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From Signals to Solutions: Exploring Early Detection of Neuropsychiatric and Neurodevelopment Disorders through Biomarkers

Zainah A. Lawman

Independent Researcher, Wellington, FL, USA
Email: lawmanzainah@gmail.com

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Abstract

In 2013, the percentage of children ranging from 5 to 17 years who reported being diagnosed with autism surged to 1.2% from 0.1% in 1997 [1]. Alongside this increase in the incidence of autism in children, there were findings of a 21% increase in children who displayed behavioral and conduct problems from 2019 to 2020 [2]. Early detection of neuropsychiatric and neurodevelopmental disorders in children is critical for timely intervention and improved long-term outcomes. With early intervention, there is better aptitude to support healthy development and give proper treatment to attain a better quality of life. This paper explores studies aimed at enhancing the early detection of these disorders through the use of biomarkers with the aim of creating a bridge between the worlds of research and clinical practice. The disorders in this paper specifically discussed are Major Depressive Disorder, Bipolar Disorder, and Autism Spectrum Disorder. With this bridge, we can foster collaborations and encourage further advancement in the field of early detection and intervention.

Keywords

Biomarkers, Neuropsychiatric Disorders, Neurodevelopmental Disorders, Autism, Depression, Bipolar, Children

1. Introduction

Research on biomarkers within neuropsychiatric and neurodevelopmental disorders is expanding and is becoming more prominent; however, more research is still needed on the subject at issue. The objective of this paper is to summarize

the available literature on the role of biomarkers in improving the prognosis of autism, major depression, and bipolar disorder. The outcomes of this paper conclude biomarkers show a correlation to disorders rather than direct causation.

2. Method

A retrospective literature review was undertaken to identify biomarkers found in neuropsychiatric disorders and neurodevelopmental disorders. The search engines Pubmed, WebMd, and Google-Scholar were used, utilizing the keywords: biomarkers, Bipolar disorder (BPD), Major Depressive disorder, (MDD), Autism Spectrum Disorder (ASD), Interleukin-6 (IL-6), children/child. The biomarkers that were selected were mentioned persistently while reviewing the disorders previously introduced: BPD, MDD, and ASD. Specific inclusion criteria were 1) comparative studies on patients with ASD, BPD, or MDD with control groups; 2) measurement of unstimulated cytokines from the blood; 3) biomarkers present within the previously mentioned disorders; 4) study subjects without major physical illness (*i.e.* diabetes, heart disease, cancer, etc.) at the time of assessment. Specific Exclusion criteria included 1) biomarkers unrelated to patients with ASD, BPD, or MDD; 2) biomarkers in elderly patients.

3. Results and Discussion

Biomarkers are measurable substances that can indicate phenomena such as disease, infection, or environmental exposure [3]. To establish the development of a biomarker, it is pivotal to demonstrate its presence before symptom onset and its specificity to the respective disorder [3]. Biomarkers can express how normal or abnormal a system in your body is, and they can be categorized into 5 major groups [3]: diagnostic, monitory, predictive, susceptibility, and prognostic. Diagnostic biomarkers will indicate that someone has a certain condition [3]. High blood sugar levels in type 2 diabetes are diagnostic biomarkers as the elevated blood sugar levels confirm the presence of the condition [4]. With regards to biomarkers that monitor, one can track markers over time to see how a condition progresses [3]. Brain natriuretic peptide (BNP) is a monitoring biomarker; tracking its levels helps guide treatment decisions regarding heart failure [5]. Predictive biomarkers measure the likelihood of response or lack thereof to treatment, while susceptibility biomarkers note how likely one is to get a condition [3]. Using prognostic biomarkers, one can determine the likely outcome of the patient using the clinical or biological characteristics the biomarkers find [3]. The protein Ki-67 is often used as a prognostic biomarker for cancers as its high levels are associated with invasive tumors [5].

Neuropsychiatric disorders are distinct, clinically acknowledged conditions wherein an individual's thoughts, perceptions, emotions, and or overt behavior lead to distress and cause disruption to their daily functions [6]. Neurodevelopmental disorders influence brain function and alter neurological development leaving those individuals with difficulty in functioning emotionally, socially, and

cognitively [7]. Standard diagnosis of these disorders is generally identified through the utilization of The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, also known as the DSM-5-TR. New ways to detect disorders are coming to light. An example would be the deep learning model, which is one newer way of detecting mental illnesses [8].

This study explored cases dealing with biomarkers found in the following disorders: ASD, BPD, and MDD: ASD, a neurological and developmental disorder that affects how people interact with others, communicate, learn, and behave, BPD, a mental illness that causes unusual shifts in a person's mood, energy, activity levels, and concentration, and MDD mental health condition that causes a persistently low or depressed mood and a loss of interest in activities that once brought joy [6].

In a comparative study involving children with ASD and a control group, significant findings emerged regarding a relation between the ASD group having two diagnostic biomarkers in 5 major proteins [9]. They manifest as follows: In the complement pathway PLG, SERPINC1, and A2M, while in the inflammatory pathway the following CD5L, ATRN, SERPINC1, and A2M [9]. The complement system acts as a nonspecific defense mechanism against pathogens. SERPINC1 and PLG both provide instructions for proteins to control blood clotting while A2M captures and inhibits major chemicals that cause cartilage damage and the breaking down of joints [10]-[12]. SERPINC1, PLG, and A2M all contribute to the protection of the body from pathogens. Multiple reaction monitoring (MRM) confirmed the precedent proteins to be notably up-regulated [9]. Through screening of a machine learning model and MRM verification two proteins (biotinidase and carbonic anhydrase1) were found to be used as possible early diagnostic markers of ASD [9]. The detected biomarkers in this study would fall under the category of diagnostic biomarkers due to their confirmed association specifically with the ASD group [3] [13].

In both BPD and MDD, the elevated cytokine, IL-6, showed as a marker [14]. In a prospective general population U.K. birth childhood study, higher levels of the marker IL-6 in childhood were linked to hypomanic symptoms in young adulthood, even when accounting for sociodemographic variables, prior psychological and behavioral issues, body mass index (BMI), and maternal postnatal depression [14]. In this study, stating the indicators as monitory and prognostic biomarkers is appropriate due to the study being done over time and giving an idea of how the inflamed marker, IL-6, would affect those in the future [3].

Evidence provided from a longitudinal study found that peripheral inflammation predates the etiology of depression [15]. The study discovered children with higher circulating levels of IL-6 at 9 years old were at a 10% greater risk of developing MDD by early adulthood (starting at 18) than the general population with low levels of IL-6 [15]. The biomarker, IL-6, concerns susceptibility by giving a percentage of how likely one is to get the following disorder [16]. Along with susceptibility, IL-6 is contestably seen as a confirming (diagnostic) biomarker as it is seen as the most consistently exalted cytokine in the blood of pa-

tients with MDD [3] [17]. In a study compared by group and sex, IL-6 showed a different inflammatory response between the sexes as the males had decreased IL-6 compared to the females [18]. The reduced inflammatory reactivity is presumed to be the result of males having a reduced inflammatory response to bacterial and viral infections compared to females [18]. Despite the study showing differences between IL-6 levels among the sexes, other studies have shown no difference [18]. The conflicting information on whether sex is associated with the inflamed cytokine suggests additional research should be conducted.

The accuracy of IL-6 being a true biomarker for BPD and MDD can be questioned due to its inflammation being flagged as a marker for both disorders. However, hypomania doesn't exclude depressive behavior. Further study and research would need to be done to fully understand the role IL-6 being upregulated would play on children. Identification is just the start.

1 in 6 children ranging from 2 - 8 years have been diagnosed with a mental, behavioral, or developmental disorder just in the U.S. [19]. The toll these disorders have on children is impactful seeing that suicide is the second leading cause of death for adolescents [20]. The etiology and pathology predating neurodevelopmental and neuropsychiatric disorders are little to none. By enabling modern and earlier detection of these disorders, an immense opportunity arises to provide children with the appropriate support and intervention they need.

4. Conclusion

While these biomarkers are related to the previously discussed disorders, no direct causation of disease has been found. Although the predictive value of IL-6 as a biomarker in BPD and MDD is not entirely sufficient to serve as the sole accurate marker, its significance remains evident. Further research and study about these biomarkers correlating with these disorders would concede further in-depth explanations and understanding in the hope of expanding and advancing the medical field through the early detection of neuropsychiatric and developmental disorders.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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