



Inside Out

Hee Jeong Yoo

Department of Psychiatry, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, Korea

In the past, when diagnoses in child psychiatry were unfamiliar and relatively rare, the word from an authoritative figure was a “marker” for a disease. Once an expert confirmed a diagnosis through careful examination and suggested ways of treatment, they were accepted as the truth, even as the gold standard. If the clinical opinion was backed up by psychological measurements, not many people would have raised concerns regarding the diagnosis, even regarding the possible prognosis. However, this is not as simple and clear today. Parents already have a vast amount of information, both correct and incorrect, and try to reconcile their pre-existing knowledge with the novel information given by the clinician. They need a second opinion from other clinicians regarding treatment options, as well as diagnostic accuracy. It is sometimes awkward for clinicians to feel like competing with random information from the community; however, facing such changes might be inevitable. It is even more evident in disorders with complex manifestations, such as autism spectrum disorder (ASD). Doctor-patient relationships in child psychiatry have tended to be paternalistic models, in which clinicians care for children and their families in a warm, holding, and sometimes firm manner; however, this is now transforming into a more informative/interpretative model. There are several sophisticated mechanisms underlying such changes, including the diversity of symptoms of neurodevelopmental disorders, the plethora of information and people’s ability to interpret them, availability of multiple doctors within the healthcare transfer system, and general skepticism about healthcare experts. Whatever the reason behind it might be, it seems clear that there is currently a significant paradigm shift towards pursuing more objective measures of underlying pathogenic mechanisms of diseases, replacing expert opinion and close behavioral observation, that is, biomarkers.

Biomarkers are objectively measured, quantifiable indicators of both normal and pathologic biological processes or biological responses to therapeutic interventions [1]. They include 1) risk biomarkers, used to identify individuals at high risk for a certain condition, such as having a family history;

2) diagnostic biomarkers used to confirm the diagnosis, identify the subtype of the disease, and stratify its severity; 3) treatment biomarkers, representing treatment responses to biological agents, including drugs; and 4) prognostic biomarkers, indicating the progression, long-term prognosis, or recurrence of the disease [1,2]. Prediction biomarkers, surrogate endpoint biomarkers, and safety biomarkers can be defined based on the classification system of biomarkers. The essential value of biomarkers in terms of precision medicine lies in diagnosis, tailoring treatment options to individual profiles, and determining prognoses. However, reliable biomarkers are not yet widely used, except for diagnostic markers for Alzheimer’s disease. In neurodevelopmental disorders, it is even less appreciated, though there have been continuous efforts to discover genetic/multiomics/biochemical/physiological markers for risk prediction and diagnosis of ASD and attention-deficit/hyperactivity disorder (ADHD) [2-4]. In the current issue, potential applications of biological measures, including electroencephalography (EEG), quantitative EEG, event-related potential, and near-infrared spectroscopy, in terms of biomarkers for a wide variety of disorders, including ASD, ADHD, anxiety disorders, and mood disorders. I trust it might be a small yet important step for the journal to raise interest in using objective measures of brain functions in the field of child psychiatry.

In the insightful animation, *Inside Out*, produced by the Pixar Animation Studio in 2015, the inside of an 11-year-old girl, Riley’s brain, is visualized and personalized. Five basic emotions, recent and remote memories, development of abstract thinking, and even prefrontal lobe function in the cognitive/emotional development of early adolescence are shown in specific but lively, vivid expressions. Spectators can *see and understand* the existence of emotion and cognition inside the child’s brain in an intuitive way without significant effort. Discovering biomarkers in child psychiatry might be a process that might mimic it, substantiating complex events inside the brain during development into a more visible form. It would enable the scientific society, as well as parents, to understand the nature of their children’s experiences more clearly. Discovering and validating biomarkers for complex developmental disorders is innately challenging because it occurs

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

in the actively changing brain; also, the phenotypes are ever-changing and multi-dimensional, and it is difficult to perform certain tests on young children; however, it is time to start considering it. First, we need to put together our experience in the form of data. Even if it might be too small to enable generalization at first, our collective intelligence, alongside precise phenotyping, would make it possible to clarify it in the near future.

REFERENCES

- 1) **FDA-NIH Biomarker Working Group.** BEST (Biomarkers, End-pointS, and other Tools) Resource [Internet] [updated 2016; cited 2021 June 20]. Available from URL: <https://www.ncbi.nlm.nih.gov/books/NBK326791>.
- 2) **Voineagu I, Yoo HJ.** Current progress and challenges in the search for autism biomarkers. *Dis Markers* 2013;35:55-65.
- 3) **Mesleh AG, Abdulla SA, El-Agnaf O.** Paving the way toward personalized medicine: current advances and challenges in multi-OMICS approach in autism spectrum disorder for biomarkers discovery and patient stratification. *J Pers Med* 2021;11:41.
- 4) **Kim JH, Kim JY, Lee J, Jeong GH, Lee E, Lee S, et al.** Environmental risk factors, protective factors, and peripheral biomarkers for ADHD: an umbrella review. *Lancet Psychiatry* 2020;7:955-970.