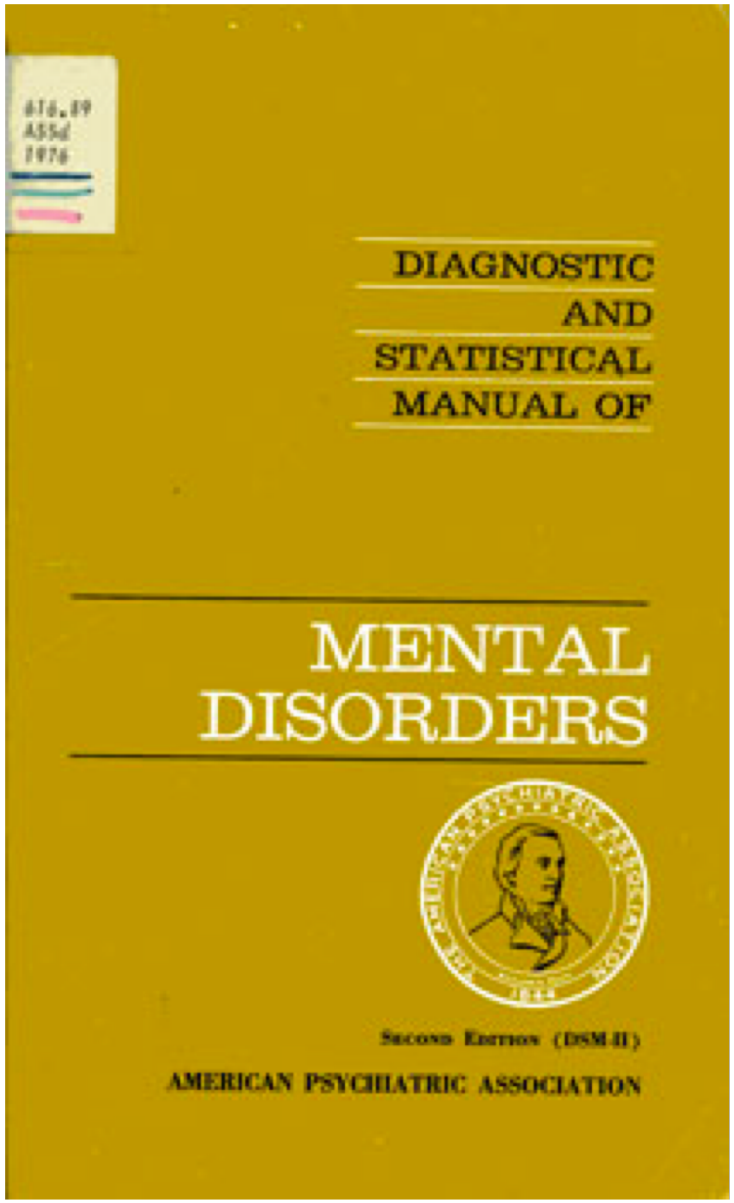


- 1911: Dementia Praecox -> the *"schizophrenias"*
- Physical disease characterized by exacerbations and declines
- Major symptoms, "4 A's"
  - flattened Affect
  - **Autism**
  - impaired Association of ideas
  - Ambivalence

LEO KANNER

- 1943: Early infantile autism
  - **Autistic** aloneness
  - Insistence on sameness
  - Speech disturbances, such as echolalia
  - Large heads, clumsy gait, excellent rote memory
- Differentiated from schizophrenia by onset of social withdrawal

DSM-II (1968)



- 295.8 Schizophrenia, childhood type
- This category is for cases in which schizophrenic symptoms appear before puberty. The condition may be manifested by autistic, atypical and withdrawn behavior; failure to develop identity separate from the mother's; and general unevenness, gross immaturity and inadequacy of development. These developmental defects may result in mental retardation, which should also be diagnosed.
- Autism does not have its own category

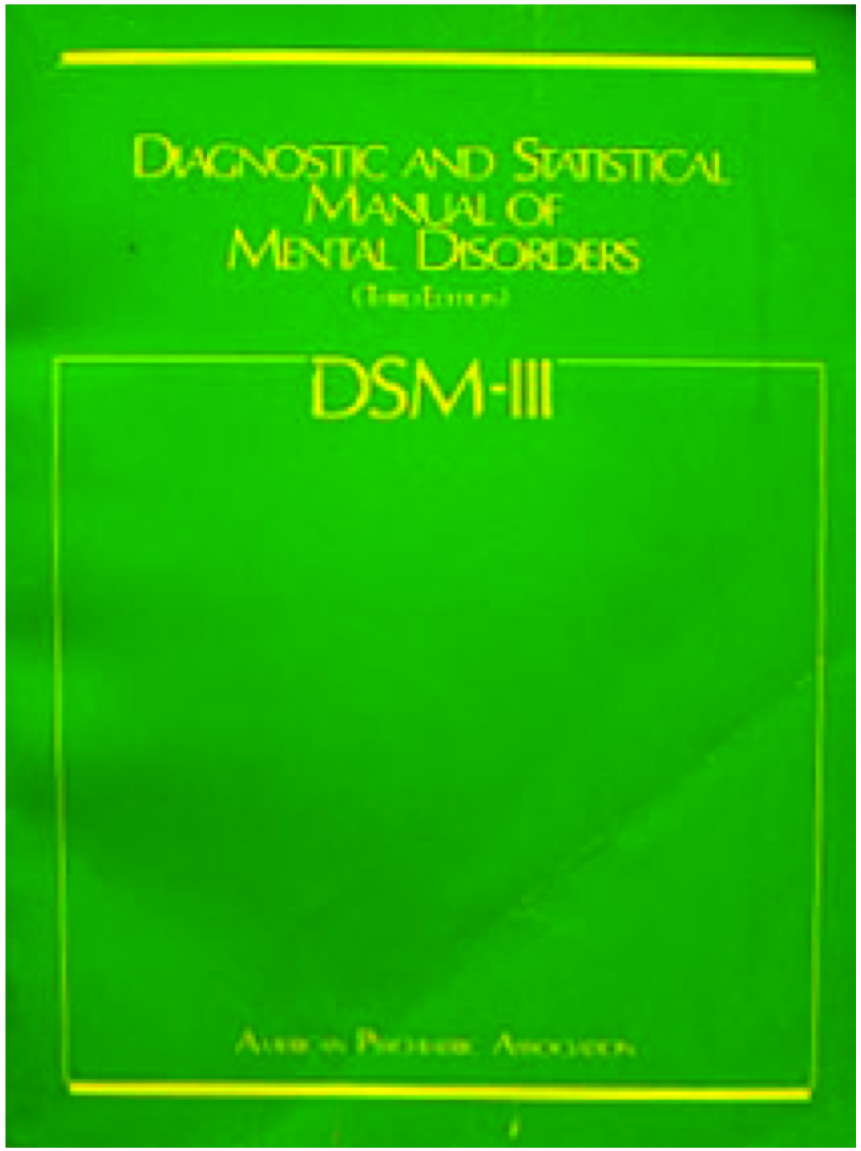
ISRAEL KOLVIN

- 1971: Studies in the Childhood Psychoses
- Three groups of psychoses in childhood, distinguished by age of onset:
  - Under 3 years (Kanner)
  - 3-5 years
  - Over 5 years (adult schizophrenia)

REMAINING SOURCES OF CONFUSION

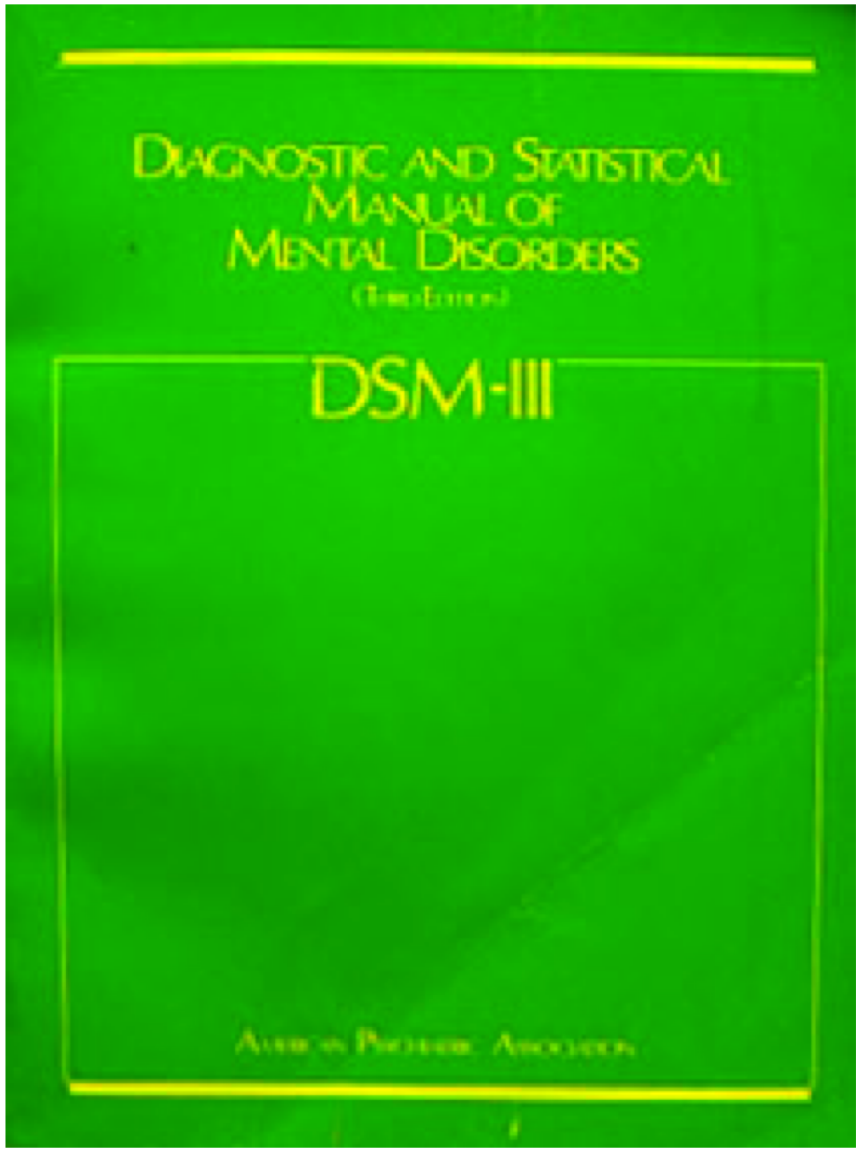
- Both disorders are schizophrenias
- Both disorders have the word "autism" at their core
- There is no separate diagnosis for autism until Infantile Autism appears in the DSM-III in 1980

DSM-III (1980)



- Infantile Autism
- A. Onset before 30 months of age
- B. Pervasive lack of responsiveness to other people (autism)
- C. Gross deficits in language development
- D. If speech is present, peculiar speech patterns such as immediate and delayed echolalia, metaphorical language, pronominal reversal

DSM-III (1980)

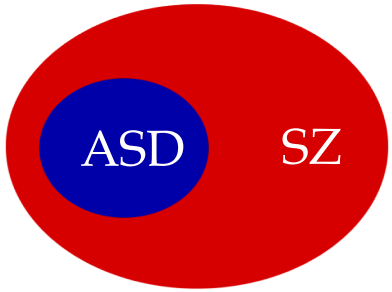


- E. Bizarre responses to various aspects of the environment, e.g., resistance to change, peculiar interest in or attachments to animate or inanimate objects.

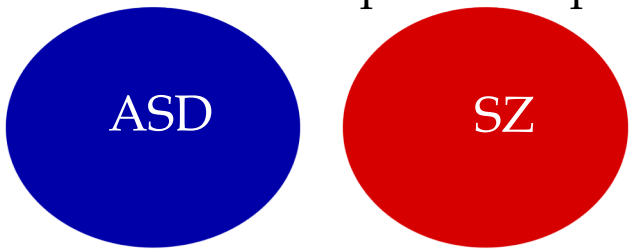
- F. *Absence of delusions, hallucinations, loosening of associations, and incoherence as in Schizophrenia.*

HISTORICAL JOURNEY OF ASD AND SCHIZOPHRENIA

Prior to DSM-III:
Autism Subsumed within Schizophrenia



After 1980:
Autism and Schizophrenia Separate



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Psychosis and autism as diametrical disorders of the social brain

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WHISPERS OF OVERLAP: CASE LITERATURE

- Petty (1984)

Autistic Children Who Become Schizophrenic

Leonora K. Petty, MD; Edward M. Ornitz, MD; John D. Michelman, MD; Emory G. Zimmerman, MD, PhD

• Infantile autism and schizophrenia have been regarded as unrelated and distinct disorders. There is, however, some evidence in the literature that supports a relationship between the two disorders in that there may be a subgroup of autistic children in whom schizophrenia develops. The diagnostic criteria used in the literature to describe infantile autism and schizophrenia in childhood has not been uniform. The three cases in this report, diagnosed on the basis of current criteria and detailed clinical descriptions, clearly point to an initial diagnosis of infantile autism followed by the development of schizophrenia.

(*Arch Gen Psychiatry* 1984;41:129-135)

PETTY (1984): CASE 1

Case 1.—Early History.—The patient was the full-term product of an uneventful pregnancy and delivery. There were no neonatal complications or congenital anomalies. The family history revealed no major psychiatric syndromes, mental retardation, or neurological disease, except for a neuromuscular defect in the patient's otherwise normal, one-year-younger sister (bilateral ptosis and epicanthus inversus).

His parents remembered him as "very good, passive, and easy" during the first six months. Breast-feeding was unsuccessful; however, he sucked well at the bottle. At the age of 8 months, he sat with support in a playpen and was responsive, affectionate, and interested in rattles and the crib mobile. His pediatrician noted "not talking much" and "trouble sleeping." The parents recalled adequate "eye contact" at the age of 1 year, but remembered that "he did not point." He stroked textured surfaces, eg, wood and wall coverings, repetitively. He said "bye bye" and "mama" at the age of 18 months.

At the age of 24 months, his vocabulary had not increased. He "pulled at hands to move the hand to pick up an object" rather than communicating in other ways. His pediatrician noted "short attention span; excessive anger, spitting."

At the age of 33 months, the pediatrician noted that the child did not speak and seemed to be extremely withdrawn, "tuning out."

At the age of 38 months, a formal audiological evaluation gave normal findings. At the age of 44 months, on enrollment in a therapeutic nursery school, he was described as having limited eye contact and being quite withdrawn. His vocabulary consisted of about 15 words. He lined objects in straight rows and would not touch any item that was slightly sticky, eg, cupcakes, cake, or paste. He touched objects gingerly at their outer edges. On initial testing, the Merrill-Palmer IQ was 73. After three months of intensive therapy, the IQ was 81. Test subscales showed wide scatter, with the highest success at the 60- to 65-month level (picture puzzle). At the age of 54 months, a Denver Developmental Screening Test showed the following:

Gross Motor—fails all tests for age; Fine Motor—fails most tests for age; language—comprehension was age level, expressive language was below age level, quantity of words below level and quality of speech far below normal; Personal-Social—interactions with peers almost non-existent. Very short attention span, then gets hung up on one activity.

At the age of 60 months, in an aphasia class, he appeared more alert and aware of others. By the age of 66 months, he had a "reading vocabulary" at grade level, ie, comprehension was severely limited, and he was restricted, literal, and concrete in his thinking.

There was a developmental "spurt" manifested by word recognition and spelling at second-grade level, at the age of 66 months, although comprehension was severely limited. Motor milestones were slightly delayed but progressed in an orderly fashion.

By 36 months of age, the patient had demonstrated sufficient autistic behavior to diagnose infantile autism (Table 1).[25,26] Such behavior was evident before 30 months of age and persisted past the age of 60 months.

PETTY (1984): CASE 1

Middle Childhood Years.—At 7 years of age, the patient began to vomit each night at bedtime. A workup was noncontributory, and the pediatrician diagnosed "psychosomatic hyperemesis."

By the age of 8 years, the initial progress in the aphasia class declined and his behavior deteriorated. Decreased attention span, conversation punctuated by irrelevant comments, and emotional lability were observed. After three weeks of trifluoperazine hydrochloride (Stelazine) therapy, his teacher reported a "truly increased attention to solitary tasks; still a loner."

At the age of 9 years, the trifluoperazine therapy was discontinued, and his pediatrician reported "deteriorating behavior" and reappearance of regurgitation. By 10 years of age, the parents sought psychiatric help. Episodic vomiting reappeared, behavior deteriorated, and he was mumbling to himself incoherently. During psychiatric examination by one of us (E.M.O.), there was intermittent hand flapping, finger wiggling, and whole-body rhythmic movement. Eye contact was fleeting. He spoke with nasal tone that did not convey adequate emotion. Speech was literal, with lack of content, but no loose associations. He told the examiner that he heard "parrotlike voices," and he saw bizarre, inappropriate details in the Rorschach test. He showed severe deficits in social judgment.

For the next two years, the patient was seen weekly by one of us (J.D.M.), and trifluoperazine therapy was reinstituted. He expressed concern that he was losing control. Loose associations developed. The patient learned to refer to them as "extra thoughts." At times they were bizarre and delusional, such as "smelling a creamy feeling" or "worrying about this decade." Other whispers and mumblings reflected age-appropriate interests contaminated by bizarre associations, such as "wanting to kiss a girl with racial feelings." Much of his thought content, however, consisted of names of television shows, advertisement jingles, key phrases from movies, lists of words that rhymed, literal puns, and word games such as "dafynitions" ("understand . . . to stand under . . . to understand!").

Adolescence.—At the age of 12 years, the patient was hospitalized for control of increasingly bizarre behavior and progressive deterioration in daily routines, including "increased insomnia."

The mental status examination on admission showed fleeting eye contact, physical agitation, and frequent hand flapping. There was much resistance and occasional noncompliance. Mood was flat; depression and suicidal feelings were denied. Thoughts included delusions of being controlled by life-threatening "witch craftery . . . the fearful force." There were hallucinations of "hearing voices," including commands. Much of the patient's language was incomprehensible because of mumbling subvocalizations and loose associations, eg, "I like the hospital all right . . . stupid, stupid, stupid . . . (whisper and giggling) what is a slapshot?" The patient was fully oriented, with excellent memory and ability to calculate.

Results of physical and neurological examinations, routine blood and urine tests, routine chest roentgenography, EEG, and hearing and vision evaluations were within normal limits. On the revised Wechsler Intelligence Scale for Children (WISC-R) verbal IQ was 91, performance IQ was 68, and full-scale IQ was 78.

Table 2 summarizes the documentation for the diagnostic criteria for schizophrenia. The requirements for chronicity were also met.[25,27] Auditory "running commentary" and two-voice hallucinations were described during the four months prior to hospital admission (when he was not taking antipsychotic medication). During hospitalization, he was again given medication. Although other schizophrenic symptoms persisted, within two weeks of initiating treatment with thiothixene hydrochloride (Navane; to 22 mg/day), the patient said, "The voices have gone away now." At the six-month follow-up examination, the patient denied "hearing voices," although incoherent muttering and whispering were observed.

WHISPERS OF OVERLAP: PSYCHOSIS PRODROME

- Acute: Mild/moderate Alterations in perception, cognition, language, will, initiative, motor function, energy level, stress tolerance
  - Social isolation
  - Negative symptoms of schizophrenia
  - Depression, anxiety
  - Difficulty with concentration, attention
  - Attenuated positive symptoms
- Further back
  - Language and other milestone delays
  - Atypical motor functioning
  - Attention problems
  - Social difficulties

WHISPERS OF OVERLAP: CHILDHOOD ONSET SCHIZOPHRENIA

- Schizophrenia diagnosed under 13
- In 97 children with COS at NIMH, 29% had a PDD diagnosis
  - Additional 39% had other developmental delays, including with language and with motor skills
- In the broader COS cohort, for any given DSM-IV ASD symptom, 16-58% of children met criteria
  - Social impairment: 100% had 1; 78% had 2+
  - Communication impairment: 84% had 1; 53% had 2+
  - RRBs: 74% had 1; 37% had 2+
  - Overall: 58% had impairment in all three categories; 100% had impairment in at least two
  - Least common overlapping symptoms were pronoun reversal, impaired non-verbal communication, deficits in imaginative play

Rapoport et al., 2009

WHISPERS OF OVERLAP: CHILDHOOD ONSET SCHIZOPHRENIA

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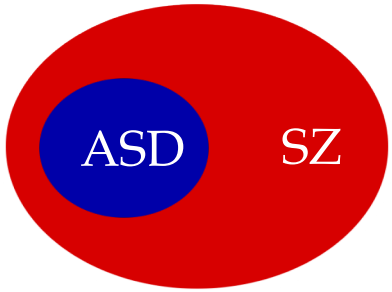

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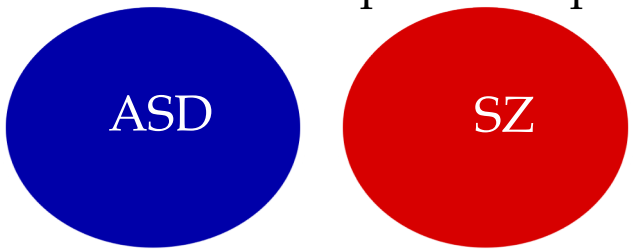

Newer Conceptualization:
Overlapping Disorders

ASD

- Stereotyped Language
- Restricted Interests
- Motor Mannerisms
- Onset under age of 5
- Limited medication effects on core symptoms

- **Social**
- **Sensory**
- **Cognitive**

SZ

- Hallucinations
- Delusions
- Onset typically early adulthood
- Responds to anti-psychotics

Shared genetic contributions?

Shared underlying neurobiology?

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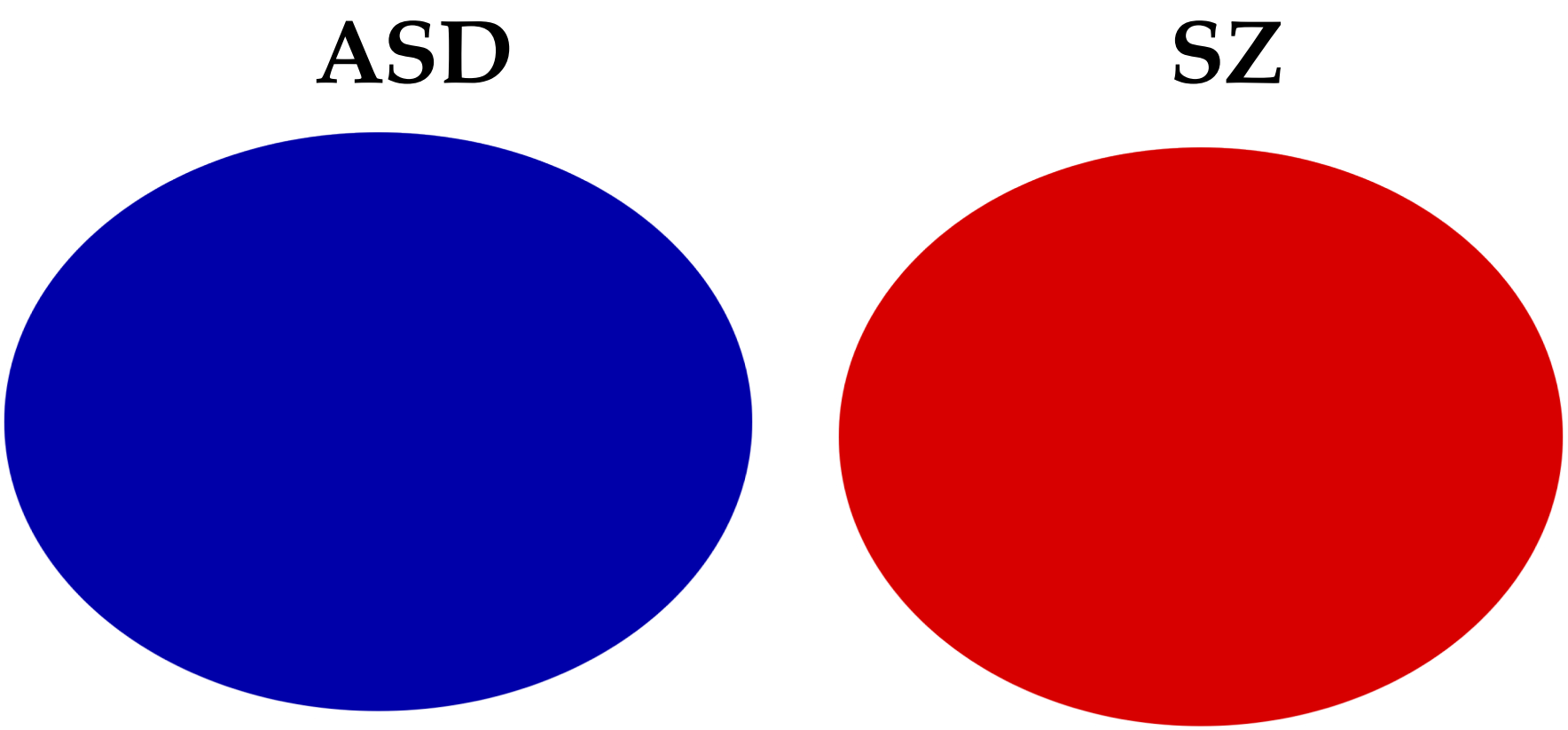
HISTORICAL JOURNEY OF ASD AND SCHIZOPHRENIA



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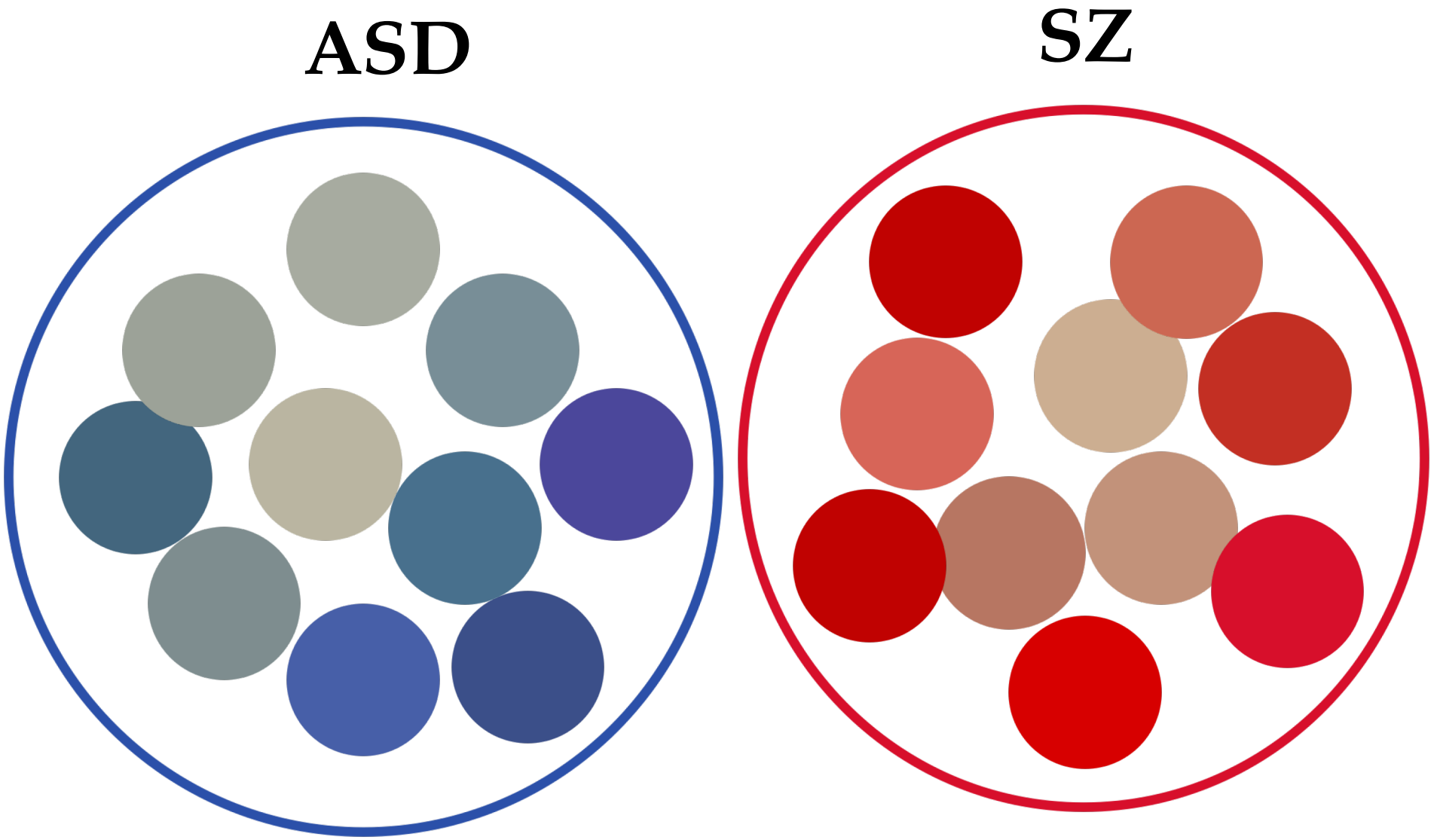

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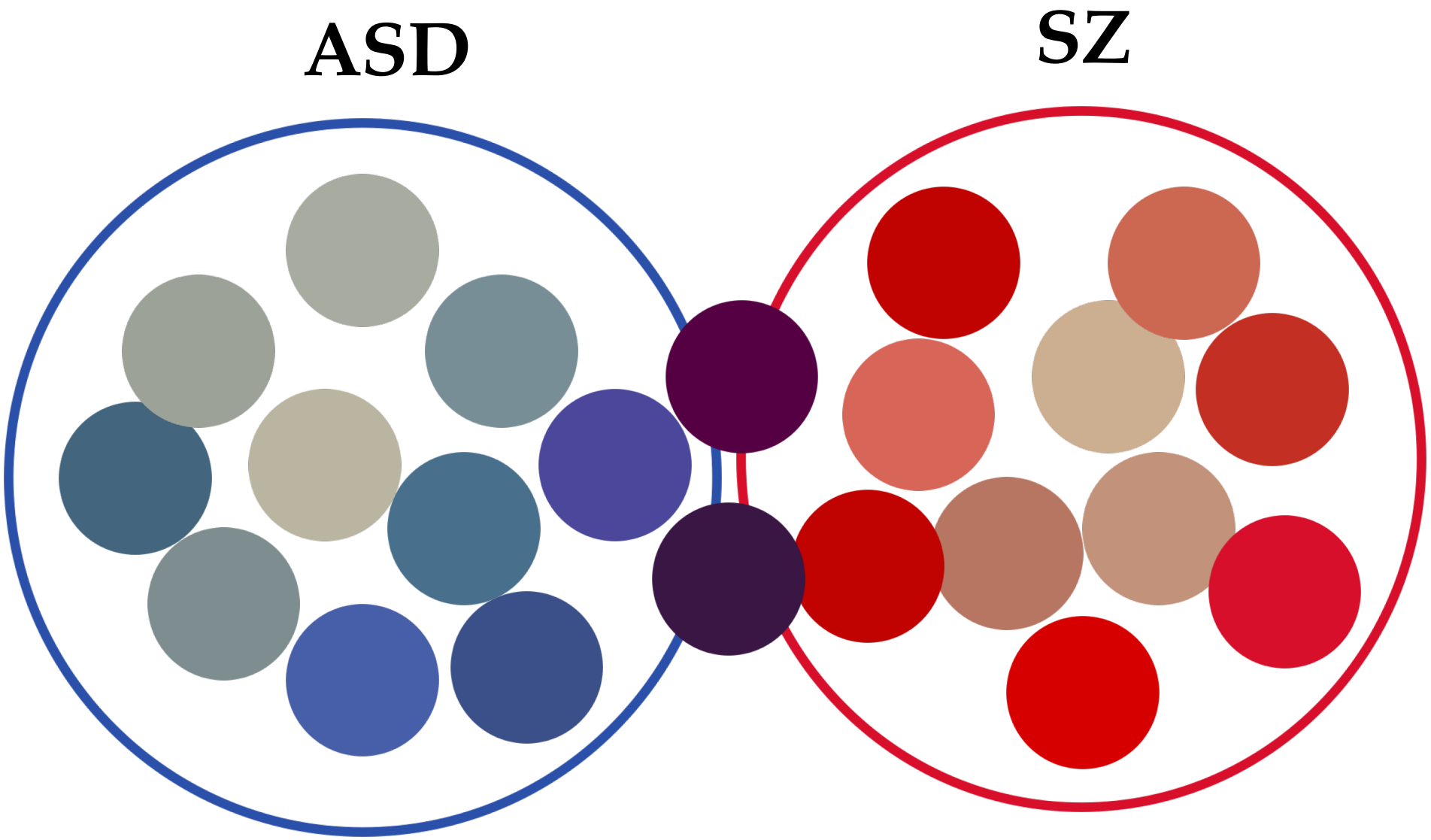

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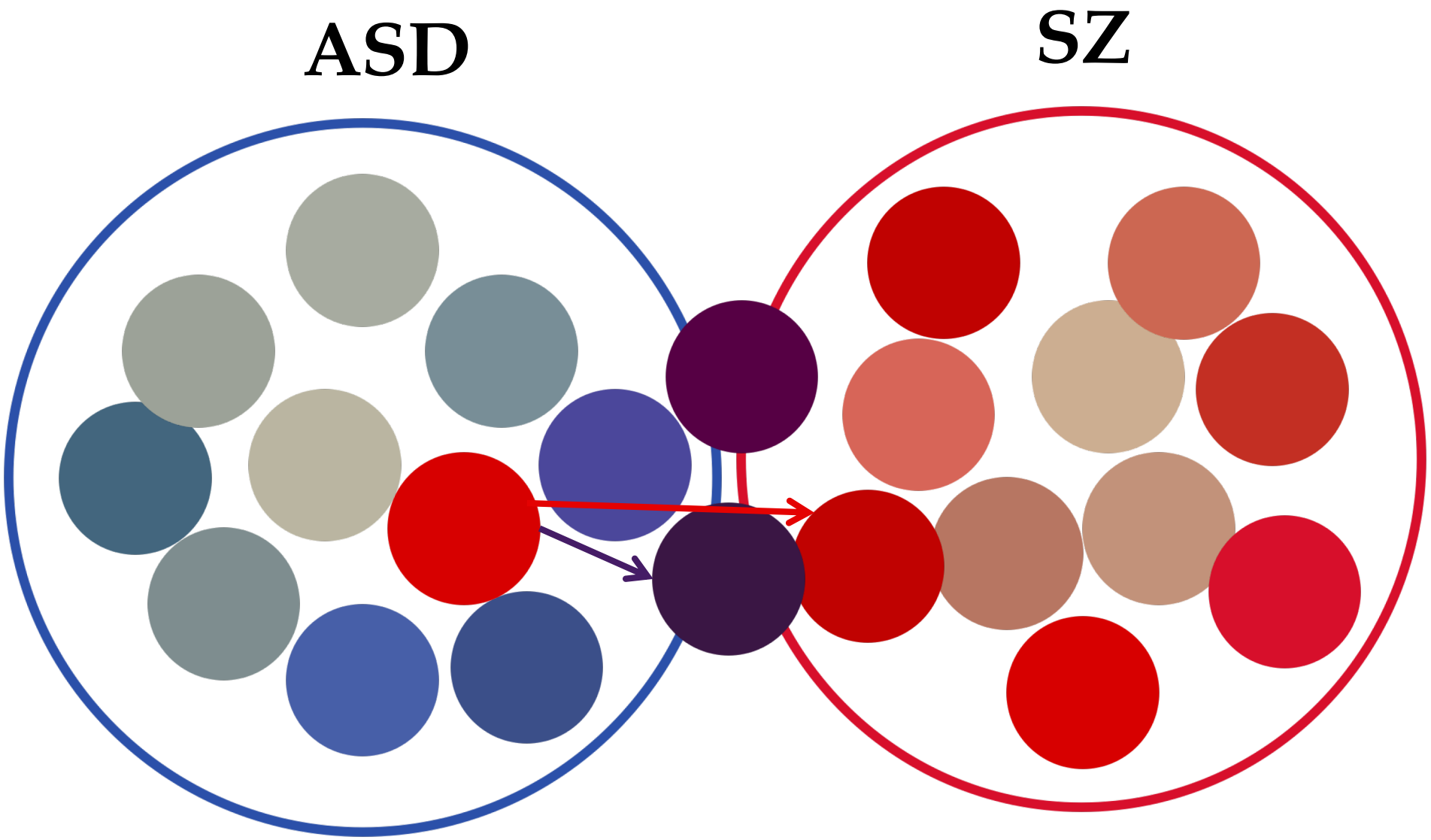

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COMMON CLINICAL RESEARCH FINDINGS

- Social
  - Theory of mind deficits
  - Face, affect, emotion, voice recognition deficits
- Sensory
  - Heightened sensory perception
  - Atypical local/global visual processing
- Cognitive
  - Impaired attention, processing speed, working memory
  - Difficulty with set-shifting, executive dysfunction

OVERLAPPING DIAGNOSES

Table 1 Psychosis and schizophrenia (SCZ) in adults with autism spectrum disorder (ASD) diagnoses

Reference	Number	Diagnosis	Age (years)	Psychotic symptoms
Tantam (1991)	85	ASD	Adult	21% psychosis 4% SCZ
Tantam (1988)	60	Autism, 46	16–65, mean 24	12% psychosis
Wing (1981)	18	ASD	16+	50% SCZ spectrum
Szatmari et al. (1989)	16	Autism, IQ >68	Mean 26	25% hallucinations
Konstantareas & Hewitt (2001)	14	Autism, high functioning	17–33, mean 25, males	50% SCZ

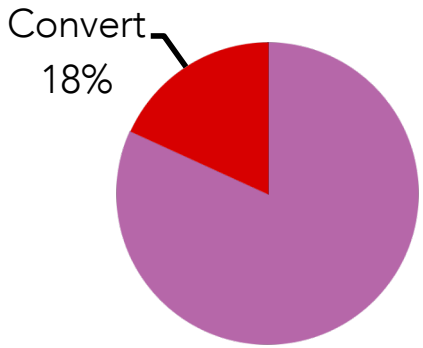
deLacy & King, 2013

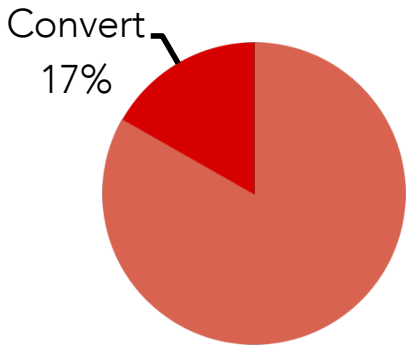
PSYCHOSIS RISK IN ASD

- Psychosis symptoms and conversion in clinical-high risk (CHR), with and without premorbid ASD diagnosis

	CHR/ASD+	CHR/ASD-
SOPS positive sx	12.12 (3.57)	11.91 (3.82)
SOPS negative sx	13.50 (4.84)	11.83 (6.10)
SOPS disorganization sx	6.08 (3.11)	5.13 (3.16)
SOPS general sx	8.65 (4.22)	9.18 (4.27)

- Social anhedonia greater in CHR/ASD+
- No symptoms less severe in CHR/ASD+





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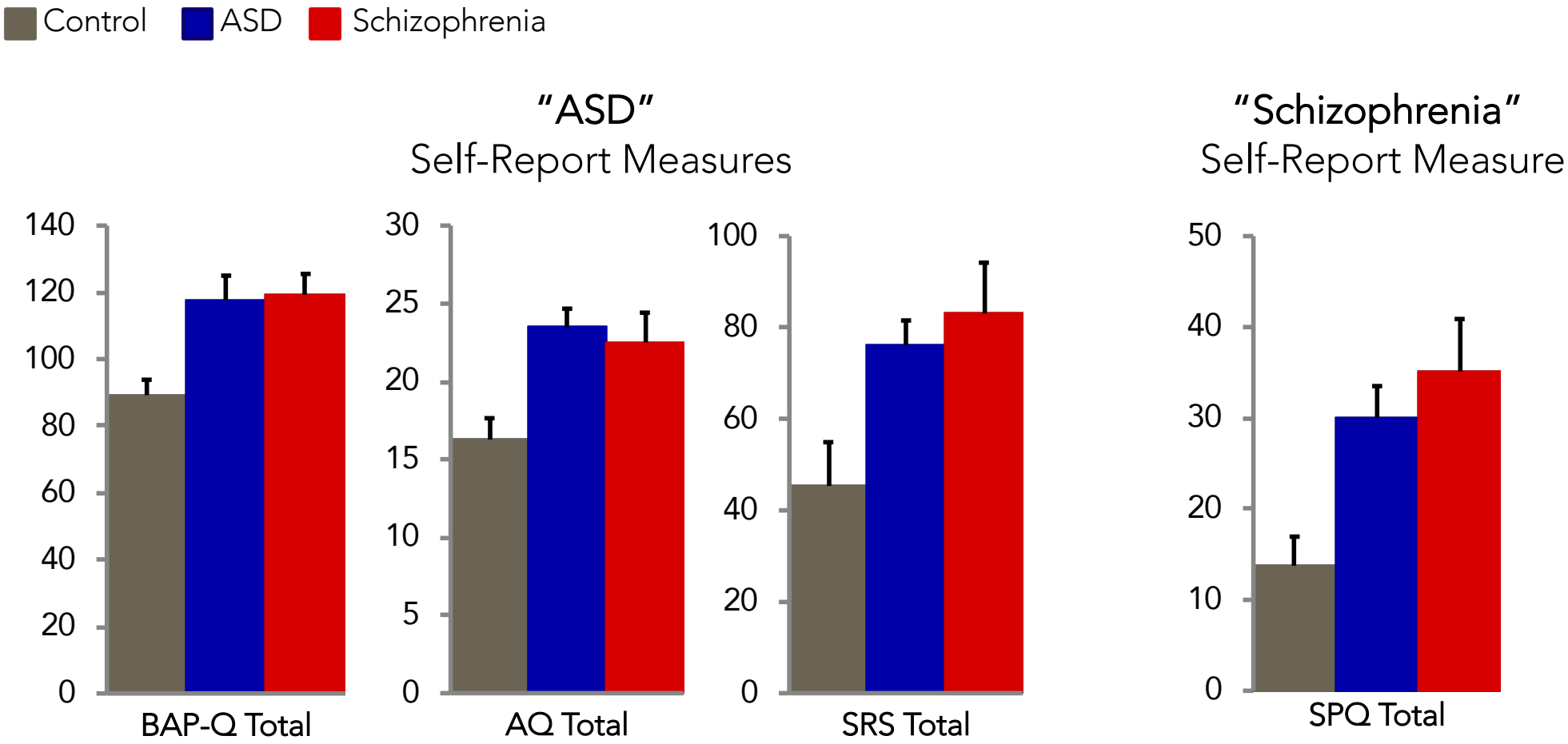
Foss-Feig, Velthorst, & NAPLS consortium, JAACAP, 2019

SELF-REPORT OF CLINICAL SYMPTOMS



- Self-report measures of ASD and schizophrenia features do not differentiate the two groups in adulthood

CLINICAL ASSESSMENT OF SYMPTOMS: ASD

ADOS SENSITIVITY AND SPECIFICITY		DSM Diagnosis	
		ASD (n=54)	Schizophrenia Spectrum (n=40)
ADOS Classification	Autism	50%	25%
	ASD	22.2%	17.5%
	Non-spectrum	27.8%	57.5%
		Sensitivity: 72.2%	Specificity: 57.5%

- Clinician-administered measures are somewhat better at differentiating diagnosis
- Over 40% of SZ participants met criteria for ASD on a "gold-standard" tool
- At least 3 participants in the SZ stream also had history consistent with ASD

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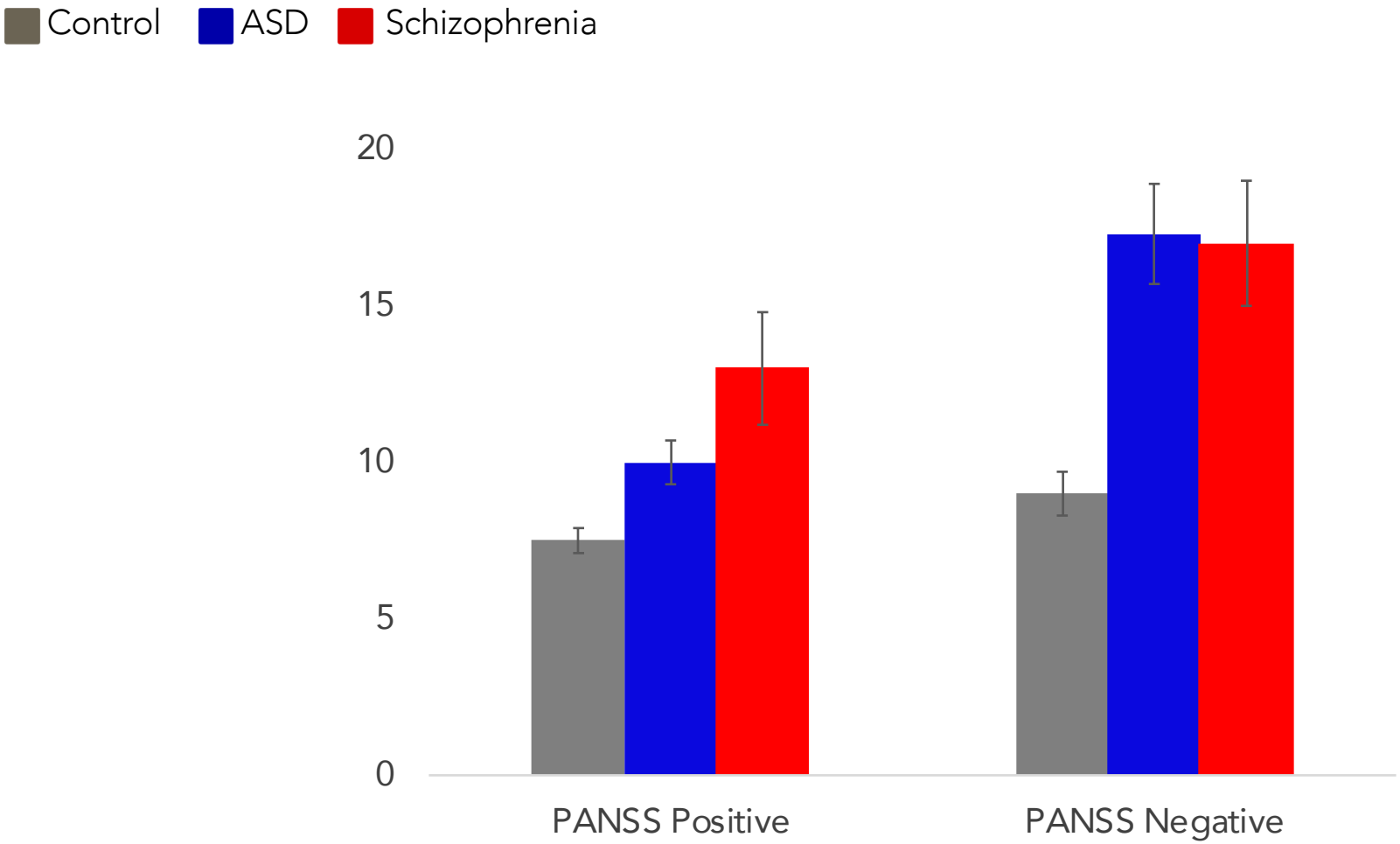
Trevesan et al., in prep

CLINICAL ASSESSMENT OF SYMPTOMS: SCHIZOPHRENIA



- Individuals with ASD displayed fewer positive symptoms of schizophrenia
- The Negative scale of the PANSS did not differentiate ASD and schizophrenia

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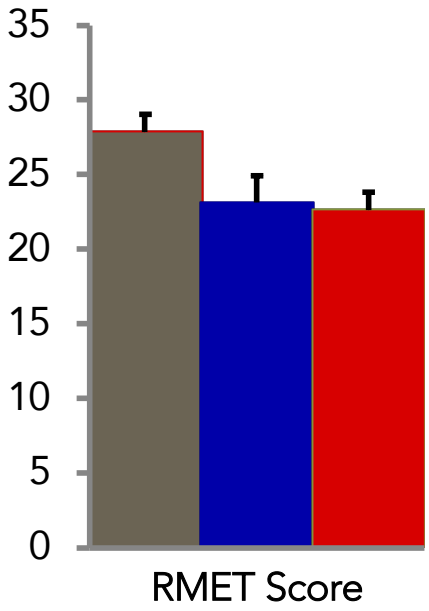
Trevesan et al., in prep

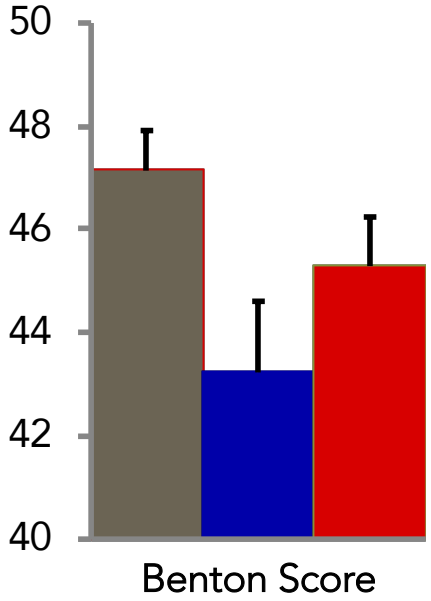
CLINICAL ASSESSMENT OF SOCIAL FUNCTION

Control ASD Schizophrenia

Underlying Process:
Emotion Recognition



Underlying Process:
Face Recognition



- Process-based measures may differentiate core features that are affected within and across groups

Altschueler et al., under review

GENETIC OVERLAP

Table II

Genomic regions and genes associated with both autism and schizophrenia

Chromosome	Gene(s)	Schizophrenia data	Autism data	Comment
22q11.2 (3 Mb hemizygous deletion)	> 50	Many studies + 4 cases COS, COS>AOS	30%PDD[71]	Nonspecific risk but both increased; [71]
16p11.2	24	500kb duplication in 2% of NIMH COS cohort[58]	1% of 5 autism populations have microdeletion or duplication[43, 48, 49]	COS CNVs both inherited; one case has comorbid PDD[58]
2p16.3	NRXN1	MZ twins concordant for COS with deletion; affected sib pair with inherited deletion[56, 58]	Deletions, disruptions, and mutations identified in several cases[48, 51, 52, 54, 72]	Growing evidence for both autism and COS; different regions of gene affected
Xq28	MECP2	1 case reported with mutation[73]	Rett's gene; autism Increased	Strong data for autism
1q42	DISC1	Disrupted gene identified in single large multiplex pedigree; numerous association studies[74]	Single association study with same haplotypes reported for schizophrenia[60]	Strong evidence for schizophrenia
7q35-q36.1	CNTNAP 2	Deletions in 2 unrelated patients[75]	Linkage, association, and gene expression in autism [76, 77]	Growing evidence in both schizophrenia and autism
7q22.1	RELN	Decreased mRNA in postmortem brain linkage[70] & association with working memory[78, 79]	Many linkage, association, and functional studies [40, 80]	
2q31.1	GAD1 (encodes GAD67)	10 studies show decreased GAD67 in schizophrenia postmortem brain[81]; 2 studies show association[82, 83]	Protein reduced in postmortem brain[84, 85]; multiple studies report linkage in region	

COS- Childhood Onset Schizophrenia, AOS – Adult Onset Schizophrenia, CNV – Copy Number Variation, MZ – Monozygous, mRNA – messenger RNA

Rapoport et al., 2009

GENETIC OVERLAP

Table 5 Candidate genes validated in both schizophrenia (SCZ) and autism spectrum disorder (ASD)

Gene	Grouping	Function	Other phenotypes
RELN	ND	Neuronal migration guidance matrix, polarization	Lissencephaly, Alzheimer's disease
DISC1	ND	Many stages of neural development, synaptic plasticity Regulates *mTOR/AKT, Wnt*	Depression, bipolar disorder
FOXP2	ND	Regulates *DISC1*, *CTNAP2*. Neural plasticity, speech	Developmental verbal dyspraxia
BDNF	ND	Neurotrophic factor. Regulates *mTOR/AKT*	Alzheimer's disease, Huntington's disease
MECP2	ND	Epigenetic regulator	Rett syndrome, PPM-X
UBE3A	ND	Epigenetic regulator	Angelman syndrome
MHC	Immune	Many candidate genes for ASD and SCZ in large complex. Immune regulation	Immune
NLGN3	Scaffold	Postsynaptic stabilization and function: complexes with NRXN	NAD
NLGN4	Scaffold	Postsynaptic stabilization and function: complexes with NRXN	ID
NRXN1	Scaffold	Presynaptic stabilization and function: complexes with NLGN	Pitt-Hopkins phenotype
SHANK3	Scaffold	Scaffold protein in postsynaptic density of glutamatergic synapse	ID
NRCAM	Scaffold	Neuronal cell adhesion and axon cone growth	Addiction
CNTNAP2 *CNTNAP4*	Scaffold	Cell adhesion, axonal differentiation	ID, Pitt-Hopkins phenotype, epilepsy, language impairment
GRIN2B	Scaffold	NMDA receptor subunit	ID, epilepsy
NTNG1	Guidance	Axon guidance	Bipolar disorder
GABRB3 *GABRA5*	NT	GABA receptor subunits	Bipolar disorder
GAD	NT	Conversion of glutamate to GABA	Epilepsy
CACNA1C	NT	Voltage-dependent calcium channel subunit	Bipolar disorder, Brugada and Timothy syndromes
SLC25A12	NT	Solute channel protein, mitochondrial membrane	Mitochondrial disorders
OXTR/OXT	NM	Oxytocin receptor Oxytocin gene	NAD
ZNF804A	Not known	Transcription regulator of *PRSS16*, *COMT*	Bipolar disorder

"Guidance" indicates dendrite and axon guidance and organization.
Abbreviations: GABA, gamma-aminobutyric acid; ID, intellectual disability; NAD, not adequately defined; ND, neurodevelopment; NLGN, neuroligin; NM, neuromodulation; NMDA, *N*-methyl-D-aspartate; NRXN, neurexin; NT, neurotransmission; PPM-X, psychosis, pyramidal signs, Parkinsonism, and macroorchidism syndrome.

Table 6 Validated copy number variants implicated in both autism spectrum disorder (ASD) and schizophrenia (SCZ)

Region	Type	Morph	Validated phenotypes	Candidate genes in region
1q21.1	Del	Y	SCZ, ASD, ID, IGE, ADHD, BAD	NAD
1q21.1	Dup	N	ASD, ID, ADHD	NAD
2p16.3	Del	N	SCZ, ASD, ID, Pitt-Hopkins phenotype, IGE	*NRXN1*
3q29	Del	Y	SCZ, ID, BAD, ASD	*PAK2*, *DLG1*
3q29	Dup	Y	ID	NAD
15q11.2	Del	Y	ID, DD, SCZ, ASD, IGE, OCD, MDD	*CYFIP1*
15q11-13	Dup	Y	SCZ, ASD, ID, IGE, ataxia	*GABRA5*, *GABRB3*, *GABRG3* + 17 others
15q13.3	Del	Y	SCZ, ASD, ID, IGE, ADHD, BAD	*CHRNA7*
16p11.2	Del	Y	SCZ, ASD, ID, learning disorder	*DOC2A*, *ERK1*
16p11.2	Dup	Y	SCZ, ASD, ID, DD, BAD	*DOC2A*, *ERK1*
16p13.11	Del	Y	SCZ, ASD, ID, IGE, ADHD	*NDE1*
16p13.11	Dup	Y	ASD, ID, ADHD	*NDE1*
17q12	Del	Y	SCZ, ASD, ID	NAD
22q11.2	Del	Y	SCZ, ASD, ID, ADHD, epilepsy (rare)	*PRODH*, *COMT*, *DGCR6*, *TBX1*
22q11.21	Dup	Y	ID, DD (mild)	*PRODH*, *COMT*, *DGCR6*, *TBX1*
22q13.3	Del	Y	ID, DD, ASD, SCZ (*SHANK3*)	*SHANK3*

"Morph" indicates dysmorphism has been noted in cases.
Abbreviations: ADHD, attention deficit hyperactivity disorder; DD, developmental delay; ID, intellectual disability; IGE, immunoglobulin E; MDD, major depressive disorder; NAD, not adequately defined; OCD, obsessive-compulsive disorder.

deLacy & King, 2013

NEUROBIOLOGICAL OVERLAP

- Atypical brain specialization
- Functional under-/over-connectivity
- Resting state alterations
- Excitatory/inhibitory neurotransmitter imbalance
- Predictive coding deficits
- Social brain dysfunction
- Neural inflammation

NEUROBIOLOGICAL OVERLAP

OPEN ACCESS Freely available online

PLOS ONE

Structural Alterations of the Social Brain: A Comparison between Schizophrenia and Autism

Daniel Radeloff[1]*, Angela Ciaramidaro[1], Michael Siniatchkin[1], Daniela Hainz[1], Sabine Schlitt[1], Bernhard Weber[2,5], Fritz Poustka[1], Sven Bölte[1,3], Henrik Walter[2,4], Christine Margarete Freitag[1]

RESEARCH ARTICLE

Shared Atypical Default Mode and Salience Network Functional Connectivity between Autism and Schizophrenia

Heng Chen, Lucina Q. Uddin, Xujun Duan, Junjie Zheng, Zhiliang Long, Youxue Zhang, Xiaonan Guo, Yan Zhang, Jingping Zhao, and Huafu Chen

Brain Imaging and Behavior (2017) 11:1823–1835
DOI 10.1007/s11682-016-9648-9

ORIGINAL RESEARCH

Diametrical relationship between gray and white matter volumes in autism spectrum disorder and schizophrenia

Serge A. Mitelman[1,2] · Marie-Cecile Bralet[3,4,5] · M. Mehmet Haznedar[1,6] · Eric Hollander[7] · Lina Shihabuddin[1] · Erin A. Hazlett[1,8] · Monte S. Buchsbaum[9]

Social Neuroscience

ISSN: 1747-0919 (Print) 1747-0927 (Online) Journal homepage: https://www.tandfonline.com/loi/psns20

Autism and psychosis expressions diametrically modulate the right temporoparietal junction

Ahmad M. Abu-Akel, Ian A. Apperly, Stephen J. Wood & Peter C. Hansen

ELSEVIER

Available online at www.sciencedirect.com
ScienceDirect
Schizophrenia Research 99 (2008) 164–175

SCHIZOPHRENIA RESEARCH

www.elsevier.com/locate/schres

Neural bases for impaired social cognition in schizophrenia and autism spectrum disorders

Amy E. Pinkham [a,*], Joseph B. Hopfinger [a], Kevin A. Pelphrey [b], Joseph Piven [c], David L. Penn [a,d]

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Schizophr Res. 2017 May ; 183: 102–109. doi:10.1016/j.schres.2017.03.009.

Social-Cognitive Brain Function and Connectivity During Visual Perspective-Taking in Autism and Schizophrenia

Shaun M. Eack[1,2,5], Jessica A. Wojtalik[1], Matcheri S. Keshavan[2,3], and Nancy J. Minshew[2,4]

OPEN ACCESS Freely available online

PLoS one

Autism Spectrum Disorders and Schizophrenia: Meta-Analysis of the Neural Correlates of Social Cognition

Gisela Sugranyes[1,2,3], Marinos Kyriakopoulos[2,4], Richard Corrigall[4], Eric Taylor[1], Sophia Frangou[2]*

146 *Current Molecular Medicine* 2015, *15*, 146-167

Common Mechanisms of Excitatory and Inhibitory Imbalance in Schizophrenia and Autism Spectrum Disorders

R. Gao[1,2] and P. Penzes[*,1,2]

)31-3998/11/6905-0026R
EDIATRIC RESEARCH

Vol. 69, No. 5, Pt. 2, 2011
Printed in U.S.A.

Schizophrenia and Autism: Both Shared and Disorder-Specific Pathogenesis *Via* Perinatal Inflammation?

URS MEYER, JORAM FELDON, AND OLAF DAMMANN

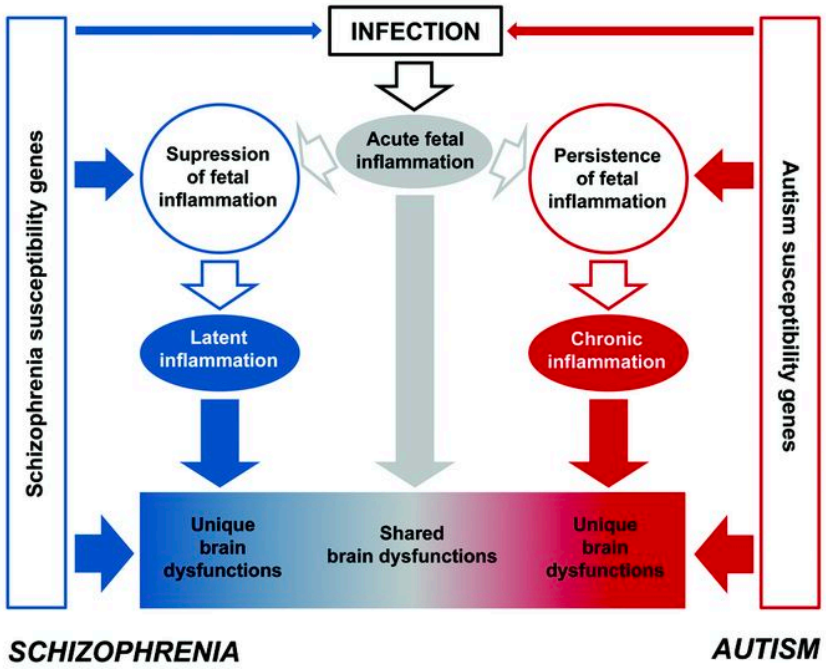
seaver autism center for research & treatment @ mount sinai

NEUROBIOLOGICAL OVERLAP

- Atypical brain specialization
- Functional under-/over-connectivity
- Resting state alterations
- Excitatory/inhibitory neurotransmitter imbalance
- Predictive coding deficits
- Social brain dysfunction
- Neural inflammation

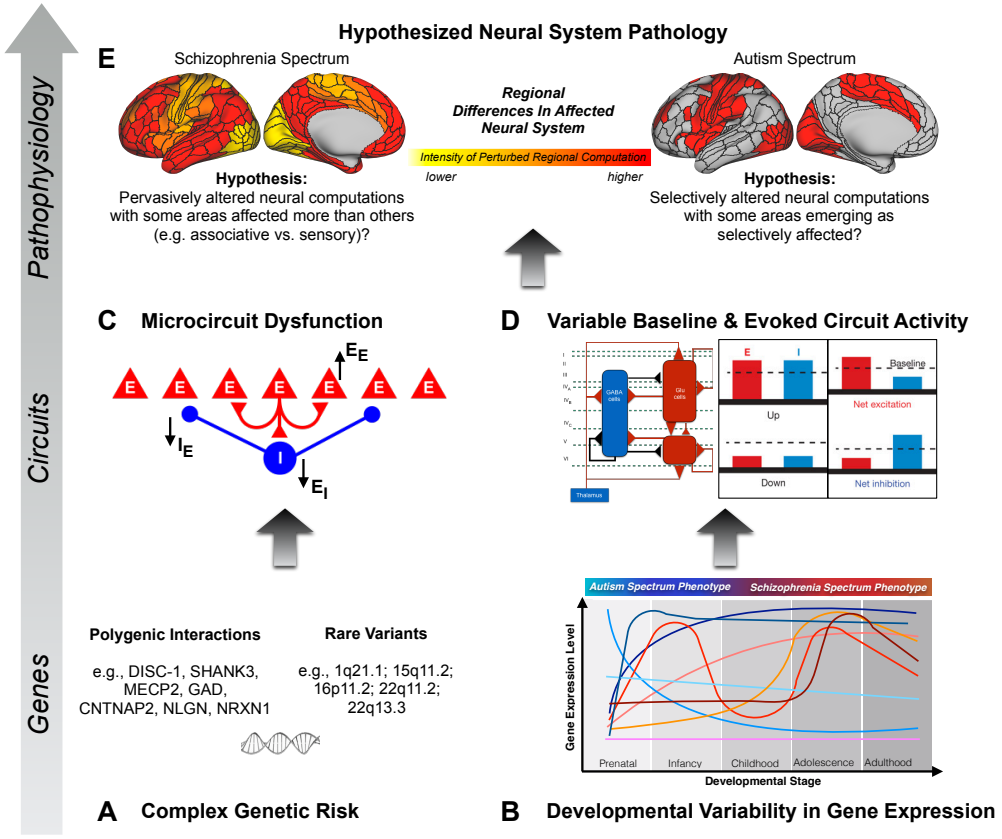
NEUROBIOLOGICAL OVERLAP

Perinatal Inflammation



Meyer et al., *2011*

E/I Imbalance



Foss-Feig et al., *Biological Psychiatry*, 2017

TALK OUTLINE

- Case Examples
- History of ASD and Psychosis
  - Diagnostic criteria and DSM
  - Psychosis prodrome
  - Childhood onset schizophrenia
- Research Findings
  - Clinical overlap
  - Genetics and neurobiology
- Clinical Implications
  - Differential Diagnosis
  - Treatment Implications

DIFFERENTIAL DIAGNOSIS: CASE EXAMPLE 3

"Elijah": 9yo M

- Delayed speech (words 2.5 years; sentences 4.5 years)
- No friends or interest in engaging peers
- Minimal conversation
- Limited eye contact
- Carries stuffed animal with him everywhere
- Past anxiety diagnosis related to compulsive behaviors and difficulties with changes in routine

But also:

- "Happy daydreams," increasing in frequency
- Communication with imaginary family, increasing in intensity and interference

CASE EXAMPLE 3: BEHAVIORAL OBSERVATIONS

- Little conversation
  - Responded to questions
  - Made social overtures by making comments, but out of context
  - Monotone speech
- Persistent body rocking
- Perseverative on specific topics
- Delayed latency in verbal responses
- Inappropriate smiling while gazing to corners of the room
- Talked to self when examiner was less engaged

CASE EXAMPLE 3: ASD ASSESSMENTS

- Lifetime History (SCQ with follow up interview)
  - Delayed language with idiosyncratic use; concrete interpretation of language
  - Limited interest in and ability to form friendships, limited shared enjoyment
  - Atypical non-verbal communication (e.c., affect)
  - Unusual preoccupations, difficulty with transitions, unusual motor mannerisms
- Current Presentation (ADOS)
  - Atypical intonation; limited complex speech
  - Few descriptive gestures and flat affect
  - Failed to pick up on bids from the examiner
  - Limited imaginative play
  - Motor mannerisms
  - Excessive focus on narrow topic of interest (train set)

CASE EXAMPLE 3: PSYCHOSIS ASSESSMENTS

- Clinical Interview
  - Reported both auditory and visual hallucinations
  - Little insight into their origin
- Parent Rating (CBCL)
  - Elevated atypicality, withdrawal; deficits in social skills and adaptability
- Teacher rating (CBCL)
  - Elevated anxiety, attention problems, atypicality, withdrawal; deficits in socials skills

CASE EXAMPLE 3: DIAGNOSTIC CONCLUSIONS

- Diagnoses
  - ASD
  - Psychosis NOS*
- Remaining questions:
  - Are these disorders comorbid for Elijah?
  - Might he have a variant of ASD/SZ that hovers the line between the two disorders?
  - Could early ASD traits have been a precursor for COS?
  - What about a genetic disorder?

CASE EXAMPLE 3: RECOMMENDATIONS

- Psychopharmacology
- Consider anti-psychotic medication
- Social skills training
- Individual therapy to build reality testing
- Parent education
- Environmental accommodations
- Longer-term follow up and continued differential

DIFFERENTIAL DIAGNOSIS GUIDELINES

- Consider developmental history
- Consider family history
- Consider change in functioning over time
  - Declines, loss of skills, change in ADLs
  - Emergence of new symptoms
- Consider "positive" symptoms of each disorder
  - Motor mannerisms, stereotyped language, restricted interests
  - Delusions, disorganized thought/speech, hallucinations

- Be wary of giving additional diagnoses
- Also be wary of not (diagnostic overshadowing)

- *Remember the opposite is also sometimes true… patients can be suspected of or diagnosed with SZ when in fact it's unidentified ASD*

POSSIBLE TREATMENT GUIDELINES

- Follow over time
- Trial of antipsychotics
  - Some research that they're effective in prodrome
  - Also approved for ASD
  - Though less effective for COS than adult SZ, response of presumed hallucinations and delusions could be informative diagnostically
    - Clozapine better than both haloperidol and olanzapine
- Psychosocial Interventions
  - Social skills training
  - Parent education and communication training
  - Individual therapy re: reality testing skills
  - Environmental accommodations
  - Cognitive remediation?

CONCLUSIONS

- There's good evidence that, at least in some cases, there's overlap between ASD and psychosis
- Research on this topic (either clinical or basic science) has been limited until quite recently
  - MCDD
  - RDoC
- Information on clinical course, prognosis, and best practice treatment is limited
  - More attention to this topic is needed

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Awarding NARSAD Grants

AUTISM SCIENCE FOUNDATION

seaver autism center for research & treatment @ mount sinai

End