

The Psychoexposome: A holistic perspective beyond health and disease

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Abstract

Background: The concept of the exposome has emerged as a new strategy for studying all environmental exposures throughout an individual's life and their impact on human health. Nowadays, electronic devices are available to collect data about an individual's geolocation, biological function, or exposure biomarkers. The appearance of "omic" sciences and advances in bioinformatics have allowed massive data-gathering and analysis from various scientific fields. **Objective:** To propose the term Psychoexposome in line with the concept of the exposome from the field of environmental sciences. **Method:** A literature review of psychological terms associated with the exposome concept was carried out and the rationale and benefits of a psychoexposome approach for psychological sciences is discussed. **Results:** The terms psychology, psychiatry and neurological diseases are scarce in the exposome approach. A long tradition in psychology of performing epidemiological studies and in the study of multifactorial influences traits places psychologists at an advantageous starting point for conducting psychoexposome studies. **Conclusion:** Psychology may take advantage from both exposome and omic sciences to create an integrated psychoexposome approach that may help in deciphering the etiology of psychological disorders and improving people's mental health.

Keywords: Psychoexposome, psychological processes, behavior, development.

Resumen

Psicoexposoma: una perspectiva holística más allá de la salud y la enfermedad. **Antecedentes:** el concepto de exposoma surgió como una estrategia para impulsar el estudio exhaustivo de las exposiciones ambientales a lo largo de la vida del individuo y su impacto en la salud. El desarrollo de dispositivos electrónicos para obtener datos de geolocalización, biológicos o biomarcadores de exposición y los avances en las ciencias "ómicas" y en bioinformática permiten la recopilación y el análisis masivo de datos muy diversos. **Objetivo:** proponer el término psicoexposoma en línea con el concepto de exposoma generado desde las ciencias ambientales. **Método:** se llevó a cabo una revisión de la literatura para buscar la inclusión de términos psicológicos asociados al concepto de exposoma. Se discute la justificación de un enfoque de psicoexposición para las ciencias psicológicas. **Resultados:** los términos psicología, psiquiatría o enfermedades neurológicas son escasos en el enfoque del exposoma. La experiencia en el control de variables ambientales sitúa al psicólogo en un punto de partida ventajoso para realizar estudios de psicoexposoma. **Conclusión:** la psicología puede aprovechar tanto las ciencias de la exposición como las ciencias "ómicas" para crear un enfoque integrado de psicoexposición que pueda ayudar a descifrar la etiología de los trastornos psicológicos y a promover la salud mental del individuo.

Palabras clave: psicoexposoma, procesos psicológicos, conducta, desarrollo.

The concept of "exposome" was created by Wild in 2005 in response to the need to develop more accurate and precise methods for assessing all the environmental exposures throughout an individual's life (Wild, 2005). The exposome encompasses all physical, biological, chemical and psychosocial environmental exposures from conception to old age. It is an all-embracing approach that feeds off a wide variety of disciplines from engineering to biological and social sciences. It is a huge undertaking that attempts to completely understand the causes

of chronic disease and complements the genome as well as other "omic" data.

Since the concept emerged, scientists have been fascinated with the idea of making a complete assessment of the causes of chronic diseases. A great body of data, multidisciplinary projects such as HELIX (Vrijheid et al., 2014) and more than 250 publications indexed in PubMed have been generated by the introduction of this concept. However, the presence of psychiatry or psychological is quite limited and only 3 to 8 outputs are obtained in PubMed when these keywords are combined with exposome.

In the particular case of Psychology and the Behavioral Sciences, epidemiological, family, twin and adoption studies have shown that genetic contribution to several psychiatric disorders is large (Faraone et al., 2005; Nemoda, Szekely, & Sasvari-Szekely, 2011). Geneticists have been studying a wide variety of candidate genes to account for either psychological traits or psychiatric

diseases. In addition, genome wide association studies have provided, important data to better understand genetic contribution to traits and disease, and to design new interventions for complex diseases (Visscher et al., 2017). Moreover, recent progress in the field of epigenetics has shown the dynamic nature of gene expression control in response to environmental exposures (Rutten & Mill, 2009). Thus, DNA and changes in chromatin structure induced by life experiences play a critical role together with polymorphisms in most psychiatric disorders and other behavioral traits observed in the general population (Barker, Walton, & Cecil, 2017; Hoffmann, Sportelli, Ziller, & Spengler, 2017). In addition, current knowledge on the interaction between the body systems indicates that life experiences, chemical, biological and physical exposures have a great impact on brain function (Aguilar, Eubig, & Schantz, 2010; Tanner, Goldman, Ross, & Grate, 2014; Xu, Ha, & Basnet, 2016). During the early stages of development, the neural circuits responsible for a variety of behaviors are programmed, which makes them especially vulnerable to any adverse alteration from the environment (Jawahar, Murgatroyd, Harrison, & Baune, 2015; Maccari et al., 2017). In this regard, there is general agreement that environmental factors play an important role in triggering psychological disorders or psychopathology (Tanner et al., 2014). Indeed, Psychology has been working for years with huge cohorts and several follow-up studies have assessed numerous environmental variables (Canals, Domènech-Llaberia, Fernández-Ballart, & Martí-Henneberg, 2002). Nonetheless, tools to accurately assess life experiences and exposures have not been introduced as quickly as tools for assessing biomarkers such as those in the “omic” sciences (Wild, 2005).

As behavioral neuroscientists, we use the term Psychoexposome in an attempt to rebuild and implement a long tradition in Psychology by introducing new tools for assessing exposure and adopting a wide multidisciplinary approach. The whole history of an individual’s exposures affecting psychological outcome must be included from a broader perspective. The concept of the Psychoexposome is not intended to narrow the holistic perspective of the exposome but to provide a better characterization of those exposures that are relevant to psychological function. From this frame of reference, there emerged the need to design new tools and improve the existing ones for assessing psychosocial challenge outcomes in an individual lifecycle. Nowadays, psychological approaches and refined assessment of many environmental exposures aligned with those from “omic” science may become a powerful tool for better understanding behavioral imbalances and resilience. Understanding how exposures throughout an individual’s life shape the nerve cells, connections and physical features that underpin behavior has the potential to design prevention, educational and therapeutic programs to fine tune adaptive behaviors.

The impact of psychosocial environmental exposures on epigenetic regulation, the importance of psychoneuroimmunology in health and disease and the recent description of the Gut-Brain axes system are examples of how psychosocial experiences shape not only behavior but also several body functions (McDade

et al., 2017). Likewise, lifelong exposures to toxins, drugs, environmental stressors such as climate changes, nutritional and/or dietary experiences, and infections, among other factors, modulate neuroendocrine, immune and inflammatory response as well as the composition and function of the microbiome (Rauh & Margolis, 2016). Remarkably, fetal life and childhood are periods of special interest in understanding the epigenetic changes induced by environmental exposures (Kundakovic & Jaric, 2017). In this regard, defective epigenetic regulation can result in the long-term reorganization of biological systems, aberrant responses to future environmental challenges (including psychological ones) or complex diseases appearing at any time of life (Hatchwell & Grealley, 2007)

As well as the concept of health and disease the psychological approach includes adaptive and maladaptive behavior (Hengartner, 2015). This can also be useful so that other disciplines can identify not only disease states but also mismatches between body response and environmental challenges. This scenario is dynamic and the phenotypic expression moves along the normal continuum to the psychopathological extreme. The psychoexposome combined with genomic and epigenomic, transcriptomic, proteomic and metabolomic data in conjunction with new technologies applied at the level of the organism could be a big step forward in our understanding of behavior and psychological processes. Combining these data could become a powerful tool for unravelling the complex mechanisms involved in the regulation and development of psychological individual differences. In turn, this knowledge must be harnessed to overcome the devastating impact of some environmental exposures on mental disease.

Exposome science, however, still has to rise to some considerable challenges. On one hand, the ways in which exposure is measured must be standardized and guaranteed to be reliable since detection methods for exposures with different accuracies may lead to incorrect attributions of causality (Turner et al., 2017). On the other hand, simultaneous exposures or highly correlated variables, associated with the origin of a pathological phenotype, are unavoidable. Complex statistical approaches need to be applied to this reality and scientists must be very cautious not to make biased or wrong predictions (Manrai et al., 2017). Needless to say, experimental approaches will still be required if causality is to be inferred.

Finally, novel techniques and biosensors are now available that can improve personal assessment of internal and external exposures, as well as baseline characteristics (genomics) and intermediate effects (omics). In combination with portable resources, such as personal cellular devices, which allow geo and chrono localization or the assessment of everyday life events (Turner et al., 2017), these are likely to provide novel data on health, disease and resilience from a biopsychosocial perspective. In this context, new concepts and tools need to be developed within a broader theoretical framework in which the organism as a whole and its lifelong Psychoexposome history will be used to explain the place and time at which the various factors contribute to the normal and pathological development of the behavior.

References

- Aguilar, A., Eubig, P. A., & Schantz, S. L. (2010). Attention Deficit/Hyperactivity Disorder: A Focused Overview for Children's Environmental Health Researchers. *Environmental Health Perspectives*, 118(12), 1646-1653. <http://doi.org/10.1289/ehp.1002326>
- Barker, E. D., Walton, E., & Cecil, C. A. M. (2017). Annual Research Review: DNA methylation as a mediator in the association between risk exposure and child and adolescent psychopathology. *Journal of Child Psychology and Psychiatry*. <http://doi.org/10.1111/jcpp.12782>
- Canals, J., Domènech-Llaberia, E., Fernández-Ballart, J., & Martí-Henneberg, C. (2002). Predictors of depression at eighteen. A 7-year follow-up study in a Spanish nonclinical population. *European Child & Adolescent Psychiatry*, 11(5), 226-233. <http://doi.org/10.1007/s00787-002-0286-y>
- Faraone, S. V., Perlis, R. H., Doyle, A. E., Smoller, J. W., Goralnick, J. J., Holmgren, M. A., & Sklar, P. (2005). Molecular Genetics of Attention-Deficit/Hyperactivity Disorder. *Biological Psychiatry*, 57(11), 1313-1323. <http://doi.org/10.1016/j.biopsych.2004.11.024>
- Hatchwell, E., & Grealley, J. M. (2007). The potential role of epigenomic dysregulation in complex human disease. *Trends in Genetics*, 23(11), 588-595. <http://doi.org/10.1016/j.tig.2007.08.010>
- Hengartner, M. P. (2015). The Detrimental Impact of Maladaptive Personality on Public Mental Health: A Challenge for Psychiatric Practice. *Frontiers in Psychiatry*, 6, 87. <http://doi.org/10.3389/fpsy.2015.00087>
- Hoffmann, A., Sportelli, V., Ziller, M., & Spengler, D. (2017). Epigenomics of Major Depressive Disorders and Schizophrenia: Early Life Decides. *International Journal of Molecular Sciences*, 18(8), 1711. <http://doi.org/10.3390/ijms18081711>
- Jawahar, M. C., Murgatroyd, C., Harrison, E. L., & Baune, B. T. (2015). Epigenetic alterations following early postnatal stress: A review on novel aetiological mechanisms of common psychiatric disorders. *Clinical Epigenetics*, 7(1), 122. <http://doi.org/10.1186/s13148-015-0156-3>
- Kundakovic, M., & Jaric, I. (2017). The Epigenetic Link between Prenatal Adverse Environments and Neurodevelopmental Disorders. *Genes*, 8(3), 104. <http://doi.org/10.3390/genes8030104>
- Maccari, S., Polese, D., Reynaert, M.-L., Amici, T., Morley-Fletcher, S., & Fagioli, F. (2017). Early-life experiences and the development of adult diseases with a focus on mental illness: The Human Birth Theory. *Neuroscience*, 342, 232-251. <http://doi.org/10.1016/j.neuroscience.2016.05.042>
- Manrai, A. K., Cui, Y., Bushel, P. R., Hall, M., Karakitsios, S., Mattingly, C. J., ..., Patel, C. J. (2017). Informatics and Data Analytics to Support Exposome-Based Discovery for Public Health. *Annual Review of Public Health*, 38(1), 279-294. <http://doi.org/10.1146/annurev-publhealth-082516-012737>
- McDade, T. W., Ryan, C., Jones, M. J., MacIsaac, J. L., Morin, A. M., Meyer, J. M., ..., Kuzawa, C. W. (2017). Social and physical environments early in development predict DNA methylation of inflammatory genes in young adulthood. *Proceedings of the National Academy of Sciences*, 114(29), 7611-7616. <http://doi.org/10.1073/pnas.1620661114>
- Nemoda, Z., Szekeley, A., & Sasvari-Szekeley, M. (2011). Psychopathological aspects of dopaminergic gene polymorphisms in adolescence and young adulthood. *Neuroscience and Biobehavioral Reviews*, 35(8), 1665-1686. <http://doi.org/10.1016/j.neubiorev.2011.04.002>
- Rauh, V. A., & Margolis, A. E. (2016). Research Review: Environmental exposures, neurodevelopment, and child mental health - new paradigms for the study of brain and behavioral effects. *Journal of Child Psychology and Psychiatry*, 57(7), 775-793. <http://doi.org/10.1111/jcpp.12537>
- Rutten, B. P. F., & Mill, J. (2009). Epigenetic Mediation of Environmental Influences in Major Psychotic Disorders. *Schizophrenia Bulletin*, 35(6), 1045-1056. <http://doi.org/10.1093/schbul/sbp104>
- Tanner, C. M., Goldman, S. M., Ross, G. W., & Grate, S. J. (2014). The disease intersection of susceptibility and exposure: Chemical exposures and neurodegenerative disease risk. *Alzheimer's & Dementia*, 10(3), S213-S225. <http://doi.org/10.1016/j.jalz.2014.04.014>
- Turner, M. C., Nieuwenhuijsen, M., Anderson, K., Balshaw, D., Cui, Y., Dunton, G., ..., Jerrett, M. (2017). Assessing the Exposome with External Measures: Commentary on the State of the Science and Research Recommendations. *Annual Review of Public Health*, 38(1), 215-239. <http://doi.org/10.1146/annurev-publhealth-082516-012802>
- Visscher, P. M., Wray, N. R., Zhang, Q., Sklar, P., McCarthy, M. I., Brown, M. A., & Yang, J. (2017). 10 Years of GWAS Discovery: Biology, Function, and Translation. *The American Journal of Human Genetics*, 101(1), 5-22. <http://doi.org/10.1016/j.ajhg.2017.06.005>
- Vrijheid, M., Slama, R., Robinson, O., Chatzi, L., Coen, M., van den Hazel, P., ..., Nieuwenhuijsen, M. J. (2014). The human early-life exposome (HELIX): Project rationale and design. *Environmental Health Perspectives*, 122(6), 535-544. <http://doi.org/10.1289/ehp.1307204>
- Wild, C. P. (2005). Complementing the Genome with an "Exposome": The Outstanding Challenge of Environmental Exposure Measurement in Molecular Epidemiology. *Cancer Epidemiology and Prevention Biomarkers*, 14(8).
- Xu, X., Ha, S. U., & Basnet, R. (2016). A Review of Epidemiological Research on Adverse Neurological Effects of Exposure to Ambient Air Pollution. *Frontiers in Public Health*, 4, 157. <http://doi.org/10.3389/fpubh.2016.00157>