

Why is it important to study fHR?

Clinical perspectives from mental health services

Dr. Michele Poletti, Azienda USL-IRCSS or Reggio Emilia, Italy,
on Behalf of Prof. Andrea Raballo, University of Italian Switzerland, Lugano

Clinical vignettes Case 1

- M.D. 11-year-old male offspring of a parent diagnosed with schizophrenia
- Help-seeking for increasing difficulties in school proficiency and increasing subjective suffering
- The multi-layer psychopathological assessment revealed:
 - Clinical High-Risk for Psychosis (CHR-P), subgroup Attenuated psychosis syndrome (APS)
 - subjective feeling of cognitive deficits, in absence of intellectual disability
 - pervasive distortions of subjective experiences (aka anomalous self-experiences, or Self-disorders)

Clinical vignettes Case 2

- C.Z., 10-year-old female, offspring of a parent diagnosed with schizoaffective disorder (depressed mood, paranoid trait)
- Exposed from birth to socially-deprived contexts, interacting only with close relatives (her family, maternal grand-parents, family of maternal uncle) in a single building house
- Attended kindergarten only from 5 years of age
- Manifests severe selective mutism and later a social anxiety disorder

Intergenerational transmission of risk for mental illness

- What is the relation (if any) between the psychopathological manifestations in the offspring and the disorder diagnosed to the parent?
- Do they play a prognostic role? Does it insist on familiarity, shared environment and/or overall concentration of enduring psychological suffering within the family?

Intergenerational transmission of risk for mental illness

Case 1

- **Homotypic continuity**
- Psychopathological manifestations appear similar across generations
- Early expressed phenotypically in the offspring in terms of schizotaxia, self-disorders, and attenuated psychosis syndrome

Intergenerational transmission of risk for mental illness

Case 2

- **Heterotypic continuity**, i.e. the psychopathological manifestations do not appear in strict continuity across generations
- Schizoaffective disorder in the parent and selective mutism + social anxiety disorder in the offspring do not formally belong to the same psychopathological cluster
- Heterotypic continuity suggests other pathomorphic factors over and above the putative familial risk
- Environmental factors may include a troubled or hypo-stimulating parenting, poorly scaffolding the development of socio-relational abilities

Intergenerational transmission of risk for mental illness

Homotypic continuity

Focus on genetic risk constraining development toward similar psychopathological manifestations in offspring

Linear perspective, easier to detect and investigate across generations

Example

Genetic vulnerability for psychosis in the Clinical High-Risk Psychosis paradigm (CHR-P)

- Genetic Risk + Functional decline (GRFD subgroup)
- Limits: role of genetic vulnerability obscured by clinical symptoms



Looking at Intergenerational Risk Factors in Schizophrenia Spectrum Disorders: New Frontiers for Early Vulnerability Identification?

Michele Poletti¹, Eva Gebhardt², Lorenzo Pelizza³, Antonio Preti⁴ and Andrea Raballo^{5,6*}

Intergenerational transmission of risk for mental illness

Heterotypic continuity

Focusing on the interaction of multiple genetic and environmental risk factors, conferring a nonspecific and non-deterministic intergenerational vulnerability for mental illness

More complex to disentangle if not limited to severe mental illness, since even parents' dysfunctional personality traits as interpersonal and emotional dysregulation may exert detectable consequences for offspring

Intergenerational transmission of risk for mental illness

Heterotypic continuity

Example of complex interactions

Nonrandom (assortative) mating between individuals with severe mental disorders is in itself an aggregator of both genetic and environmental risk factors

Mental health vulnerabilities may aggregate across the family tree and exponentially may increase the concentration of environmental early risk factors, from in utero exposure to obstetric complications and enduring familial stressful conditions, such as heightened expressed emotions, inadequate parenting, and social stigma.

Intergenerational transmission of risk for mental illness: translational preventive considerations

Applying Transgenerational Scientific Evidence
to the Next Wave of Early Identification Strategies
for Psychopathological Risk—Transdiagnostic,
Developmental, and Personalized

- Empirical evidence suggests that, in case of genetic risk for mental illness, unspecific endophenotypic features (especially in the neurocognitive and behavioral domains) are early expressed in childhood, with more specific psychopathological manifestations in adolescence
- This progression of risk suggests that early intervention may go beyond traditional transdiagnostic clinical staging (which mainly operates along symptom severity thresholds, from subclinical to clinically overt conditions) to adopt a broader, prevention-oriented transgenerational and developmentally sensitive stratification.

Intergenerational transmission of risk for mental illness translational preventive considerations

Applying Transgenerational Scientific Evidence
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- Such extended risk staging should incorporate early developmental dimensions of risk (deviations from developmental milestones, nonsecure attachment, early difficulties in peer relations and in school performance) along with consolidated evidence from transgenerational, family high-risk studies (family history of mental illness, presence of pervasively dysfunctional traits, poorly sensitive parenting)
- Such personal and family ecosystem—centered early Intervention may support prevention strategies and suitable service redesign, considering that parenting is a modifiable risk factor

Intergenerational transmission of risk for mental illness translational preventive considerations

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- An appropriate identification of potentially vulnerable parenting for stable or transient parent mental health conditions may be a reasonable preventive strategy that would allow low-burden, low-risk interventions aimed at supporting prenatal caregiving and the postnatal transformation of the family system.
- For example mothers with post-partum depression or severe mental illness may be less responsive to and less attuned with offspring needs, possibly triggering the developmental structuration of unsecure or disorganized attachment in children (an established risk factor for lifetime psychopathology).

Intergenerational transmission of risk for mental illness

Summary

Key points

- Homotypic vs heterotypic continuity across generations
- Genetic risk is not-deterministic and may lead to clinical expressivity if interacting with multiple (early and enduring) environmental risk factors
- Current early-intervention preventive strategies need to give more emphasis to developmental and fHR issues
- Preventive strategies may focus on modifiable risk factors as parenting

Thanks for attention