# Biomarkers in the Sphere of Neuropsychology: An Avant-Grade Stamping Ground By Dint of Histological Tack

**Harisoorya A. U. [1*], & Vidya N. [2]**

[1*] Research Scholar, Institute of Social Sciences and Humanities, Srinivas University, Mangalore, Karnataka, INDIA,
ORCID-ID: 0000-0003-0013-2444; E-mail: vishnuau1@gmail.com

[2] Associate Professor, Institute of Social Sciences and Humanities, Srinivas University, Mangalore, Karnataka, INDIA,
ORCID-ID: 0000-0002-3390-567X; E-mail: vidyakrithi.n@gmail.com

**Area/Section:** Health Management.
**Type of the Paper:** Clinical Data Analysis.
**Type of Review:** Peer Reviewed as per |C|O|P|E| guidance.
**Indexed in:** OpenAIRE.
**DOI:** https://doi.org/10.5281/zenodo.7187959
**Google Scholar Citation:** IJHSP

**How to Cite this Paper:**
Harisoorya, A. U., & Vidya, N., (2022). Biomarkers in the Sphere of Neuropsychology: An Avant-Grade Stamping Ground By Dint of Histological Tack. *International Journal of Health Sciences and Pharmacy (IJHSP)*, *6*(2), 110-123. DOI: https://doi.org/10.5281/zenodo.7187959

**International Journal of Health Sciences and Pharmacy (IJHSP)**
A Refereed International Journal of Srinivas University, India.

Crossref DOI: https://doi.org/10.47992/IJHSP.2581.6411.0088

Received on: 23/09/2022
Published on: 13/10/2022

# Biomarkers in the Sphere of Neuropsychology: An Avant-Grade Stamping Ground By Dint of Histological Tack

**Harisoorya A. U. [1*], & Vidya N. [2]**
[1*] Research Scholar, Institute of Social Sciences and Humanities, Srinivas University, Mangalore, Karnataka, INDIA,
ORCID-ID: 0000-0003-0013-2444; E-mail: vishnuau1@gmail.com
[2] Associate Professor, Institute of Social Sciences and Humanities, Srinivas University, Mangalore, Karnataka, INDIA,
ORCID-ID: 0000-0002-3390-567X; E-mail: vidyakrithi.n@gmail.com

## ABSTRACT

**Purpose:** *An astonishing amount of work has been put out in recent years to pinpoint biomarkers as possible resources for enhancing psychiatric preventive care, diagnosis, therapeutic response, and therapeutic development. In contrast to those other ailments, psychological illnesses include a diverse range of symptoms that are grouped into diagnostic categories. As a result, persons that have the same psychological disorder have a large deal of therapeutic variation. The above aspect, together with our poor understanding of the neurochemical imbalances driving dissociative ailments, leads to the existing pharmaceutical choices' low effectiveness. In this regard, the discovery of biomarkers in psychology or psychiatry, or any other clinical mental health sciences area is turning out to be crucial for facilitating diagnosis and through the creation of markers that enable the stratification of individuals inside this condition, which may then result in more targeted therapy choices. This evaluation presents a practical description of therapeutic development along with an overview of the idea and several categories of biomarkers to throw light on the subject. Additionally, the developments in this area were compiled and divided into the following groups, including "genetics, transcriptomics, proteomics, metabolomics, and epigenetics".*

**Objective:** *The main objective of this paper is to shed some light on the area of neuropsychological disorder and its variations as well as common biomarker assessment methods to detect it. Another core objective of this paper is to rule out "omics" techniques used in the domain of neuropsychology or general psychiatry to detect some complicated and common mental disorders.*

**Design/Methodology/Approach:** *This clinical paper is prepared by using secondary data from various official and authentic websites and journal papers. In order to make the paper more accurate and scientific in nature, primary data has also been utilized to build this paper. Expert opinions from neuropsychologists, general psychiatrists, and researchers who are doing research in the domain of neuropsychology have also been taken to guarantee the reliability of the paper.*

**Findings/Result:** *Despite the positive outcomes, there have been few biomarker studies, particularly those that focus on the treatment of mental illnesses. This study's outcome makes a comment on the difficulties that will need to be overcome in the possible future in order to generate credible, trustworthy, and widely applicable biomarkers for mental diseases and their intervention. An essential first step towards the construction of more customized therapy is the detection of characteristics that forecast response to therapy since doing so will decrease drug switching based on trial and error and facilitate the development of novel successful medicines.*

**Originality and Value:** *A scientific and more comprehensive approach has been taken to provide better information about neuropsychological/general psychiatric disorders and their detection by using histological or any other clinically proven methods. A new stratagem is applied to shed light on the topic of neuropsychological illnesses and their detection by using the biomarker method.*

**Paper Type:** *Clinical analysis/interpretive paper*
**Keywords:** Biomarkers, Neuropsychology, Mental Health Sciences, Omics, Transcriptomic biomarker, Genomic biomarker.

## 1. INTRODUCTION :

Additionally, there are few ineffective pharmaceutical therapy choices for all forms of mental disease. According to multiple investigations, there are major limits to the existing pharmaceutical therapies regarding healing as well as relapse. The World Health Organization reports that the recurrence, fatalities, disability, and disability percentages associated with mental illness are horrifying [1]. An individual's longevity is reduced by Thirteen to thirty-two years if they have a significant mental condition. Vital evidence in this regard was provided by several potency trials funded by the "National Institute of Mental Health (NIMH)" in the USA. Also, this therapeutic paradigm is influenced by a number of things. In this aspect, the intricacy and variability of mental illnesses are high. Patients with mental illnesses had a variety of signs that had to do with their actions, thoughts, emotions, and/or interpersonal interactions [2]. The "Diagnostic and Statistical Manual of Mental Diseases", Fifth Edition (DSM-IV) or the "International Statistical Classification of Diseases and Related Health Problems", Tenth Edition (ISC-10) classify mental disorders into diagnostic categories with a long list of symptoms to aid in diagnosis (ICD-11) [3]. As a result, persons who share the same psychological illness have a large deal of therapeutic variation. Additionally, a number of mental diseases share indicators, which sometimes makes the assessment challenging [4].

However, psychological illnesses have a significantly higher rate of comorbidities. In between eighty-five percent in terms and ninety percent of individuals suffering from depression, emotional problems also were present. Psychological comorbidities are frequent in people with schizophrenia. Over forty-seven percent of patients have received a lifetime experience diagnosis of concomitant drug-related disorders, and almost 50% of patients experience distress. When two or more mental conditions coexist, the aggravation, pharmaceutical sensitivity, and suicide probability are all increased compared to when one or the other is present unilaterally [5].

Notwithstanding all these grim statistics, advancements in the study of the human nervous system and brain and the advancement of technology, which includes “omics” technologies, present a chance to alter the course of mental illness care as well as its results in the not-too-distant. In this regard, the discovery of biomarkers has emerged as a brand-new, exciting tool for assisting in specific diagnosis, forecasting results, and ultimately advancing our knowledge about the pathophysiology of psychological conditions [6].

This analysis provides a comprehensive outline of the state of biomarkers in psychiatry or psychology today with the true goal of highlighting several other achievements to date and outlining the challenges that still need to be overcome to create valid, trustworthy, and widely applicable biomarkers for psychological conditions as well as their therapies. For this reason, the study defines historical biomarker ideas, discusses several forms of biomarkers and their possible applications in clinical practice, as well as emphasizes the most popular samples and methods. Due to the 'omics' field's significant advancement in recent years, its significance is detailed in more depth. The conclusion discusses the constraints and restrictions of the existing neuropsychological biomarkers methodologies as well as the upcoming obstacles to advancement in this field [7].

## 2. RELATED WORKS :

Exposure to cerebral specimens is especially important for illnesses of the brain's central nervous system (C.N.S), including such psychological and cognitive conditions [8]. Human post-mortem brain tissues, which are often donated through brain banks, are essential in this regard. Nonetheless, comprehensive metabolic studies utilizing these collections are rare, constrained, and unfeasible, mostly as a result of the inability to track the progression of the illness [9]. In this regard, advancements in "functional neuroimaging" have made it possible to analyze various neural processes, such as changes in regional brain blood flow, and mitochondrial biogenesis, including chemical binding site distribution as well as activation throughout illness progression [10]. However, because of its substantial financial expenses, "functional neuroimaging" cannot reveal a lot about the degree of cell biology, consequently, the availability of this technology is restricted. Blood cells have attracted particular focus in this scenario when looking for collateral indicators [11]. Lab tests make it simple to separate lymphocytes, which may then be regularly analyzed to track the progression of the illness. In contrast, peripheral

lymphocyte-released interleukin alters CNS activities such as circulatory regulation, hormonal reactivity, as well as psychological reactions [12]. The operation, as well as metabolic activity of lymphocytes, may also change in tandem with changes in serotonin and even the "hypothalamic-pituitary-adrenal" (H.P.A) axis in the central nervous system. Several genetic factors, including c-fos, "interleukins (IL-2, IL-4, IL-6, IL-10)", "brain-derived neurotrophic factor (B.D.N.F)", "nerve growth factor (NGF)", cholinergic, G.A.B.A.A. receptors, "B2-adrenergic receptors", "glucocorticoid receptors", "mineralocorticoid receptors", "D3-dopaminergic receptors", as well as "serotonin receptors", have indeed been utilised in neuropsychology [13]. This makes the identification of biochemical identifiers in psychology, psychiatry, or in any other field of clinical mental health disciplines increasingly important for aiding in the assessment and the development of markers that allow the stratification of people with the disorder, which may then lead to more focused treatment options [14]. This analysis provides a detailed explanation of clinical application, an outline of the concept, and a number of types of assays to help gain a deeper understanding [15].

## 3. OBJECTIVES :

This paper's main goal is to provide some insight into the field of neuropsychological dysfunction and the many widely used biomarker evaluation techniques for its detection. The application of "omics" methods used in neuropsychology or general psychiatry to identify some complex and widespread mental diseases would be another important goal of this study. Some other main objectives are listed below.

(1) To comprehend the fundamental workings or characteristics of biomarkers.
(2) To describe several categories of biomarkers and how neuropsychology and general psychiatry use them.
(3) To clarify how the "omics" biomarker is used in neuropsychology to recognize different neuropsychological diseases.

## 4. METHODOLOGY :

This scientific study was created utilizing secondary information from several reputable, authoritative sources and journal articles. Primary data has also been used to develop this study in order to increase its accuracy and scientific rigor. To ensure the validity of the study, independent views from neuropsychologists, general psychiatrists, and researchers working in the field of neuropsychology have also been obtained. To determine the essential material, more than fifty clinical articles with a high degree of scientific credibility were thoroughly and rigorously reviewed. To obtain reputable and scientific data, articles from Google Scholar Academia and Researchgate have often been utilized.

## 5. “BIOMARKERS” WHAT EXATLEY THEY ARE? A GENERAL OUTLINE :

In 1973, the word "biomarker" was first coined to denote the existence or dearth of biological material. The idea was first mentioned as a "biochemical marker" in the year 1949 and as a "biological marker" in 1957, though. The U.S.-backed Biomarker Classification Research Group was formed in 2000. "A trait that is reliably monitored and assessed as a signal of natural physiological systems, pathogenic processes, or pharmacological reactions to a treatment" is how the National Institutes of Health (NIH) described a biomarker [16]. This concept has two significant drawbacks. The very first has to do with the reality that a biomarker may occasionally be determined by arbitrary criteria. The latter is the exclusion of new processes or reactions not included in the specification. The term "biomarker" was revised by Fitzgerald in the year of 2016 as "a functional variation or quantitative measure of a biological function that indicates or displays the progression of or propensity to a disorder or a response to a medication." However, this definition does not take into account structural variations and descriptive indices here as possible biomarkers.

The 'Food and Drug Administration (FDA)', in coordination with the 'NIH Combined Leadership Council', established the FDA-NIH Biomarker Steering Committee in the year of 2016 to standardize the word "biomarker." The explanation of a biomarker as just being "a defining characteristic that is measured as an indication of normal biological processes, pathogenic processes or reactions to an exposure or intervention" was condensed by this committee [17].

The above explanation of a biomarker, which is simpler and even more precise, identifies its main uses devoid of adding any extraneous complication or contradicting details. A robust biomarker should also be assessed with sufficient regularity, have a sizable signal-to-noise percentage, and, most significantly,

satisfy the requirement of being adjusted in a progressive and uniformity as the therapeutic situation progresses to its clinical application. A biomarker should also be available for identification and quantification, just like a plasmatic indicator or protein would be, or it may be found using histology or picture techniques [18].

## 6. USES OF BIOMARKERS IN THE DAY TO DAY CLINICAL PRACTICE :

Biomarkers might offer more details about the problem or potential treatment options depending on their usage. Any time after the pathogenesis, the start of the initial clinical signs, the assessment, the course of therapy, or the recuperation, biomarkers may be discovered. According to their major therapeutic use, the 'FDA-NIH Biomarker Working Group' classified various types of biomarkers into the following categories and they are as "diagnostic, monitoring, pharmacodynamic/response, predictive, prognostic, safety, and susceptibility/risk biomarkers". A biomarker may satisfy various requirements for various purposes or possess certain characteristics that allow for that usage [19]. Types of biomarkers are given below:

1. Diagnostic Biomarker
2. Monitoring Biomarker
3. Pharmacodynamic/Response Biomarker
4. Predictive Biomarker
5. Safety Biomarker
6. Susceptibility Biomarker

**Table 1:** Shows the scientific definition of all main biomarkers and its common examples [1].

| S. No | Type of Biomarker | Definition | Examples |
|---|---|---|---|
| 1 | Diagnostic | To confirm or detect the presence of a disease or identify subtypes | Levels of Aβ42 and T-tau proteins in cerebrospinal fluid of patients with dementia |
| 2 | Monitoring | To monitor the status of a disease and the response to the clinical intervention | Quantification of creatinine and/or potassium serum levels |
| 3 | Pharmacodynamic or Response | To evaluate the response to a medical condition or clinical intervention | Levels of macrophage migration inhibitory factor in schizophrenia |
| 4 | Predictive | To predict the probability to develop any effect as consequence of a clinical intervention | Specific SNPs in schizophrenic patients as predictor of better olanazapine treatment response |
| 5 | Prognostic | To identify the probability of develop a clinical event in patients with a disease or clinical condition | Number of trinucleotide CAG repetitions in patients with Huntington's disease |
| 6 | Safety | To evaluate the probability of developing signs of toxicity as an adverse event of the intervention | Number of active CYP2D6 genes, that modify risperidone metabolization including side effects |
| 7 | Susceptibility or risk | To measure the risk of an individual to develop a disease or medical condition | IL-6 and CRP levels as an indicator of schizophrenia |

| Type of Biomarker | Examples |
|---|---|
| Biochemical markers | high-sensitivity, C-reactive peptide, plasma B-type natriuetic peptide, plasma homocysteine, urinary albumin excretion, plasma renin activity |
| Physiologic markers | Blood pressure, heart rate, pulmonary artery pressure, pulmonary capillary wedge pressures, ventricular premature beats |
| Anatomic measures | Coronary vessel diameter (by coronary angiography), carotid intima media thickness (ultrasound), atherosclerotic plaque burden (intravascular ultrasound) |
| Histologic markers | Tissue biopsy specimens |
| Physical markers | Skin color, weight, height |

**Fig. 1:** Shows other markers also to get a better understanding [20].

### 6.1 Diagnostic Biomarker:

Includes a wide range of biomarkers that are applied to determine if an ailment or other medical problem exists or not. Using this kind of biomarker, illness subcategories can also be determined [21]. The emergence of targeted therapy underlines the notion that testing biomarkers help categorize a sickness and identify in categorizing a sickness and identifying to categorizing sickness but also in identifying people who have it. This is a crucial characteristic as most illnesses have subgroups with varying prognoses or reactions to therapy. As a result, detecting biomarkers would indeed enhance customized treatment and boost the efficacy of the treatment outcomes [22]. Such biomarkers could be extremely important as assessment is used to determine diagnostic accuracy predictors. The levels of "A42" as well as "Total-tau (T-tau)" in the CSF fluid of people living with dementia and diagnostic biomarkers for Alzheimer's disease are two examples [23].

### 6.2 Monitoring Biomarker:

This group encompasses biomarkers that are examined over time to track the progression of an illness or other situation as well as a patient's reaction to therapy, such as exposure to a drug or an ambient toxin. Alterations in biomarker readings are used as assessments of the pharmaceutical response and other treatments as well as signs of how the health manifestations are progressing [24]. The increase in blood creatinine and/or potassium values following a medicinal or physiological therapy is an illustration of a monitoring biomarker. These values are frequently employed as indicators of the likelihood to experience negative impacts. Screening biomarkers can be used in a variety of contexts, such as clinical practice, drug testing, the start of a patient's treatment regimen, the creation of a health supplement, as a way to assess the risk associated with acquiring a disease or to assess the pharmacokinetic profile of the treatment [25].

**Table 2:** Shows the use of monitoring biomarkers in Neuropsychology [1].

| S. No. | Type/Category of Intervention | Usefulness |
|---|---|---|
| 1 | Medical care or scientific trial | To assess the clinical state of the patient before, all through, or after the therapy |

| | | |
|---|---|---|
| 2 | Before management initiation | To recognize the symptoms and/or indications of an ailment or health condition as a prognostic indicator. To evaluate if early intervention is necessary. |
| 3 | Medical product progress | To explain more about a medication's benefits and risks |
| 4 | Public health | To advise people about the likelihood that they may get any ailment or other illness |
| 5 | Pharmacodynamics research or studies | To offer supporting evidence for a treatment outcome |

| Test | Abnormal Findings |
|---|---|
| Glucose | *low glucose*: insulin overdose in an adolescent with diabetes, insulinoma with anxiety and delirium, alcoholism, anorexia nervosa |
| | *high glucose*: delirium, metabolic syndrome, acute pancreatitis, treatment with atypical antipsychotics, and other drugs |
| Calcium | low calcium in alcoholism, cirrhosis, laxative abuse, vitamin D deficiency |
| Albumin | low albumin is a risk factor for delirium and an indicator of liver dysfunction, and can suggest that free rather than total drug levels should be used |
| Total protein | low in undernutrition |
| Sodium | abnormal in polydipsia, diabetes insipidus, the syndrome of inappropriate antidiuretic hormone secretion (SIADH), beer potomania, hypopituitarism and in patients treated with SSRIs, carbamazepine, oxcarbazepine, and other psychotropic drugs |
| Potassium | abnormal in starvation, bulimia nervosa, psychogenic vomiting, alcoholism, and in patients treated with lithium or anabolic steroids |
| Carbon dioxide | abnormal in eating disorders due to purging, alcoholism, alcoholic ketosis, dehydration, head injury, and liver disease |
| Chloride | elevated with hyperventilation, salicylate intoxication; decreased with water intoxication, overuse of antacids |
| Blood urea nitrogen | elevated in renal failure and dehydration, with associated psychiatric signs and symptoms, including delirium |
| Creatinine | may be elevated with lithium treatment; elevated in renal failure and dehydration, with associated psychiatric signs and symptoms, including delirium |
| Alanine transaminase (ALT) | elevation may suggest liver disease |
| Aspartate transaminase (AST) | elevation may suggest liver disease; isolated elevation may suggest early liver disease |
| Bilirubin | elevated in alcoholism, cirrhosis, pernicious anemia, and cancer of the head of the pancreas and as a drug reaction (e.g., to chlorpromazine or other phenothiazines) |
| Alkaline phosphatase | may be elevated in alcoholism and cirrhosis; significant elevation coupled with normal transaminases suggests a cholestatic drug reaction |

**Fig. 2:** Shows more examples of monitoring and diagnostic biomarkers [26].

### 6.3 Pharmacodynamic or Response Biomarker:

A health problem or therapeutic procedure, such as medication therapies, can alter a pharmacodynamic biomarker. This kind of biomarker is typically regarded as a surveillance or monitoring biomarker due

to the periodic pattern of its measurement. This biomarker's primary use is to direct clinical care and provide important data for choosing if or not to sustain the therapy. Pharmacodynamic biomarkers, therefore, control the course of the therapy [27].

### 6.4 Predictive Biomarker:

When a marker's existence or alteration makes it possible to identify which client or group of individuals is so much more susceptible to developing a negative effect as a result of exposure to a medication or ambient contaminant, the indicator is referred to as a "predictive biomarker". These biomarkers are widely employed in clinical testing that is randomized, regulated, and testing novel treatments. The biomarker is utilized in this situation to stratify patients into intervention groups or choose individuals for engagement. If the biomarker foretells a favorable impact, its existence may indicate that the brand-new approach is having a stronger impact than the control therapy. Thus, the utilization of predictive biomarkers makes it easier to choose particular individuals who are more likely to react to medication or not [28].

### 6.5 Prognostic Biomarker:

The term is used to describe the probability of experiencing a therapeutic event in individuals who have been classified with an illness or health problem. Mortality, illness growth or reappearance, or the occurrence of a new serious illness is examples of such events. Prognostic biomarkers are used in clinical trials to identify individuals who are more likely to experience a clinical incident or progression, allowing researchers to identify high-risk groups. Prognostic biomarkers are utilized as insertion or exclusion criteria in this setting [29].

### 6.6 Susceptibility or Risk Biomarker:

As an illustration, consider a hereditary biomarker that may be found years or even decades well before pathological changes or indicators of the disease appear. These research avenues raised the possibility of a link between "interleukin-6 (IL-6)" and "C-reactive protein (CRP)" levels and the risk of SCZ. Lower CRP levels have been hypothesized as a possible highly susceptible biomarker for this neuropsychiatric illness, along with the blockage of I.L-6 signaling, which dramatically raises the chance of SCZ [30].

| TEST | DISEASES |
|---|---|
| Albumin | decreased in malnutrition, hepatic failure, carcinomas |
| Aldolase | increased in bulimic patients and schizophrenia (60-89%) |
| Amylase | increased in bulimia nervosa |
| Antinuclear antibodies (ANA) | found in systemic lupus erythematosus (SLE) and drug induced lupus, secondary to e.g. anticonvulsants; SLE can be associated with delirium, psychotic disorders and mood disorders |
| Bicarbonate | decreased in panic disorder<br>increased in bulimia nervosa |
| Combs tests direct and indirect | hemolytic anemias secondary to psychotropic medication |
| Copper, urine | elevated in Wilson's disease |
| Cortisol (hydrocortisone) | increased in Cushing's disease associated with anxiety, depression |
| Ebstein-Barr (EBV) Cytomegalovirus (CMG) | EBV is causative agent for mononucleosis, which can manifest with depression and personality change<br>CMG may produce: anxiety, confusion and mood disorders |

**Fig. 3:** Shows some examples of the same [31].

## 7. OMICS BIOMARKERS AND ITS USE IN NEUROPSYCHOLOGY/NEUROSCIENCES/ OSYCHIATRY :

This section outlines the key benefits of every 'Omics' approach in the quest for biomarkers for hazard analysis, assessment, tracking therapeutic effectiveness, and clinical outcome forecast in neuropsychological illnesses.

### 7.1 Genomic Biomarkers:

By offering potential targets for illness characterization, early identification, as well as higher management, genomic biomarkers are advancing our comprehension of disease pathophysiology and guiding clients toward the most liable profit based on their distinct profiles. A 'genomic biomarker' is described as "a detectable DNA and/or RNA feature that is an indication of normal biologic processes, pathogenic processes, and/or response to therapeutic or other interventions," by the 'European Medicines Agency' (E.M.E.A) [32]. Those quantifiable characteristics have included a gene's transcription, operation, as well as control. Single nucleotide polymorphism (SNPs), "variability of short sequence repeats," "haplotypes," "deletions or insertions of (a) single nucleotide (s)," 'copy number variation', as well as cytogenetic permutations like "translocations," "duplications," "deletions," or "inversions" can all be used to describe all such attributes in the DNA [33]. "Understanding various mental illnesses like SCZ required the application of genetic tools for the investigation of 'candidate gene', "genome-wide research", as well as "polygenetic risk score analysis". These methods also include "genome sequencing", "exome sequencing", "microarray", as well as "comparative genomic hybridization" (CGH). A small example is given below to understand the concept precisely [34].

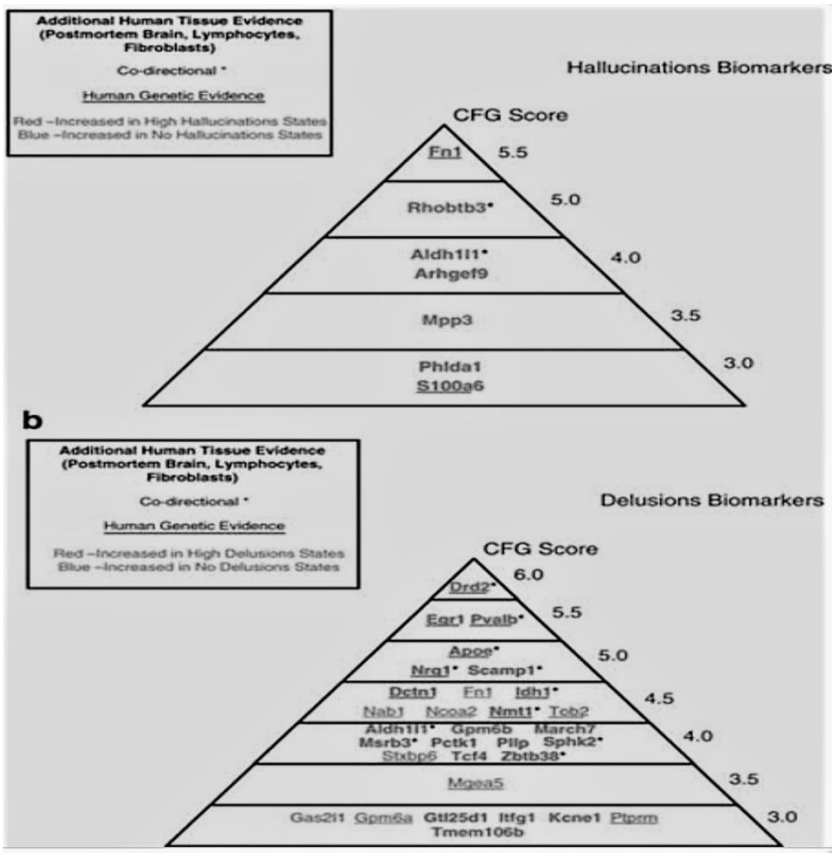


**Fig 4:** Shows examples of genomic biomarkers to diagnose schizophrenia [35].

The discovery of putative genetic biomarkers in many neuropsychological, as well as drug-use diseases, has been made possible by "genome-wide association studies". For instance, the "Collaborative Study of the Genetics of Alcoholism" (C.O.G.A) has linked the 'SNPs rs4780836' "[A > C; chromosome 16:19974071", "rs2605140 A > G chromosome 17:1825306", "rs11690265 chromosome 2: C > T; chr2:27418655 rs692854" "non-functional Se" (FUT2) "gene allele" (AUD) [36].

### 7.2 The Use of Transcriptomic Biomarkers In Neuropsychology/Psychiatry:

The whole collection of Biomolecules in a single cell or a cluster of tissues at a key developmental cycle or biological state is known as the transcriptome. The transcriptome is therefore fluid as well as an accurate reflection of the cellular status. Superior perception of human maladies and their pharmacotherapies would result from monitoring the appearance of an organism's genes as an image in different parts of the body, situations, or time points. This would also enable the discovery of promising therapeutic biomarkers when differences in clinical outcome eventuate [37].

In addition, transcriptomics research has shown that the effectiveness of medications is correlated with modifications in the transcriptome's overall pattern of gene expression. Changes in the "MMO28" and "KXD1 genes", which encode for the proteins "matrix metallopeptidase 28" as well as "KxDL motif-containing protein 1", correspondingly, were linked to a higher sensitivity to nortriptyline in depressed patients in transcriptome research. This information could help characterize the molecular processes that underlie the effectiveness of antidepressants better.

Furthermore, a clinical investigation connected novel miRNAs like "miR-146a-5p, miR-146b-5p, miR-24-3p, and miR-425-3p" to the efficiency of psychiatric drugs like 'duloxetine', "escitalopram", as well as "nortriptyline" in M.D.D patients. These 'miRNAs have a significant role in the regulation of the "mitogen-activated protein kinase" (M.A.P.K) and "Wnt signaling pathways", which are connected to stress-response and M.D.D. They are widely expressed and strongly correlated in blood and brain tissue [38].

### 7.3 The use of proteomic biomarkers in neuropsychology:

Considering plasma, erythrocytes, or serum are physiological specimens that are often employed for therapeutic tests in clinical practice, proteomics techniques employing these materials are a strongly wanted tool for biomarker screening of mental illnesses. Additionally, because of its closeness to the brain, 'cerebrospinal fluid' (C.S.F) is a specimen of special interest in neuroscience and psychology for the discovery of putative proteomic biomarkers. Due to the invasive method entailed, even though its collection is quite sophisticated, it carries far fewer proteins than plasma. As a result, the protein structure "buffering" is substantially weaker, which tends to make it harder to find possible proteomic indicators.

Neurobehavioral illnesses frequently have difficulties with diagnosis and require help as soon as possible. Similar is the situation with SCZ, which is identified by possible symptoms as well as indications but not by quantifiable and distinguishable inborn traits. In this regard, proteome analyses of plasma proteins, serum, and post - mortem nerve cells from SCZ patients reported changes in proteins important for inflammation and immune responses, calcium-homeostasis, and signaling, energy-metabolism, oxidative-stress, cytoskeleton, neuronal communication, and synaptic operation. As potential biomarker contenders for SCZ predictions, diagnosis, and drug surveillance, these proteins have been put forth [39].

### 7.4 The use of metabolomics biomarkers in neuropsychology:

There is an increase in metabolomics indicators for pharmaceutical research. This method concentrates on detecting tiny chemicals called metabolites in a variety of complicated composites, including cerebral spinal fluid, serum, urine, and saliva, as well as other bodily fluids. The metabolome provides an immediate program evaluation of mitochondrial biogenesis and biological factors since it is naturally more dynamic as well as time-sensitive than the "proteome and genome". The combination of ecological, inherited, pathogenic, evolutionary, and lifestyle variables result in changes in the metabolome.

There isn't just one metabolite that defines a marker from metabolomics. Instead, they are a group of linked metabolites that identify particular pathological conditions or the reaction to the medical or psychopharmacological procedure. Presently, the primary analytical platforms employed in the hunt for metabolomics biomarkers are "gas chromatography-mass spectrometry" (G.C-M.S), "liquid chromatography-mass spectrometry" (L.C-M.S), as well as "nuclear magnetic resonance" (N.M.R).

The discovery of putative metabolomics markers in various mental conditions has been the subject of many investigations. For instance, it has been suggested that urine metabolomics may be a valuable method for pinpointing networks that may be implicated in the mode of action of particular medicines. Furthermore, fewer metabolomics biomarkers, particularly in neuroscience and psychology, have satisfied the regulatory requirements for their utilization in clinical practice. This is mostly because

there aren't any reliable assays for routinely quantifying putative biomarkers and because studies are heterogeneous [40].

### 7.5 Neuropsychology and the application of epigenetic biomarkers:

Due to their potential significance in the emergence of human illnesses, particularly psychiatric disorders, dynamic alterations in the structure of chromatin—which alter gene expression but do not alter DNA sequence—have received attention. In light of this, epigenetics could offer a useful gateway between phenotype, genotype, as well as environmental stressors.

"Any epigenetic mark or altered epigenetic mechanism that can be measured in the body fluids or tissues defining a disease; predicts the outcome of a disease; responds to therapy; monitors responses to therapy or medication; and predicts the risk of future disease development" is the definition of an epigenetic diagnostic marker. Epidemiological studies are one method that has been developed to date for analyzing epigenetic alterations that take place in particular areas of the genome as well as mechanisms at the level of distinct genes. Although they are not the only methods, "DNA methylation assays" and "DNA methylation sequencing" are the most commonly employed markers [41].

## 8. CONCLUSION :

As shown in this article, the development of "omics" technology has made it possible to correlate several numbers of proteins, substances, and genes with specific neuropsychological illnesses. None of these, although, has shown to be reliable and practical biomarkers in clinical practice. Despite the limits and difficulties that each "omic" presents, three crucial main goals are shared to enhance the hunt for biomarkers in neuroscience and psychology: (1) Accurate clinical demographic identification, (2) shorter duration, and (3) standardization of sample process parameters. These things can be used to treat any illness, but psychological diseases are of particular importance.

The clinical population being investigated is more heterogeneous due to the wide range of phenotypes seen in clients with the same mental condition and the convergence of some features or patterns among several neuropsychological disorders, which may frequently make diagnosis challenging. Emerging "omics" research has concentrated on the discovery of possible biomarkers for particular features in order to address this problem. The process of integrating the vast amount of data gleaned from each "omics" in order to arrive at a comprehensive realization of a "systems biology" knowledge of the physiological topic remains one of the most difficult tasks to be completed. Techniques for biostatistics have been developed specifically to comprehend the promise of "omics technology" in this aspect.

A further issue is that the existing form of assessment for biomarkers is time-consuming as well as difficult. Essentially, this approach entails two steps: technique evaluation (based on the properties of the assay used) as well as therapeutic testing (to offer proof that the marker is particularly associated with the illness or treatment outcomes under scrutiny) [42]. Large-scale longitudinal holistic "omic" research will be crucial in guaranteeing responsiveness, precision, diagnostic accuracy, as well as probability proportion by evaluating biomarkers in a substantial proportion as well as enabling thorough assay testing. Significant advances in this area are anticipated to happen in the upcoming years.

## REFERENCES :

[1] García-Gutiérrez, M. S., Navarrete, F., Sala, F., Gasparyan, A., Austrich-Olivares, A., & Manzanares, J. (2020). Biomarkers in psychiatry: concept, definition, types and relevance to the clinical reality. *Frontiers in psychiatry*, *11*(1), 432-455. Google Scholar↗

[2] Ilyas, A., Chesney, E., & Patel, R. (2017). Improving life expectancy in people with serious mental illness: should we place more emphasis on primary prevention?. *The British journal of psychiatry*, *211*(4), 194-197. Google Scholar↗

[3] Chesney, E., Goodwin, G. M., & Fazel, S. (2014). Risks of all-cause and suicide mortality in mental disorders: a meta-review. *World psychiatry*, *13*(2), 153-160. Google Scholar↗

[4] OECD. Publishing, & Organisation for Economic Co-operation and Development. (2012). *Health at a glance: Europe 2012*. Organisation for Economic Co-operation and Development, *4*(1), 210-223. Google Scholar↗

[5] Swartz, M. S., Stroup, T. S., McEvoy, J. P., Davis, S. M., Rosenheck, R. A., Keefe, R. S., ... & Lieberman, J. A. (2008). Special section on implications of CATIE: what CATIE found: results from the schizophrenia trial. *Psychiatric services*, *59*(5), 500-506. Google Scholar↗

[6] Sinyor, M., Schaffer, A., & Levitt, A. (2010). The sequenced treatment alternatives to relieve depression (STAR* D) trial: a review. *The Canadian Journal of Psychiatry*, *55*(3), 126-135. Google Scholar↗

[7] Parikh, S. V., LeBlanc, S. R., & Ovanessian, M. M. (2010). Advancing bipolar disorder: key lessons from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). *The Canadian Journal of Psychiatry*, *55*(3), 136-143. Google Scholar↗

[8] Gorman, J. M. (1996). Comorbid depression and anxiety spectrum disorders. *Depression and anxiety*, *4*(4), 160-168. Google Scholar↗

[9] Angst, J., & Merikangas, K. (1997). The depressive spectrum: diagnostic classification and course. *Journal of affective disorders*, *45*(1), 31-40. Google Scholar↗

[10] Pincus, H. A., Tew Jr, J. D., & First, M. B. (2004). Psychiatric comorbidity: is more less?. *World Psychiatry*, *3*(1), 18-29. Google Scholar↗

[11] Green, A. I., Canuso, C. M., Brenner, M. J., & Wojcik, J. D. (2003). Detection and management of comorbidity in patients with schizophrenia. *Psychiatric Clinics*, *26*(1), 115-139. Google Scholar↗

[12] Buckley, P. F., Miller, B. J., Lehrer, D. S., & Castle, D. J. (2009). Psychiatric comorbidities and schizophrenia. *Schizophrenia bulletin*, *35*(2), 383-402. Google Scholar↗

[13] Mundkur, B. D. (1949). Evidence excluding mutations, polysomy, and polyploidy as possible causes of non-Mendelian segregations in Saccharomyces. *Annals of the Missouri Botanical Garden*, *36*(3), 259-280. Google Scholar↗

[14] Porter, K. A. (1957). Effect of homologous bone marrow injections in x-irradiated rabbits. *British Journal of Experimental Pathology*, *38*(4), 401-423. Google Scholar↗

[15] Biomarkers Definitions Working Group, Atkinson Jr, A. J., Colburn, W. A., DeGruttola, V. G., DeMets, D. L., Downing, G. J., ... & Zeger, S. L. (2001). Biomarkers and surrogate endpoints: preferred definitions and conceptual framework. *Clinical pharmacology & therapeutics*, *69*(3), 89-95. Google Scholar↗

[16] FitzGerald, G. A. (2016). Measure for measure: biomarker standards and transparency. *Science translational medicine*, *8*(3), 343-358. Google Scholar↗

[17] Cagney, D. N., Sul, J., Huang, R. Y., Ligon, K. L., Wen, P. Y., & Alexander, B. M. (2018). The FDA NIH Biomarkers, EndpointS, and other Tools (BEST) resource in neuro-oncology. *Neuro-oncology*, *20*(9), 162-172. Google Scholar↗

[18] Olsson, B., Lautner, R., Andreasson, U., Öhrfelt, A., Portelius, E., Bjerke, M., ... & Zetterberg, H. (2016). CSF and blood biomarkers for the diagnosis of Alzheimer's disease: a systematic review and meta-analysis. *The Lancet Neurology*, *15*(7), 673-684. Google Scholar↗

[19] Califf, R. M. (2018). Biomarker definitions and their applications. *Experimental Biology and Medicine*, *243*(3), 213-221. Google Scholar↗

[20] Retrieved from Google Image on 20/09/2022. https://images.app.goo.gl/u4d2Gq6fmSH2nR6z5

[21] Kraus, V. B. (2018). Biomarkers as drug development tools: discovery, validation, qualification and use. *Nature Reviews Rheumatology*, *14*(6), 354-362. Google Scholar↗

[22] Prata, J., Santos, S. G., Almeida, M. I., Coelho, R., & Barbosa, M. A. (2017). Bridging Autism Spectrum Disorders and Schizophrenia through inflammation and biomarkers-pre-clinical and clinical investigations. *Journal of neuroinflammation*, *14*(1), 1-33. Google Scholar↗

[23] Pu, S., Setoyama, S., & Noda, T. (2017). Association between cognitive deficits and suicidal ideation in patients with major depressive disorder. *Scientific reports*, *7*(1), 1-6. Google Scholar↗

[24] Rosén, C., & Zetterberg, H. (2013). Cerebrospinal fluid biomarkers for pathological processes in Alzheimer's disease. *Current opinion in psychiatry*, *26*(3), 276-282. Google Scholar↗

[25] Wiecki, T. V., Antoniades, C. A., Stevenson, A., Kennard, C., Borowsky, B., Owen, G., ... & Frank, M. J. (2016). A computational cognitive biomarker for early-stage Huntington's disease. *PLoS One*, *11*(2), 148-169. Google Scholar↗

[26] Retrieved from Google on 21/09/2022. https://psychnews.psychiatryonline.org/doi/full/10.1176/appi.pn.2017.4a31

[27] Okazaki, S., Hishimoto, A., Otsuka, I., Watanabe, Y., Numata, S., Boku, S., ... & Sora, I. (2018). Increased serum levels and promoter polymorphisms of macrophage migration inhibitory factor in schizophrenia. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *8*(1), 33-41. Google Scholar↗

[27] Zhou, W., Xu, Y., Lv, Q., Sheng, Y. H., Chen, L., Li, M., ... & Qin, S. (2019). Genetic association of olanzapine treatment response in Han Chinese schizophrenia patients. *Frontiers in pharmacology*, *10*(1), 177-190. Google Scholar↗

[28] Ghosh, R., & Tabrizi, S. J. (2018). Huntington disease. *Handbook of clinical neurology*, 1(4), 255-278. Google Scholar↗

[29] Llerena, A., Berecz, R., Dorado, P., & de la Rubia, A. (2004). QTc interval, CYP2D6 and CYP2C9 genotypes and risperidone plasma concentrations. *Journal of psychopharmacology*, *18*(2), 189-193. Google Scholar↗

[30] Hartwig, F. P., Borges, M. C., Horta, B. L., Bowden, J., & Smith, G. D. (2017). Inflammatory biomarkers and risk of schizophrenia: a 2-sample mendelian randomization study. *JAMA psychiatry*, *74*(12), 126-140. Google Scholar↗

[31] Retrieved from Google on 21/09/2022. https://images.app.goo.gl/v9fMgsoNGvrS7H2c7

[32] Lescuyer, P., Hochstrasser, D., & Rabilloud, T. (2007). How shall we use the proteomics toolbox for biomarker discovery?. *Journal of proteome research*, *6*(9), 371-386. Google Scholar↗

[33] Gladkevich, A., Kauffman, H. F., & Korf, J. (2004). Lymphocytes as a neural probe: potential for studying psychiatric disorders. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *28*(3), 559-576. Google Scholar↗

[34] Elenkov, I. J., Chrousos, G. P., & Wilder, R. L. (2000). Neuroendocrine regulation of IL-12 and TNF-α/IL-10 balance: clinical implications. *Annals of the New York Academy of Sciences*, *917*(1), 94-105. Google Scholar↗

[35] Retrieved from Google on 21/09/2022. https://images.app.goo.gl/fBsZVbZD12UL5r5x7

[36] Peng, S., Li, W., Lv, L., Zhang, Z., & Zhan, X. (2018). BDNF as a biomarker in diagnosis and evaluation of treatment for schizophrenia and depression. *Discovery medicine*, *26*(1), 127-136. Google Scholar↗

[37] Annunziata, P., Cioni, C., Mugnaini, C., & Corelli, F. (2017). Potent immunomodulatory activity of a highly selective cannabinoid CB2 agonist on immune cells from healthy subjects and patients with multiple sclerosis. *Journal of Neuroimmunology*, *3*(1), 66-74. Google Scholar↗

[38] de Campos-Carli, S. M., Araújo, M. S., de Oliveira Silveira, A. C., de Rezende, V. B., Rocha, N. P., Ferretjans, R., ... & Teixeira, A. L. (2017). Cannabinoid receptors on peripheral leukocytes from patients with schizophrenia: Evidence for defective immunomodulatory mechanisms. *Journal of psychiatric research*, *8*(1), 44-52. Google Scholar↗

[39] Ilani, T., Ben-Shachar, D., Strous, R. D., Mazor, M., Sheinkman, A., Kotler, M., & Fuchs, S. (2001). A peripheral marker for schizophrenia: Increased levels of D3 dopamine receptor mRNA in blood lymphocytes. *Proceedings of the National Academy of Sciences*, *9*(2), 625-628. Google Scholar↗

[40] Lima, L., & Urbina, M. (2002). Serotonin transporter modulation in blood lymphocytes from patients with major depression. *Cellular and molecular neurobiology*, *22*(5), 797-804. Google Scholar↗

[41] Hernández, E., Lastra, S., Urbina, M., Carreira, I., & Lima, L. (2002). Serotonin, 5-hydroxyindoleacetic acid and serotonin transporter in blood peripheral lymphocytes of patients with generalized anxiety disorder. *International immunopharmacology*, *2*(7), 893-900. Google Scholar↗

[42] Novelli, G., Ciccacci, C., Borgiani, P., Amati, M. P., & Abadie, E. (2008). Genetic tests and genomic biomarkers: regulation, qualification and validation. *Clinical cases in mineral and bone metabolism*, *5*(2), 149-161. Google Scholar↗

*******