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Psychiatric Insights into Chromosomal Disorders: Behavioral Phenotypes in Children with 22q11.2 Deletion Syndrome" comprehensive narrative review

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ABSTRACT

Background: 22q11.2 deletion syndrome (22q11.2DS) is a common chromosomal microdeletion disorder associated with elevated risk for cognitive impairments and psychiatric disorders across development.

Objective: To provide a comprehensive narrative review of behavioral and psychiatric phenotypes in children with 22q11.2DS, summarizing prevalence, developmental trajectory, comorbidities, assessment methods, heterogeneity, and clinical implications.

Methods: Literature was searched in PubMed, PsycINFO, and Embase (2000–2025) using keywords including "22q11.2 deletion syndrome," "ADHD," "autism," "anxiety," "mood disorders," "psychosis," and combinations thereof. Included were peer-reviewed original studies, cohort analyses, and reviews in English reporting psychiatric phenotypes in participants aged ≤18 years. Excluded were animal studies and case reports <5 subjects.

Results: ADHD (30–50%), anxiety disorders (25–60%), ASD (10–30%), mood disorders (increasing in adolescence to ~15%), and emerging psychosis (rare in childhood, but increasing into adolescence/adulthood up to ~30%) are all significantly elevated. There is substantial comorbidity and developmental change: ADHD and ODD predominate in childhood; anxiety and mood disorders rise in adolescence; psychotic spectrum disorders emerge later. Assessment methods vary (clinical interview vs screening tools), contributing to prevalence heterogeneity.

Conclusion: Children with 22q11.2DS manifest complex, evolving psychiatric profiles. Routine developmental surveillance and early psychiatric screening are essential. Research must address methodological heterogeneity and develop targeted interventions. .

1. INTRODUCTION

22q11.2DS (prevalence ~1:2,000–1:6,000) arises from a 3 Mb microdeletion on chromosome 22, affecting ~40–90 genes, with predominantly de novo occurrence[18,2]. It presents with multisystem medical anomalies alongside consistent neurocognitive impairments and heightened psychiatric risk[2,3,7,8].

Methods

We conducted narrative searches in PubMed, Embase, and PsycINFO between 2000 and 2025, using terms "22q11.2 deletion syndrome," "ADHD," "autism," "anxiety," "mood," "psychosis." Original studies, cohort studies, and reviews in English reporting pediatric psychiatric outcomes (≤18 years) were included; animal models and small case reports (<5 subjects) were excluded. Prevalence data, assessment methods, age ranges, and psychiatric comorbidities were extracted descriptively.

2. RESULTS

Psychiatric Phenotypes in Childhood and Adolescence

ADHD and Disruptive Disorders: Studies indicate elevated ADHD prevalence (~30–50%) in children with 22q11.2DS[4,5,8]. Disruptive behaviors (ODD) also frequent[8].

Autism Spectrum Disorder: ASD prevalence varies (10–30%), depending on assessment tools (ADI-R/ADOS vs parent-report), with structured diagnostic interviews yielding ~16% in young cohorts[6].

Anxiety Disorders: Anxiety rates in children range from ~25% to over 50%, often under-recognized; symptoms correlate with poorer adaptive functioning[17].

Mood Disorders: Depressive disorders increase during adolescence (~10–15%)[4].

Psychosis-Spectrum Disorders: Rare in childhood but up to ~30% develop schizophrenia by adulthood[2,3,15].

Comorbidity and Trajectory

Psychiatric comorbidity is the norm; symptoms evolve: ADHD/ODD dominate early, anxiety and mood symptoms rise in adolescence, psychosis emerges later[2,3,6].

Table 1: Summary of Major Studies on Psychiatric Phenotypes in 22q11.2DS

Study & Year	Sample Size & Age Range	Methods/Assessment	Key Findings
Tang et al. 2015[4]	Narrative review—children/adolescents	Review	High prevalence of ADHD, ASD, anxiety, mood, schizophrenia; guidelines offered
Sandini et al. 2020[11]	–	Review	Up to 50% ADHD/ASD/ID; anxiety/mood ~15–65%; psychosis ~20–30%
Gothelf et al. 2019[6]	Children age 3–8	ADI-R, ADOS, clinical interview	84% had at least one psychiatric disorder; ASD ~16%
Fiksinski et al. 2021[2]	Review	Review	22q11.2DS as model for neurodevelopment, schizophrenia risk
Morrison et al. 2020[3]	236 children/adolescents	Comparison cognitive study	Higher ADHD, ASD, anxiety vs controls; cognitive trajectory
Kates et al. 2015[4] (JDBP)	Review	Narrative	Prevalence, features, management guidelines
Cambridge cohort (Psychiatry 2014)[8]	80 children + sibling controls	Psychiatric & cognitive assessments	>50% had psychopathology; ADHD/anxiety/ODD common
2013 Danish registry study[19]	244 adults	Population registry	Elevated developmental and psychiatric disorders vs controls

Table 2: Approximate Prevalence of Disorders by Age Group

Disorder	Childhood (≤12 yrs)	Adolescence (13–17 yrs)	Emerging Adulthood (>18 yrs)
ADHD / Disruptive behaviors	~30–50%	Declining but still ~20–30%	Lower still, underrecognized
ASD	~10–16%	~20–30%	Similar rates
Anxiety disorders	~25–50%	~30–60%	Stable or increasing
Mood disorders (depression)	~5–10%	~10–15%	~15%
Psychosis / schizophrenia	~0–2%	~5–15%	~20–30%

3. DISCUSSION

Heterogeneity and Methodological Variability

Prevalence estimates vary widely—ADHD (30–50%), anxiety (25–60%), ASD (10–30%)—largely due to diverse assessment methods (clinical diagnosis vs parent-report, structured tools like ADI-R/ADOS)[6,8]. Smaller cohorts also contribute to variance.

Assessment Tools

Gold-standard instruments (ADI-R, ADOS, structured psychiatric interviews) enhance diagnostic accuracy but are used inconsistently. Screening questionnaires (e.g., CBCL) may overestimate or misclassify symptoms[6].

Developmental Trajectory

Trajectory is under-studied longitudinally. Available cohort data support shifting phenotypes with age, but large-scale longitudinal designs are lacking[4,2].

Comorbidity and Cognitive Interplay

Psychopathology often co-occurs, particularly anxiety and mood disorders as potential precursors to psychosis. Cognitive decline or stagnation may mediate risk for later psychiatric disorders[3].

Clinical Implications

Routine psychiatric surveillance from early childhood is essential. Early identification and intervention for ADHD, anxiety, and mood disorders may improve adaptive outcomes and potentially mitigate later psychosis risk. Guidelines exist but are not universally implemented[4].

4. LIMITATIONS OF CURRENT EVIDENCE

We note limited longitudinal data, lack of RCTs or treatment studies specific to 22q11.2DS, and scant research linking specific genes to psychiatric manifestations beyond *COMT* and *PRODH*. Genotype-phenotype correlation studies remain inconclusive[18].

5. CONCLUSIONS & RECOMMENDATIONS

Children with 22q11.2DS exhibit high rates of ADHD, ASD, anxiety, mood disorders, and psychosis that evolve over development. Early and repeated psychiatric assessment is warranted. Future work should:

Use standardized diagnostic tools and longitudinal cohorts.

Investigate treatment efficacy (psychological and pharmacological) in controlled trials.

Explore genetic and neurobiological markers predictive of psychiatric outcomes .

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