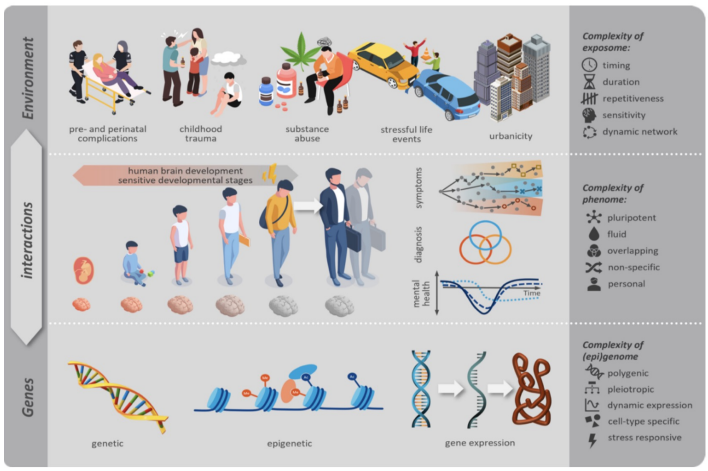
The Youth-GEMs project:

Gene environment interactions underlying trajectories of mental health in youth across Europe

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Introduction: Most mental disorders emerge before age 24, yet the mechanisms shaping youth mental health trajectories remain poorly understood. Evidence suggest that gene-environment interactions shape trajectories of mental health, albeit that robust evidence is scarce to date. Here, we present the Youth-GEMs consortium performing a multidisciplinaryresearch project funded by a European Union Horizon-Staying-Healthy-2021 grant.

Figure 1. Concept of gene-environment interplay

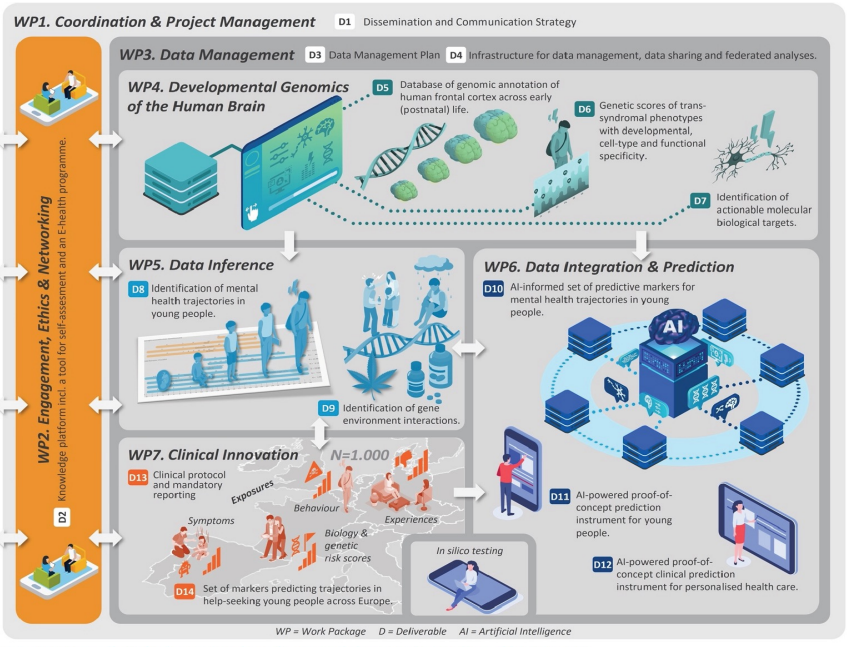


Methodology and approach: The Youth-GEMs project (Gene Environment interactions in Mental health trajectorieS of Youth) has an integrated, developmental framework that examines how genetic, epigenetic, and environmental factors dynamically interact to influence risk and resilience across adolescence and young adulthood. The project combines developmental (epi)genomic mapping of the human brain, genomic analyses of trans-syndromal phenotypes, exposome-wide environmental assessment, and Artificial Intelligence-based modelling to identify predictive and actionable markers of mental health trajectories of young people. By harmonizing multimodaldata from existing population-based cohorts and by establishing the first international, trans-syndromal clinical cohort of help-seeking young people, Youth-GEMs is generating biologically informed polygenic and exposomic scores, cell-type-specific regulatory annotations, and interpretable machine-learning models. Continuous engagement with young people, clinicians, and stakeholders ensures that findings translate into tools for early detection, monitoring, and personalized intervention.

Outcomes and results: To forge evidence-based breakthroughs, the Youth-GEMs project is providing and has (partially) provided the following outcomes and results

1. a multimodal set of studies on developmental trajectories based on a knowledge base of functional (epi)genomics of the human brain, see e.g. PMID: 40997811;
2. a multimodal robust, trans-syndromal mental health assessment battery for help-seeking young people;
3. innovative analyses in psychiatric genetics identifying genetic components of trans-syndromal phenotypes in a neurodevelopmental and environmental context;
4. assessment of the exposome in interaction with genetic background for mental health trajectories of young people,
5. employing Artificial Intelligence-based methodology to characterize mental health trajectories and to identify predictive and actionable markers of personal mental health trajectories;
6. scientific and social innovations and participation of young people, people with lived experiences and health care professionals directly in the project.

Figure 2. Overview of the project and work packages (WPs).



Conclusion: Together, these efforts are expected to advance mechanistic understandings of youth mental health, improve prediction of emerging illness, and support the development of evidence-based, developmentally sensitive approaches to prevention and care.

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