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Exposome

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The genome, the complete set of genes in each nucleated cell, contains the basic building blocks of human development, but environmental exposures can shape development in profound ways that lead to significant variation in health, biology, and behavior. The *exposome* refers to the totality of environmental exposures that an individual will experience across the life span from conception onward. These exposures encompass the broadest definition of environment, including individual-level toxicological, nutritional, social, and lifestyle experiences, and societal- or global-level events, such as discrimination or climate. The exposome can also include internal metabolic, immunological, neurobiological, and endocrine environments. These exposures collectively create a multilayered context for the genome and development that are critical to predicting individual differences in health trajectories.

The term *exposome* was first introduced in 2005 to highlight the need to complement advances in comprehensive profiling of the genome with comparable measures of environmental exposure in an effort to characterize the gene–environment interaction and interplay that contributes to disease risk. However, the concept of the exposome also serves to illustrate the complexity of defining and measuring environmental factors across the life span within the study of human development. This entry describes issues regarding the definition and measurement of environment that are raised within an exposome perspective, with particular focus on the temporal features and biological markers of environmental exposures.

Defining Environmental Exposure

The environment is a complex and multilayered construct. The definition of environment within the context of any given study will typically be field-dependent and vary based on the particular level of analyses being considered. Moreover, these levels are not independent of each other. For example, hormonal changes (e.g., increased/decreased insulin, leptin, estrogen, testosterone) will shape the cellular environment of the body, with consequences for cellular/molecular processes. These hormonal changes may be the product of other biological changes, such as aging or reproductive status (i.e., pregnancy or lactation) or of environmental changes at the level of the individual, such as dietary changes and psychosocial or physical stress. Individual-level environmental exposures will also likely occur within the context of broader changes in the environment, such as famine, political instability, or immigration. Thus, environments can also be the consequence of environments, with proximal biological environments (e.g., metabolism, hormones) being shaped by more distal ecological shifts in the environment. Several different environmental exposures may also cluster together. For example, children who grow up under conditions of poverty may be more likely to also experience exposure to pollutants, poor diets, and psychosocial stress. The concept of the exposome illustrates that environmental exposures are multifaceted, with any individual being constantly exposed to varying environmental signals over developmental time. This concept also liberates *exposure* from classic domains of study, such as toxicology, psychology, and sociology, to create a more integrative perspective of the experiences of an individual across the life span.

Measuring the Exposome

Acknowledging that the totality of human environmental exposure is diverse and multifaceted is the first step toward a more integrative understanding of human experience across the life

span. The challenge posed by this view, however, is in the actual assessment of the exposome. The classic approach to the study of environmental exposures is to choose a particular environmental feature—such as exposure to lead, prenatal choline in the maternal diet, or variation in socioeconomic status—and focus measurement on that feature. Although studies typically include multiple measures of the environment, these additional measures would likely be used as covariates to assess the relative impact of the environmental exposure of interest when other exposures that influence outcome are taken into account. For example, studies of the impact of prenatal choline intake on childhood cognition indicate that elevated maternal intake of choline during the second trimester of pregnancy results in improved learning and memory scores in childhood and that this effect persists even when statistically controlling for the impact of maternal intelligence, paternal education, maternal age, ethnicity, education, parity, smoking, intake of fish, vitamins, and energy during pregnancy and overall quality of the home environment. These results suggest a robust effect of prenatal choline in the context of other exposures and highlight the value of assessment of multiple exposures when attempting to infer a causal pathway between a single exposure and an outcome. However, exposome research aims to go beyond this selection of targeted exposures to examine, in an unbiased way, the total exposure profile of an individual and how that profile relates to outcome.

Temporal Features of the Exposome

Within studies of environmental influences, there is increasing use of technology that can monitor mood, social interactions, air quality, physiology, and nutrition and that can provide insight into the moment-to-moment exposures of an individual. This technology allows for more detailed exposure data that incorporate dynamic changes in exposure over time that can be used in a prospective study design. Change in an exposure over time may be a critical variable when considering outcome. For example, circadian fluctuations in hormone levels are a highly conserved feature of biology that leads to circadian variation in mood, activity levels, and food intake. Altered rhythmicity rather than absolute levels of these exposures may be critical in predicting a specific long-term outcome and may be the consequence of prior exposure to stress or immune activation. Only by assessing change over time with multiple assessments of exposure, the dynamic nature of the exposure can be captured.

Timing of assessment of the exposome within the life span of an individual is also a critical aspect of any experimental design. Development is a dynamic process, and systems will be differentially impacted if an exposure occurs during the prenatal period, infancy, childhood, adolescence, or in adulthood. However, it may be necessary to use different assessments of exposure at these different life stages. For example, an adolescent or adult may be able to create a moment-to-moment log of their mood state, but this assessment would not be possible at early developmental time points. An additional challenge of assessment occurs when a prospective study design is not possible. In cross-sectional studies, the characterization of the exposome during early development may depend on retrospective reports. Although there is evidence that retrospective and prospective reports of environmental quality (e.g., childhood adversity) are correlated, these reports may differ in their prediction of outcome measures, with retrospective reports being influenced by trait-like personality characteristics. An exposure can be measured objectively (e.g., air quality assessment with a digital sensor) or subjectively (e.g., asking an individual to rate what they perceive to be the air quality). Both measures are elements of the exposome.

Biological Markers of Environmental Exposure

In light of the challenges in characterizing the exposome through assessments of environmental quality, there has been increased interest in using biomarkers as a proxy measure of exposure. For example, if air quality sampling is not possible as a tool for determining exposure to polycyclic aromatic hydrocarbons (a product of the combustion of organic matter), it is possible to use polycyclic aromatic hydrocarbon-DNA adducts, a segment of DNA bound chemically to polycyclic aromatic hydrocarbon in exposed tissues to infer the level of exposure. The level of DNA adducts can then be used to predict outcome measures, such as obesity, cardiovascular disease, or cognition. In addition to DNA adducts, there is increasing interest in using broad biological profiling to infer exposures. Proteomics, transcriptomics, and epigenomics are examples of just a few of the -omic approaches to biological characterization that mirror the genomewide sequencing initiatives in their relatively unbiased assessment of proteins, ribonucleic acid, and epigenetic variation. Assessment of these profiles captures elements of the exposome through detailed characterization of the cellular/molecular environment. However, what remains to be determined is whether these measures can also be useful as proxies for broader external environmental exposures and whether they are predictive of specific health outcomes.

The concept of the exposome is increasingly being integrated into studies of the environmental impact on health and development. This concept is evolving in response to developments in the field of genetics, where genomewide approaches have supplanted targeted gene approaches in an effort to create more robust experimental designs. However, in contrast to the analyses of DNA sequence variation within the genome, analyses of the exposome require consideration of both external and internal environments that are dynamically changing and interacting. The questions of what to measure, how to measure it, and when to measure pose significant challenges when assessing the exposome. Although there is an increasing focus on the use of biomarkers of exposure, the utility of these approaches for approximating exposure and predicting outcome has yet to be determined.

See alsoDevelopment; Epigenetics; Gene–Environment Interplay; Genomics

- environmental exposure
- exposure assessment
- air quality
- biomarkers
- DNA
- prospective studies
- pregnancy

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Further Readings

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