

Predicting the Pathways of Adolescents and Young Adults at High-Risk for Psychosis: Moving from Being Highly Vulnerable to Expressing Full-Scale Pathology using an Integrated Dynamic Network Approach Mapping Digitally Collected Ecologically Valid Data

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Introduction

Consolidated knowledge affirms that the early detection of Adolescents and Young Adults (AYAs) at high clinical risk for the development of psychosis (CHR-P) may lead to its prevention [1-4]. Acknowledging that in AYAs at high risk psychosis is a disorder of the developing brain and that behavior is the last step of a cascade that starts long before problems manifest themselves, implies that we probably should start with the brain development, wiring, and connections, with its ways of interacting with its surroundings and with its susceptibility to context [5]. Much variation exists in how the brain is wired and functions [6-8]. Still, this variation does not exclude the existence of some possible and predictable set of factors that put AYAs at a high risk of moving from being vulnerable to develop full-blown psychosis or, on the other hand, predicting who will not transition to psychosis [10-13]. Furthermore, knowing that experiences are biologically embedded, defining the (biological) susceptibility of each AYA to its environment would move us towards a novel understanding of risk and disability, future functioning, and resilience [14-16]. Considering this, the resulting phenotype is the emergent outcome of a dynamic system of progressively changing functions and structures that continuously interact with each other and with the environment [17].

Furthermore, high risk AYAs represent an enormously heterogeneous group, and currently identified risk factors cannot distinguish individual trajectories. At the same time, no treatment modality has proved to prevent the development of full-blown psychosis. Early recognition and prediction of the risk trajectory over time are even more critical, considering that psychosis does not need

to be a chronic disease if young individuals at heightened risk are detected early and preventive measures are put into place promptly [18-21]. However, if the distinct clinical pathways of AYAs at high risk for the development of psychosis are to be detected, predicted, and prevented and, consequently, personalized treatment modalities developed, then a paradigm shift is essential [22-24].

Description

New conceptual thinking will result in increasingly explanatory and predictive models [25,26] which may offer a more realistic image of the strengths and vulnerabilities of AYAs at CHR-P by stressing the dynamic nature of the underlying processes, which are context-sensitive, and, incidentally, tend to change over time. Abnormal phenotypic outcomes develop from modifications in basic procedures early in development (such as pruning, synaptogenesis, density of neurons, neuro/glia ratio) that are highly flexible, plastic, and open to extensive environmental influences [27,28]. Many individual predictive measures exist but little is known on how they relate to each other. The main challenge then is not to understand the role of each factor and context but the relationships and connections among them by constructing a dynamic network of interacting biological, genetic, behavioral, and psychosocial determinants to explain the individual variances of these young patients at heightened risk for psychosis. Using signs together with symptoms, objective indicators and behavioral symptoms, and screening indices would provide more quantitative measures of deficits, avoiding the exclusive use of clinical rating scales [29-31]. Furthermore, fractioning problems in various subtypes based on specific patterns of cognition, emotion,

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and behavior variables together with a more ecological risk assessment will improve the understanding of individual risk [32,33]. Innovative digital health technologies offer such an approach when incorporated into existing infrastructures and enable the use of various data sources. AYAs are not usually involved in the early design and research concerning their present and future health. Still, they want a role that genuinely influences the development of treatments for their unmet needs/priorities. To accomplish this, we need to build a new and trusted ecosystem that will allow data collection *via* mobile phones, tablets, Ecological Momentary Assessments (EMA), and other digital technologies, enabling these young patients to participate from home, regardless of geographical location, with tools they are highly familiar with. One of the important questions to face now is how can maximize the benefits of DHT and innovative analyses while minimizing their risk [34-37].

Conclusion

A combination of network analysis with a digital approach and direct patient involvement in their health integrates the so-called P4 or precision medicine: predictive, preventive, personalized, and participatory. The latter is significant because it will increase the confidence of the adolescent to shift from a passive receiver of care to an active, responsible, and aware driver of their future wellbeing.

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