Proposal Preview

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Research Project Title
Mismatch Negativity and EEG Measures for Quick, Accurate and Reliable Measurements in the Management of Schizophrenia

Executive Summary
Schizophrenia is a debilitating mental disorder and one of the ten leading causes of disability worldwide. It is a chronic mental disorder associated with significant and long-lasting health, social and financial/economic burden, not only to sufferers but also on their families, public health care system as well as the wider society. Therefore, early diagnosis of schizophrenia is very important as the longer the period of untreated psychosis, the poorer the prognosis. In

addition, life expectancy in patients with schizophrenia is one to two decades shorter when compared to the general population. Hence, prompt and correct diagnosis of schizophrenia is of public health importance. In the clinical setting, the diagnosis of schizophrenia is made using diagnostic criteria based on symptoms, this is unlike other medical specialties where diagnosis is often based on aetiology and supported by objective laboratory investigations. For schizophrenia our understanding of its aetiology, neurophysiology and neuropathology is still limited, and there are no objective laboratory investigations for diagnosis of schizophrenia due largely to the poor understanding of its aetiology.

The observation that mismatch negativity (MMN) is consistently impaired in schizophrenia has made it one of the most viable measures upon which objective laboratory tests for this condition can be based. Further investigation on the use of MMN however has shown that while MMN outperforms other candidate measures, it solely is not accurate enough for clinical use. Hence, this project proposes a technique to improve the accuracy of MMN by combining its performance with those of fuzzy entropy and Auditory Steady-State Response (ASSR) extracted from the patient's electroencephalography recordings. It is expected that the integration of these multiple measures into a single index will result in an objective and more accurate diagnosis and classification of schizophrenia in addition to existing clinical diagnostic criteria. This study could lead to an accurate and easy-to-administer laboratory test for the diagnosis and classification of schizophrenia, which would have profound impact on the management of the disorder globally.

Keywords: Schizophrenia, EEG, MMN, ASSR, Fuzzy Entropy, Diagnosis
Duration of Research: 24 months (January 2021 – December 2023)

1.0 GENERAL BACKGROUND OF THE RESEARCH PROJECT

1.1 Introduction [Provide a general background of the problem and justification leading to the proposed research project]

Schizophrenia is the heartland of psychiatry and the core of its clinical practice, it is a disorder characterized by hallucinations, delusions, grossly disorganized speech and behaviour, and a range of negative symptoms, along with impairments in sensory and higher cognitive function. It affects about 7 per thousand of the adult population, mostly in the most productive age group (15-40 years) and it has been reported that 90% of individuals with untreated schizophrenia are in developing countries (WHO, 2001). When the symptoms of schizophrenia are not treated, the effects can be devastating to the individual with the disorder, the relatives, as well as the society at large.

Vulnerability to psychosis is believed to be mediated by a complex interplay of factors including genetics, temporal and environmental factors, and intense emotional stimuli. Despite recent progress in understanding schizophrenia however, major gaps still exist at all levels of research. A notable aspect of schizophrenia has always been the wide range of potential symptoms that accompany it, which has led some to consider it a heterogeneous group of disorders rather than a single condition. Historically, a symptom-based nosology has been embraced, starting from Kraepelin's classification under dementia praecox, through Bleuler's reclassification, which is the basis for the Diagnostic and Statistical Manual of Mental Disorders (DSM) classifications by the American Psychiatric Association. While this approach to psychiatric nosology has proved to be effective for clinical practice, attempts to isolate definitive pathophysiological correlates have been largely unsuccessful. Consequently, while the behavioural symptoms of the disorder have been studied for a century, there is still no universally-accepted framework to link them to underlying neurophysiology/neuropathology. This affects both the validity of diagnosis and management of the disorder.

Given what remains unknown about its pathogenesis and pathophysiology, diagnosis is still primarily based on assessment of the presence and severity of some symptoms, and for research purposes use of standard questionnaires such as the Structured Clinical Interview (SCID13), Positive and Negative Symptoms Schedule (PANSS) etc. This approach to diagnosis is accurate when applied to patients who have already progressed to psychosis, but is problematic for a number of reasons. First, it is a subjective tool, rather than a proper laboratory test. In fact, psychiatry is the only branch of medicine that does not routinely use diagnostic laboratory tests. The result is that clinicians may have difficulties discriminating between disorders whose symptoms overlap, such as bipolar I, schizophrenia, psychotic depression, and schizoaffective disorders. More importantly, for a disease with such a huge economic and emotional burden, there is a great need for prognostic tools to identify at-risk populations at "premorbid" stage, especially since, even with current medications, early intervention dramatically affects outcome. Present diagnostic tools are of little use for this; hence the ongoing search for biomarkers for the disorder. The development of such a test would have immense ramifications for the study, management, perception, and outcome of the disorder globally. This is the primary long-term goal of this project.

Recently, Mismatch Negativity (MMN) has emerged as a viable candidate endophenotype for schizophrenia. MMN is an event-related potential (ERP) generated in response to deviant auditory ("oddball") stimuli. Deficits in MMN generation in schizophrenia were first reported in 1991, and since then, a few dozen studies have demonstrated preferential reduction in MMN in schizophrenia patients compared with normal populations and other patients with mental disorders (Rissling et al, 2014). Other than being the most consistent marker identified till date, interest in MMN is based on the fact that it appears to be temporally stable, is heritable, and is based on EEG, a neuroimaging modality that has high temporal resolution, and which is both cheap and easy to administer.

Despite the strong link between MMN deficit and schizophrenia, the accuracy of detection is still inadequate for clinical use. In almost every study, the average MMN deficit for schizophrenia populations is higher than the average for other populations. There are however overlaps between the distributions of the different populations. On average, MMN is more attenuated in people with schizophrenia than normal, but there is no absolute threshold; a random normal may have more attenuated MMN than a random schizophrenia patient, and vice versa (Erickson MA, Ruffle A, Gold JM, 2015). A viable approach would be to augment the MMN measure with some other metrics which correlate to some degree with schizophrenia predisposition or psychosis. It turns out that there are a few such candidate measures such as EEG spectral power, coherence, synchrony, and entropy.

Mirroring the progress made in understanding the role of MMN in schizophrenia, important results that could assist in the search for biomarkers have accumulated in other areas. For one, well-known associated effects in schizophrenia are volumetric reductions in white and central grey matter in regions such as the hippocampus and thalamus, along with increase in cerebral ventricles. While exact mechanisms are not clearly understood, these result in certain abnormalities consistently observed in EEG tracings of people with schizophrenia. For example, higher gamma power over the left temporal lobe is viewed as a definite observation in schizophrenia patients (McNally JM, McCarley RW, 2016).Neuroimaging studies have provided credible evidence that schizophrenia is a disorder of connectivity between brain structures and regions. Using measures such as coherence and synchrony, brain connectivity studies at the structural, functional, and effective levels have provided relatively consistent results. For instance, numerous studies have indicated reduced beta and gamma band phase synchrony in schizophrenia patients (McNally JM, McCarley RW, 2016).
A well-known symptom of schizophrenia is auditory hallucinations, which suggests a distortion of the auditory cortex of the brain or some other related characteristic or structure of the brain. This has prompted the study of auditory spectral responses in the brain, of which the auditory steady-state response (ASSR) has produced interesting results. Auditory steady-state responses (ASSR) a type of event response potential (ERP) which test the integrity of the auditory pathway (Brenner et al, 2009) is observed at frequencies up to 50Hz,. Report has shown that patients with schizophrenia show a reduction in power, at 40Hz but not at 20 or 30Hz, they also have delayed onset of phase synchronization and delayed resynchronization

also to 40Hz power (Mulert et al, 2011). ASSR deficits in the range of 30-40Hz are reported to be suggestive of auditory cortex disturbances (O'Donnell et al, 2016).
In the proposed project, a study will be conducted to improve the accuracy and specificity of MMN as a marker for schizophrenia by combining MMN scores with other indices developed from oscillatory abnormalities (ASSR) and measures of connectivity and complexity such as Fuzzy entropy. No previous study anywhere in the world has tried this approach to developing informational correlates of schizophrenia vulnerability or progression. The project will then evaluate the possibility of developing an objective, accurate, and easy-to-administer test for schizophrenia based on the study results.

The implications of the proposed study for the diagnosis and management of schizophrenia, not just in Nigeria but globally, could be far-reaching. With prevalence rates of around 1% of the global population, and average cost of care per year estimated at around $2000 per patient, and costs in excess of £2.6billion annually for England alone, no disease has a greater impact on productivity.

1.2 Aims, General and Specific Objectives of the Research Project:

The aim of this project is to develop a new technique for improved diagnosis and management of schizophrenia.
The general objective of the project is to develop a theoretical framework by which accurate biomarkers for schizophrenia can be identified, and used as the basis for laboratory tests for the disease.

The specific objectives of the project are to:

1. Determine the pattern and severity of symptoms of schizophrenia.
2. Develop an ensemble classifier combining mismatch negativity, Fuzzy entropy and ASSG
3. Acquire electroencephalography (EEG) data from a population of schizophrenia patients classified into subtypes and control subjects
4. Correlate the index developed in (2) with schizophrenia type and severity
5. Develop a prototype diagnostic system based on (4);
6. Assess the effectiveness of the developed system for the diagnosis of first-episode schizophrenia.

1.3 Statement of the Problem [Why does this research need to be conducted?]

Schizophrenia is a severely debilitating mental disorder that affects more than 1.7 million Nigerians. Due to significant knowledge gaps in the aetiology and pathophysiology of the disorder, management of this condition is often life-long. The drugs of choice for its management often lead to unpleasant side effects. This leads to considerable losses to Nigeria, both in productivity, and in directly-quantifiable economic terms. An objective, simple and accurate diagnostic tool for the disorder would greatly reduce the overall cost-of-care for the disease, but the best candidate for such a test is not accurate enough for clinical use. The proposed project is motivated by the urgent need to develop new approaches and tools for the diagnosis and management of Schizophrenia as a way of easing the severe burden of the disease on sufferers, their loved ones, and the nation.

1.4 Conceptual framework of the Study [Clearly identify and define the central concepts or ideas of the study]

The study is based on the following important concepts:

1. Mismatch Negativity: Mismatch negativity (MMN) is an event-related potential generated in response to deviant auditory ("oddball") stimuli. It is a negative-going potential expressed most strongly at fronto-central electrodes that is generated around 50ms after a deviation from a previously-established pattern of auditory stimuli, and lasts for a few hundred milliseconds. Dozens of studies over the last two decades have established a correlation between MMN deficit and schizophrenia. It is now generally considered one of the most viable candidate endophenotypes for schizophrenia, although its accuracy as a diagnostic metric falls short of requirements for clinical use.

2. Schizophrenia as an abnormality of connectivity: in the past, the disease was viewed as a disease affecting specific brain networks and regions. This view was strengthened by neuroimaging studies that showed distinct anatomical changes in particular regions. One oft-noted effect is the reduction in white and grey matter volume, with reductions of up to 10% reported in regions including the hippocampus, the heteromodal association cortex including the prefrontal, anterior cingulate, superior temporal and parietal cortex as well as the thalamus. Currently however, there is mounting evidence in support of the "dysconnectivity" model of the disease. This model hypothesizes that the disorder arises due to pruning or "dysfunction" of connections between brain structures and regions. Were it to be validated, this hypothesis would provide a basis to expect variations in measures of connectivity such as coherence, and measures of complexity such as Fuzzy entropy.

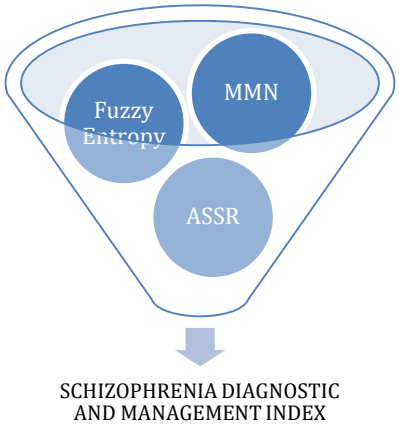
3. Heterogeneity of the disease: The evidence in support of treating schizophrenia as a spectrum of related disorders is significant. One of the most perplexing aspect of exploratory studies into the disease is the often inconsistent and sometimes contradictory results. A central premise of this study is that the inconsistencies are at least partly caused by an implicitly monolithic view of the disorder, which is not supported by existing evidence. The majority of studies reported in literature lump all schizophrenia patients into one group. This study will instead, identify subtypes of the disorder based on existing literature, and correlate statistical measures to specific subtypes, rather than lumping all schizophrenia suffers as a monolithic group.

4. Electroencephalogography (EEG) signals are considered unstable and non-linear. Recently, the analysis of complexity of time series, such as EEG signals, has witnessed notable advances. These advances have provided intuitive understanding and insights into the study of EEG signals. Over the years various entropy based-measures such as Approximate Entropy (ApEn), Sample Entropy (SamEn), Fuzzy Entropy (FuzzyEn) have been used to investigate the complexity of EEG time series signals. The Fuzzy Entropy is regarded as the most robust and reliable complexity measure. Entropy as a measure is used to quantify the disorder and degree

of chaos of a time series signal. The entropy index increases as the degree of irregularity of the time series signal increases.

Fuzzy Entropy defined as the negative natural logarithm of the conditional probability that two vectors similar for m points remain similar for the next $m+1$ points. Fuzzy entropy can serve as a measure of the information content of certain portions of scalp-acquired EEG data. It is directly linked to the complexities of the underlying neurophysiological processes. This is significant because one of the oldest noted anatomical changes accompanying schizophrenia is the reduction in both volume and the complexity and density of connections between brain regions, which are all reflected in EEG. In addition, the dysconnectivity model predicts alterations in the information-bearing capacity of structures and regions during psychosis. Fuzzy entropy can therefore be used as a means of inferring the complexity of underlying brain anatomy from EEG data.

This study hopes to combine the mismatch negativity MMN with Fuzzy entropy and the auditory steady state response (ASSR) into a single index to be used for diagnosis of Schizophrenia



1.5 Project Goals [Provide a summary of the short and long-term goals of the project. Indicate clearly the problems the project will help to address]

The short-term goals for the project are:

1. Identifying EEG patterns of schizophrenia patients and compare same with normal individuals;
2. Developing an objective laboratory test based on an index that combines MMN, Fuzzy entropy, and other brain electrical activity measures, that can be used in the diagnosis and subtyping of schizophrenia; and
3. Mentorship of at least one Resident Doctor and a Masters student.

Long-term goals

4. To determine the neuropathological basis of schizophrenia which will help with identifying possible preventive measures against this very debilitating condition.
5. This project will also provide baseline data on MMN and ASSR among patients with schizophrenia in Nigeria.
6. Correlate subtypes of schizophrenia with prognosis

1.6: Project Impact: [Provide information on the long-term impact of the project within the context of social, economic and technological benefits.]

Social Impact: Few medical conditions are associated with the social burden and stigma of schizophrenia. The results of the proposed project would lead to a shift in how the disorder is perceived, thus reducing associated stigma and thus helping many more receive needed care

Economic Impact: The economic cost of schizophrenia is significant. If its objectives are met, the proposed project would result in more effective and early diagnosis and treatment for the disorder. The disorder is highly debilitating because it affects people in the prime of their life's thus impacts the productivity of sufferers, but early diagnosis is known to greatly improve outcome. The current diagnostic tool is ineffective until sufferers' progress into the psychosis stage. An objective test such as the one being developed would allow earlier intervention with the possibility of full recovery, thus allowing the individual contribute to economic development rather than becoming a burden.

Technological Impact: The project would develop a ground-breaking test for schizophrenia that can be administered with ease and very cheap when compared with other forms of imaging techniques used today. Diagnostic algorithms developed will be combined with EEG devices to form stand-alone test stations, which would only need qualified medical technicians to set up.

2.0 RESEARCH DETAILS

2.1 Literature Review

Schizophrenia is a severe psychiatric condition with symptoms such as hallucinations, delusions, grossly disorganized speech or behaviour, and a range of negative symptoms (Uhlhaas and Singer, 2010), with symptoms varying in severity across time and across individuals. The disorder has a peak onset in young adulthood, with onset and prevalence both modulated by gender. Vulnerability to schizophrenia is highly heritable. Environmental and stochastic factors such as migrant status, older fathers, Toxoplasmosis gondii antibodies, prenatal famine, lifetime cannabis use, obstetrical complications, urban rearing, and season of birth, are also known to play important roles in determining whether an at-risk individual progresses to psychosis (Stephan et al., 2009).

The view of schizophrenia as a consequence of pathological interaction between brain regions dates back to at least 1906. However, structural and functional connectivity analysis tools needed to verify the hypothesis did not become available till the 1980s. Consequently, the preponderance of evidence on the pathophysiology of schizophrenia has traditionally been with respect to focal brain anomalies. Prominent among these are volumetric reductions in white (Paillere-Martinot et al., 2001) and grey (Paillere-Martinot et al., 2001; Kasparek et al., 2007; Yamada et al., 2007) matter.

Widespread availability of PET and MRI has allowed the re-emergence of the dysconnectivity hypothesis. This hypothesis holds that abnormal connection between anatomically distinct brain regions is a characterizing neurophysiological feature of schizophrenia. The term "dysconnection" is preferred to "disconnection" to emphasize that connections become abnormal, rather than reduced (Stephan et al., 2009). The formal dysconnection hypothesis suggests that the underlying cause of dysconnectivity in schizophrenia is a specific impairment in synaptic plasticity, resulting from aberrant modulation of N-methyl-D-aspartate receptor (NMDAR) functions by dopamine, acetylcholine, or serotonin (Stephan et al., 2009). There is significant evidence in support of the hypothesis. Neuroimaging studies confirm dysconnectivity localizations in the frontal lobe (Garrity et al., 2007; Wolf et al., 2009; Lynall et al.,2010), and to a lesser extent, fronto–temporal (Wolf et al., 2009) corpus callosum (Lynall et al., 2010) and anterior cingulate gyrus (Honey et al., 200; Tu et al., 2010) dysconnectivity to other cortical and subcortical regions. These trends have been observed for all stages of the disorder (Pettersson-Yeo et al., 2010).

While structural connectivity studies have depended primarily on MRI and PET, EEG and MEG have been very useful for functional connectivity studies due to their excellent temporal resolution. EEG in particular, has been used for schizophrenia research for decades. One of the oldest observed abnormalities EEG anomalies in schizophrenia is the preponderance of slow rhythms (Boutros et al., 2008) with shifts in the central frequencies of the alpha band to lower values and beta bands moving to higher frequencies but with lower amplitudes (Elbert et al., 1992). In most studies, the abnormal rhythms were localized to the frontal regions (John et al., 1994; Takeuchi et al., 1995; Omori et al., 1995; Knott et al., 2001). Others have noted more pronounced changes in the left hemisphere of schizophrenics than normals (Karson et al., 1988).

More recent EEG approaches have mirrored the emergence of the dysconnection hypothesis. Measures such of synchronization, correlation, and coherence have been extracted from EEG signals (Uhlhaas and Singer, 2010; Weiss and Rappelsberger, 2000). Abnormal oscillations or distance synchronizations have been observed both in the resting state and in task-induced states such as perceptual grouping, attention, and working memory (Breakspear et al., 2003; Uhlhaas and Singer, 2010).

One EEG-derived measure in particular is seen as a viable candidate in the search for endophenotypes of schizophrenia. Mismatch negativity (MMN) is "a pre-attentive auditory event-related potential (ERP) that is automatically generated when a stimulus is presented that deviates in some physical features, such as frequency, duration, and intensity, from previously repeatedly presented standard stimuli" (Umbritch et al., 2003). Its main generators lie within the primary and secondary auditory cortices, and the signal is usually expressed most strongly at fronto-central electrodes (Li et al., 2008; Weickert et al., 2013) MMN is estimated by subtracting the magnitude of the ERP elicited by regular auditory events from the ERP elicited by the violating events (Lieder et al., 2013). Deficits in MMN generation in schizophrenia were first reported in 1991 (Shelley et al., 1991), and since then, multiple studies have observed preferential reduction in MMN in schizophrenia patients compared with normals or populations

with other psychiatric disorders (Stephan et al., 2009, Rissling et al, 2014). The current view is that MMN deficit represents a possible biomarker of schizophrenia (Weickert et al., 2013, Rissling et al, 2014).

There however exists a major challenge in the path to clinical use of MMN in diagnosis: its specificity. While the average MMN response for schizophrenia is lower than that for other populations, there are substantial overlaps in the values for individuals from all populations (Umbritch, 2013). Consequently, it is impossible to classify individuals into populations solely by MMN deficit. One possible way to improve the specificity of the MMN deficit measure is to combine it with other measures reported in literature to correlate to lesser extents with the disorder. Among these are EEG power spectrum (for a review, see Boutros et al., 2008), coherence and synchrony (Uhlhaas and Singer, 2010) and entropy (Bassett et al., 2012; Bachiller et al., 2015). It is interesting that no attempt to improve the accuracy of MMN in this manner has been reported in the literature. That is the knowledge gap targeted by this study.

Entropy measures have been applied to a wide range of biological data studies. Kannathai, N, et al 2005, performed the detection of Epilepsy from EEG time series data using entropy measures, while the recognition of positive and negative emotions based on sample entropy of EEG was presented by Xiang J, et al, 2014. Simons, S. et al, 2018, studied EEG data from Alzheimer's disease (AD) using sample Entropy and Fuzzy entropy measures. Xiang J, et al, 2019 investigated the abnormal entropy modulation of the EEG signal in patients with Schizophrenia during auditory paired-stimulus.

Pincus et al 1991 in their seminal work developed the approximate entropy (ApEn) algorithm. However, the ApEn suffers from vector self-mating and it is heavily impacted by the length of the time series data. To overcome these setbacks of ApEn, the Sample Entropy (SamEn) was proposed in 2001 by Richaman and Moorman. However, due to the heaviside binary function employed in ApEn and SamEn, their entropy values presented dis-continuity for close boundary data sequences. To avoid this discontinuity, Chen et al in his 2007 paper proposed a new algorithm that employs an exponential fuzzy membership function instead of the usual binary Heaviside function.

The Fuzzy entropy is regarded as the most robust and reliable entropy measures (Simons, S. et al, 2018). Hence, in this proposal the Fuzzy Entropy measure is adopted for the study of complexity measures of EEG signals for the improvement of the clinical diagnosis, classification and management of Schizophrenia patients.

The study of 40 Hz signals in the brain began in the 1940s, in the 1980s, the 40 Hz ERP [2] and then the middle latency response were of interest and these were used for the characterization of the brain and clinical hearing testing (Jaaskelainen et al, 2004). More recently, the Auditory Steady-State Response (ASSR) has been studied for its use in diagnosing Schizophrenia. This is due to the fact that some Schizophrenia symptoms sometimes include hallucinations and a distortion of the schizophrenic's auditory perception (Raas et al, 2012).

2.2 Research Methodology [Give detailed methodology of the proposed research project]

The study will be conducted in two phases.
PHASE I: Developing the diagnostic Index XYZ (Combining MMN, Fuzzy Entropy and ASSR)

SAMPLE SIZE: The required sample size for the study group was calculated using the formula according to Fleiss et al (2013)

$$N = C \frac{[2\ (Pc)\ +\ Qc]}{d^2} + \frac{2}{d} + 2$$

Where: C is a constant that depends on the values for alpha (significance level) and beta (power), with alpha set at 0.05 and beta at 90%, then C = 10.51
Pc: the estimate of the proportion of outcome set at 50% (0.5)
Qc = 1 - Pc
d = differences in the outcome (1 - 0.5) = 0.5

$$N = \frac{10.51\ [2\ (0.5)\ +\ 0.5]}{0.5\ X\ 0.5} + \frac{2}{0.5} + 2$$

N = 69.06
Adding 10% attrition rate = 6.906 + 69.06 = 75.97
A sample size of 100 was chosen in order to increase the statistical power. Thus, each of the two study groups (patient with schizophrenia and apparently healthy control) comprised of 100 sample subjects making a total sample population of 200.

Participants

The patients will be recruited from the outpatients' Mental Health Clinics of the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife, Osun State (both Ife Hospital Unit and Wesley Guild Hospital, Ilesa will be used) and those attending the outpatient clinic of the Department of Behavioural Science, University of Ilorin Teaching Hospital Ilorin Kwara State. Patients that meet the inclusion criteria and give written consent will be consecutively recruited until the required number is complete. Age and sex matched healthy control subjects will also be recruited simultaneously..

The inclusion criteria for patients to be included into the study will be:

1. Patients aged 18 years and above
2. Diagnosis of schizophrenia must be based on ICD – 10 research diagnostic criteria, this will be confirmed by the researchers using the Mini International Neuropsychiatric Interview (MINI) English Version 5.0.0 (Sheehan et al, 1998).

The exclusion criteria for the patients will be:

1. Any neurologic illness or major head trauma that would result in abnormal EEG; electroconvulsive therapy.

2. Presence of any other current psychiatric comorbidities such as psychoactive substance use disorder
3. Presence of organic disease or mental retardation and significant physical illness such as stroke, severe hypertension and diabetes mellitus.
4. Patients with hearing difficulty in either or both ears will be excluded

The healthy control subjects will be randomly selected from the community, they will be matched for age and sex; potential healthy controls will be excluded if there is past history of any psychiatric illness or a family history of psychiatric illness in the first degree relative as well as any current treatment with drugs known to act on the central nervous system. In addition, they will also be excluded if they are suffering from significant physical illness such as severe hypertension and diabetes.

The study will be cross-sectional survey. One hundred patients and hundred controls will be recruited for the study. Approval of the research protocol by the Ethics and Research Committee of Obafemi Awolowo University Teaching Hospitals Complex will be obtained and written informed consent will be obtained from the subjects after the aim of the study had been explained to them.

Measures:

Mini International Neuropsychiatric Interview (MINI): The diagnosis of schizophrenia will be ascertained with the Mini International Neuropsychiatric Interview (MINI), English Version 5.0.0 (Sheehan *et al.*, 1998). The MINI was designed as a brief structured interview for the major AXIS I psychiatric diagnoses in the DSM IV and ICD-10. Validation and reliability studies done comparing the MINI to other similar structured interviews such as the Structured Clinical Interview for the DSM-IV Patient version (SCID – P; First *et al.*, 1994) and the Composite International Diagnostic Interview (CIDI; Smeets & Dingemans, 1993) have shown high validity scores. The lifetime diagnosis version will be used in this study. The instrument has been used in Nigeria (Akinsulore *et al.*, 2015). A semi–structured questionnaire will inquire about socio-demographic and illness related variables of the subjects. The information included: age, sex, marital status, religion, ethnicity, highest level of formal education, occupation, current employment status. Also, information about duration of the illness, age of onset and number of active symptoms of schizophrenia, past history of hospital admissions and number of hospital admissions will be obtained.

Positive and Negative Syndrome Scale (PANSS; Kay *et al.*, 1987): Psychopathological symptoms will be assessed with the Positive and Negative Syndrome Scale (PANSS; Kay *et al.*, 1987) which will include a structured interview to assess patients on 30 items covering positive, negative and general symptoms. For each item, ratings will be made on a 1 – 7 scale of symptom severity. The scale has been used in Nigeria (Akinsulore *et al.*, 2014; 2015).

The World Health Organization Disability Assessment Schedule (WHODAS II) will be used to measure disability as well as functioning. The 36-item interviewer-administered version of the

WHODAS II will be used for the study and it measures the difficulty the individual has had with performing particular daily activities over a period of 30 days. It consists of 36 Likert formatted questions, divided into six domains: understanding and communicating (six items); getting around (five items); self-care (four items); getting along with others (five items); life activities (eight items); and participation in society (eight items). The final scores range from 0 to 100 with lower scores indicating greater functioning.

Procedure:

Each respondent (Case) will complete the socio-demographic questionnaire after which they will be interviewed using the MINI, PANNS and WHODAS, this will be done in a quiet room in the clinic. They will then be taken for EEG recording.
Selected control subjects will also complete the socio-demographic questionnaire
The data collected at this stage will be used to determine the Index (XYZ)

EEG recordings will be acquired from 28 scalp locations with a 32-channel device. Electrode placement will follow the international 10/20 system using standard Ag-Cl electrodes. An electrode placed on the nose will serve as reference. Electrode/skin impedance will be kept below 5 kΩ, and signals amplified with a band pass of .1 to 100 Hz (6 dB down) and digitized continuously at a sampling rate of 500 Hz.

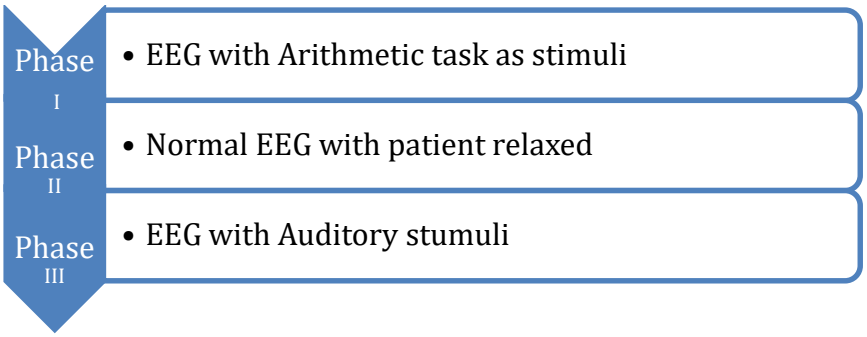
EEG acquisition will be done in three phases. The first two phases will acquire data for the computation of EEG spectral analysis and entropy. The first phase will have subjects performing an arithmetic task, while the second will be with subjects at rest. The third phase will be for the generation and detection of the mismatch negativity ERP. Prior to EEG acquisition, subjects will be familiarized with the EEG equipment and signal acquisition procedure, and given the chance to practice the arithmetic task.

The arithmetic task of phase 1 will require the subject to assign numerical values to each letter of two randomly-selected sentences from well-known sources (such as the National Anthem or songs known by the subject). Subject will then be required to add up all the numerical values of the letters consecutively for a 4-minute recording time. Participants will be advised to be as accurate as possible, and to take their time, as there would be no bonus for completing the task before the expiration of the 4-minute duration. To determine whether subjects had successfully performed the task, their reported answers will be compared to the known accurate answers (at the last letter reached by the subject), and deviations of less than 20% would be taken to indicate successful completion of the task. The data for subjects who do not successfully complete the task will be discarded.

At the completion of the 4-minute arithmetic task, subjects will be asked to simply relax as much as possible with their eyes closed to avoid muscle and eye movement. They will be asked not to follow any particular train of thought. Additional EEG will be recorded for up to 4 minutes. Users will then be given a chance to take a short break before the third section if they so desire.

For the third phase, auditory stimuli will be presented binaurally through disposable foam insert earphones. Auditory stimuli will consist of three classes of tones. Tone A (“standard”) will have

duration of 100 ms and frequency 1 kHz. Tone A will be intermixed with two deviant signals (Tone B will be a frequency deviant with duration of 100 ms and frequency of 2.5 kHz, and Tone C will be a duration deviant with duration 250 ms and frequency 1 kHz). Rise time for all stimuli will be maintained at no less than 5 ms, and nominal intensity will be 75 dB sound pressure level. A random series of 600 tones consisting of Tones A, B and C (with probabilities of occurrence of 0.70, 0.15, and 0.15 respectively) will be pre-recorded, and the same identical recording will be played back to all subjects. The playback will be done using a computer which will be time-locked to the EEG data acquisition for accurate detection of the MMN ERP. For subjects taking the test a second time, a different randomly-generated series of tones will be pre-recorded and played back. All subjects taking the test for an n^{th} time will have the same n^{th} pre-recorded sequence played to them. During the application of auditory stimuli, subjects will watch a silent video film to divert attention from the tones, and to minimize boredom. Short breaks will be offered if subjects become restless or animated before the completion of the test.



PHASES OF EEG MEASUREMENTS.

Extraction of EEG Measures:

EEG data will be converted to the EDF+ data format so that data processing can be carried out in Matlab. The data analysts will be blind to the clinical subtype and other traits of each patient and control. Data from some of the 28 electrodes will be used for analysis. The exact electrodes have not been determined at this time. Signals will be passed through a fourth order Butterworth filter with pass band between 1 Hz and 70Hz to eliminate artifacts.

To extract a measure from the EEG power spectral density, a short time Fourier transform (STFT) will be used to analyse the time-frequency information extracted from data from selected electrodes for all three phases. This sliding temporal window technique will be used to obtain the temporal evolution of signal power spectral density (PSD). EEG data will be broken into 400 ms epochs (with each epoch containing 200 samples). Each epoch will further be split into 84 ms temporal segments (or 41 samples) with 90% overlapping. Thirty-two time intervals will thus be obtained.

Given time series of data length of N points, the Fuzzy entropy measure can be computed using the following steps.
i) From the given N points of the time series $\{x(n); 1 \leq n \leq N\}$, such that $\{x(n)\} = x(1), x(2), x(3), \ldots . x(N)$, while, $1 \leq i \leq N - m + 1$, form the m-vectors,

$X_m(1),,X_m(2),,X_m(3),\ldots,X_m(N-m+1)$, where m is length of the compared window dimension and with $X_m(i)$ is defined as;

$X_m(i) = [x(i), x(i+1), x(i+2), x(i+3), \ldots, x(i+m-1)] - x0(i)$.

$X_m(i)$ denotes m consecutive x values commencing at the i^{th} point with the baseline $x0(i)$ removed.

Note $x0(i) = m^{-1} \sum_{j=0}^{m-1} x(i+j)$.

ii) Define the distance, $d^m{}_{i,j}$, between the vectors $X_m(i)$ and $X_m(j)$as the maximum absolute difference between their scalar components;

$d^m{}_{i,,j} = d\,[X_m(i), X_m(j)] = max_{k\in\{0.m-1\}}|(x(i+k) - x0(i))\text{- }(x(j+k) - x0(j))|$.

iii) Given n and torelarance, , calculate the similarity degree, $D_{i,j}{}^m$ of the vectors $X_m(i)$ and $X_m(j)$ using the exponential fuzzy function:

$$D_{i,j}{}^m = \mu(d^m{}_{i,,j}, r) = exp(\frac{-(d^m{}_{i,,j})^n}{r})$$

iv) Define the function $\emptyset_m$ as:

$$\emptyset_m(r) = \frac{1}{N-m}\sum_{i=1}^{N-m} (\frac{1}{N-m-1}\sum_{j=1,j\neq 1}^{N-m} D_{i,j}{}^m)$$

v) Increase the length of the compared window from m to $m+1$, then form the vectors $X_{m+1}(i)$ and similarly obtain the function $\emptyset_{m+1}$ by repeating the steps ii to iv. above.

vi) For a finite time series with N sample length, the FuzzyEN can be evaluated as:

$FuzzyEn(m.r)$ =ln$\emptyset_m$(r)-ln$\emptyset_{m+1}$(r).

For the computation of MMN deficit, epochs will be constructed from phase 3 data, consisting of a 100 ms pre-stimulus baseline, and a 500 ms post-stimulus interval. Epochs will be averaged for each subject and stimulus type, and digitally filtered with a low-pass filter of 15 Hz (24 dB down). The epochs to standard stimuli immediately after a deviant stimulus will be excluded from the averaging process.

Mismatch negativity waveforms will be obtained by subtracting waveforms evoked by Tone A from waveforms evoked by Tone B or Tone C stimuli. To assess the overall strength of the MMN response to standard and deviant stimuli respectively, and to increase the signal-to-noise ratio, average waveforms will be mathematically referenced to an average- mastoid reference. Using a mathematical operation that is yet to be decided, an index will be generated to represent the mismatch negativity deficit.

The measures derived from spectral power, entropy, and mismatch negativity will be combined into a single measure, tentatively termed “Measure XYZ”. The most appropriate mechanism for the combination will be determined after the initial sets of data are analysed, but a simple mean may be sufficient.

PHASE II: Prototype and Testing

Depending on the results of statistical analysis, all algorithms initially implemented in Matlab will be ported to a compiled programming language such as C#. A proper user interface will be developed, automating the process from EEG data acquisition to the generation of Measure XYZ for subjects. The developed application will be tested in clinical settings at the outpatient department of the Obafemi Awolowo University Teaching Hospitals Complex and University of Ilorin Teaching Hospital, Ilorin Kwara state.

For the clinical testing of the developed Index:
Patients meeting with first episode psychosis (100) defined as patients presenting with psychotic symptoms the first time and symptoms starting within the last 12months and who gave consent to be included in the study after the objectives of the study had been explained to them. This patients will be interviewed using MINI, PANNS and WHODAS, and then sent to have EEG done. (Both EEG technicians and the researchers analysing the EEG will be blind to the diagnosis of each patient).
The developed index (XYZ) will then be used to determine the diagnosis, classification and severity of the illness.
Correlation between clinical diagnosis and diagnosis using the developed index (XYZ) will be determined using appropriate statistical analysis. Sensitivity, Specificity, positive and negative predictive powers of the developed index will be determined

Statistical Analysis

Measure XYZ will be correlated with diagnostic measures generated from MINI, CIDI, etc. The Statistical Product and Service Solutions (SPSS) software (version 23) will be used for analysis. A descriptive analysis will be performed to explore data distribution while inferential statistics will involve the use of Student t-test and Chi-square statistics to study the differences between the two groups (patients with schizophrenia and the healthy controls). Correlations between psychopathology, symptom pattern and EEG index will be studied using Pearson's Product Moment Correlation Co-efficient.

2.3 Project Activities and Output [Give details of expected output from the research grant i.e. results to be obtained/produced within the proposed time frame of the project]

	Activity	Expected Output
1	Evaluation of candidate EEG metrics	Formulation of a model by which a measure ("Measure XYZ") combining MMN, fuzzy entropy, and ASSR can be used as a diagnostic or theranostic index.
2	Study design	Protocols for main study clearly defined.
3	Training of graduate students, research assistants, and Mental Health clinic staff.	Study protocols understood by participating clinical and research personnel.
4	Recruitment of subjects for study	Appropriate number of controls and patients recruited for the main study.
5	Study to extract EEG from schizophrenia patients and normals	EEG data acquired from large population of mental health patients and controls.
6	Analysis of study data	Data and evidence of the correlation of Measure XYZ with schizophrenia disposition or progression.
7	Development of software application to implement algorithm to automatically determine value of Measure XYZ from EEG data	Working software that accurately computes value of Measure XYZ from EEG data.

8	Development of laboratory test protocol	Streamlined procedure for acquiring EEG data, and using the software developed in Activity 6, generate a Measure XYZ value for a subject.
9	Assessment of prototype test with clinical populations	Test developed in Activity 7 administer to schizophrenia patients and used as a diagnostic or theranostic tool.
10	Presentation and dissemination of findings	At least one workshop held; findings from the study discussed on at least one TV program; at least one publication presented at a conference; at least one paper published in a journal.
11	Mentorship	At least two academic staff and at least one graduate student mentored.

2.4 Time Frame: [Provide a timeline for the major activities of the project.]

S/N	Description of Activity	Duration months)	Quarter (Year 1)				Quarter (Year 2)			
			1st	2nd	3rd	4th	1st	2nd	3rd	4th
1	valuation of candidate EEG etrics	3								
2	tudy design	2								
3	raining of graduate students, search ssistants, and Mental Health clinic aff.	1								
4	ecruitment of subjects for study	6								
5	tudy to extract EEG from chizophrenia atients and normals	4								
6	nalysis of study data	3								
7	evelopment of software plication implement algorithm to utomatically determine value of leasure XYZ from EEG data.	4								
8	evelopment of laboratory test rotocol	3								

9	ssessment of prototype test with inical populations	6								
10	resentation and dissemination of ndings	6								
11	lentorship	24								

2.5. Activity Indicators [Clearly state the indicator(s) of each major activity of the project]

Activity	Expected Outcome
Evaluation of candidate EEG metrics	i. Quantity and currency of literature used. ii. Number of candidate metrics considered. iii. Data on performance of each metric will be obtained.
Study design	i. Clarity of definition of roles of study personnel and subjects.
Training of graduate students, research assistants, and Mental Health clinic staff.	i. Number of participants who can clearly articulate the study goals and their roles.
Recruitment of subjects for study	i. Subjects who meet the inclusion criteria for the study will be recruited. ii. Percentage of invited individuals who submit signed consent forms. Iii Percentage and characteristics of those who refuse to participate in the study will be determined
Study to extract EEG from schizophrenia patients and normal controls	i. Number of successfully-completed EEG sessions.
Analysis of study data	i. Percentage of total acquired EEG data importable into data-processing software. ii. Numerical values for Measure MMN, Fuzzy Entropy and ASSR, and correlation with schizophrenia status.

Development of software application to implement algorithm to automatically determine value of Measure XYZ from EEG data.	i. Number of syntax and semantic errors in the source-code (should be zero). ii. Computed numerical values for Measure MMN, Fuzzy Entropy and ASSR.
Development of laboratory test protocol	i. Parsimony of the protocol guidelines.
Assessment of prototype test with clinical populations	i. Numerical data on accuracy of diagnosis.(Specificity and Sensitivity of index assessed)
Presentation and dissemination of findings	i. Number of workshops held. ii. Two local conferences and two international conferences attended. iii. Two publications.
Mentorship	i. Two resident doctors or engineering graduate students who co-author publications. ii. Two resident doctors or engineering graduate students who play key roles in the main study and other activities.

2.6 The Study Location

The main study will be conducted at the Obafemi Awolowo University Teaching Hospitals Complex and the University of Ilorin Teaching Hospital Ilorin, Kwara State. (Both the Ife hospital unit and the Wesley Guild Hospital units will be used). Data processing and software development will be carried out on Obafemi Awolowo University campus.

2.7 Data Management and Analysis

EEG data is usually acquired and saved in vendor/proprietary formats. All raw data acquired for the study will be converted to the open EDF+ neuroimaging data format, and stored on a dedicated computer secured with a password. Subject-related information and other study data will be entered into the same computer, with access restricted where necessary through the use of proper security measures.

Analysis of EEG data will be carried out using Matlab release 2017a, while statistical analysis will be done using the SPSS version 23.

2.8 Ethical and Environmental Considerations

Ethical Considerations: Ethical clearance for the project will be obtained from the Obafemi Awolowo University Teaching Hospital ethics committee. EEG is a non-invasive technique, and generally poses no danger whatsoever to study participants. Study data and relevant health records of study participants will be handled following international best practices.

Environmental Considerations: The project will have no adverse effect on the environment.

2.9: Monitoring and Evaluation Mechanism [State clearly the monitoring and evaluation mechanisms you will adopt in achieving the stated objectives.]

1. The principal investigator will ensure that selected participants meet the research and diagnostic criteria of the ICD 10 in both centers to be used for the study.

2. He will also make sure that all questionnaires are fully completed before they are entered into the computer software SPSS.

3. Prof. Mosaku, Dr Akinsulore and Prof. Ajiboye will coordinate the EEGs, ensuring that they are done in the same room with little or no distractions to reduce artifacts from affecting the result. They will monitor the technologists that will perform the EEGs.

4. The testing equipment will be properly calibrated and standardized before use.

5. Results will be compared with findings in the literature from other countries.

6. There will be monthly meetings at which activity indicators stated in Section 2.5 of this proposal will be used as bases for assessing the progress of the project. During the study, assessment of outcomes will be done fortnightly.

2.10: Dissemination Strategies [Indicate the steps you will take to ensure the project outcomes are brought to the attention of stakeholders.]

1. At the onset of the project, a sensitization seminar will be organized to inform and sensitize stakeholders, including mental health professionals (psychiatrists, psychologists, mental health nurses, social workers etc.), Non-Governmental Organizations (NGO) with the care of schizophrenia patients as their focus, other NGOs, administrators and government officials on the burden of schizophrenia and the proposed project.
2. At the end of the project, the results will be presented at the annual meeting of the Association of Psychiatrists in Nigeria and at one or more International Conference(s) on Schizophrenia.
3. The result will also be published in a reputable international journal on biological psychiatry.
4. Adequate media coverage of the study and its results will be ensured by inviting electronic and print media houses to all events. Also, members of the research team will participate in television and radio programs to effectively reach the general public, and policy makers.

3.0 The Research Team

Prof S.K Mosaku is an adult psychiatrist with interest in the study of psychopathology of mental disorders. He is a seasoned researcher and administrator who has over 60 published articles in reputable National and International Journals. He is a member of the WHO, Global Clinical Practice Network (GCN) which has the goal of furthering research and practice in global mental health and belongs to several International Organizations including the International Society for Quality of Life Studies (ISQOLS), International College of Psychosomatic Medicine and the Society for Neurosciences.

Dr. Kayode P. Ayodele is an electrical engineer with focus on bioinstrumentation, signal processing and control. His previous and ongoing work on biomedical systems includes brain-computer interfaces for stroke rehabilitation, rehabilitation robotics, and the development of the first general device in the literature for automatic medical percussion. In recent times, his methods have included the application of deep learning classifiers such as convolutional neural networks.

Dr Adesanmi Akinsulore is a seasoned community psychiatrist who has over 40 articles in reputable National and International journals. He is currently the principal investigator for the research on developing and pilot testing a mental health intervention to reduce the psychological impact of COVID 19 on health care workers. This is a project sponsored by the Global Effort on Covid 10 (GECO).

Prof Ajiboye is a seasoned researcher with over 60 publications to his credit. His research interest is in the area of psychopathology of schizophrenia, anxiety and depression. He is a member of the American Psychiatric Association and an associate member of the Royal College of Psychiatrists in the United Kingdom. He recently published a work on the pattern and outcome of EEG on management of neuropsychiatric disorders.

Dr Enoruwa Obayiuwana is currently working on TV white space broadband to deliver low-cost and reliable wireless communication for rural areas in Nigeria, this project which is in collaboration with the University of York, York United Kingdom is funded by the EPSRC. He is also part of the group working

on wireless communication based vehicle crash detection and reporting system, this is in conjunction with the Federal Road Safety Corps (FRSC) in Nigeria, sponsored by the Nigeria Communication Commission (NCC). He is proficient in the use of "Math Works®" Matrix Laboratory programing Language for numerical computations.

3.2. Research Work to Date

List the relevant team publications. Also list not more than 3 relevant on-going research works

The Computational Psychiatry research group is a new one, and was formed specifically because there is no record of research or publications in this area in the country, despite the fact that there is ample domain expertise in the individual disciplines that constitute this multi-disciplinary research area. The publications below represent some publications of team members with bearing on their roles in the new group, and this project.

i. Mosaku K., Akinyoola A., Olasinde A., Orekha O. (2014) Predictors of posttraumatic stress in patients admitted to a trauma unit following road traffic accident (RTA). *Journal of Psychiatry*. 17(3);dx.doi.org/10.4172/psychiatry.1000121

ii. Mosaku S.K., Akinpelu V.O., Ogunniyi G.M. (2015) Psychopathology among a sample of hearing impaired adolescents. *Asian Journal of Psychiatry*

iii. Seun-Fadipe CT**, Mosaku K**, Komolafe MA. (2018) Circadian Sleep Preferences Sleep quality, Daytime Sleepiness and Sleep Hygeine amongst Undergraduate students of a Nigerian University Sleep DOI:10.1093/sleep/zsy061.654

iv. Adebiyi MO, **Mosaku SK**, Irinoye OO.(2018) Socio-Demographic and Clinical Factors Associated with Relapse in Mental Illness. International Journal of Africa Nursing Sciences, DOI.ORG/10.1016/J.IJANS.2018.05.007

v. Aloba O.O., Mapayi B.M., Akinsulore A. (2014) Insight into illness in a sample of Nigerian Patients with Schizophrenia: Sociodemographic and clinical correlates. Ife PsychologiA 22 (1): 80 – 91.

vi. Akinsulore A., Aloba O.O., Mapayi B.M., Oloniniyi O.I., Fatoye F.O., Makanjuola R.O.A. (2014). Relationship between Depressive Symptoms and Quality Of Life in Nigerian Patients with Schizophrenia" Social Psychiatry and Psychiatric Epidemiology. 49: 1191-1198.

vii. Akinsulore A., Makanjuola R.O.A., Fatoye F.O., Aloba O.O., Mapayi B.M. (2015). Disability assessment as an outcome measure: a comparative study of Nigerian outpatients with schizophrenia and healthy control. Annals of General Psychiatry 14:40. Doi:10.1186/s12991-015-0079-6.

viii. Ejidokun, T.O., **Ayodele, K.P**. and Yesufu, T.K., 2011. Development of an Eye-Blink Detection System to Monitor Drowsiness of Automobile Drivers", Ife Journal of Technology. 19(2). pp. 51-55.

ix. Moninuola, O.A., **Ayodele, K.P**., Kehinde, L.O. and Yesufu, T.K., 2009. A Platform for Inertial Motion Capture and Modelling of Human Movement. Ife Journal of Technology.18(2). pp. 63 – 71.

x. **Ayodele, K. P**., Akinboboye, E. A., & Komolafe, M. A. (2020). The performance of a low-cost bio-amplifier on 3D human arm movement reconstruction. Biomedical Engineering/Biomedizinische Technik, 1(ahead-of-print).

xi. **Ayodele, K. P.,** Ikezogwo, W. O., Komolafe, M. A., & Ogunbona, P. (2020). Supervised domain generalization for integration of disparate scalp EEG datasets for automatic epileptic seizure detection. Computers in Biology and Medicine, 103757.

xii. **Ayodele K.P.**, Akinniyi O.T., Oluwatope A.O., Jubril A.M., Ogundele A.I., Komolafe M.A. (2021). A Simulator for Testing Planar Upper Extremity Rehabilitation Robot Control Algorithms. Accepted for publication by Nigerian Journal of Technology.

xiii. Ayodele, K.P.,Olugbon, F.J., Ogunlade, O., Akinwale O.B., Akinniyi O.T., & Kehinde L.O. (2020). A Mobile Percussograph for Medical Examination of the Torso. FUOYE Journal of Engineering and Technology. DOI: 10.46792/fuoyejet.v5i2.560

xiv. **Ayodele K.P**., Kehinde L.O., Yesufu T.K. and Inyang I.A.,2009. A USB Interface for a Thermal Sigma-Delta Wind Sensor. The Journal of Computer Science and its Applications.16(2). pp. 31-40.

xv. Ajiboye PO, Abiodun OA, Ogbebor AI (2017). An investigation of the patterns and outcome of electroencephalographic (EEG) recording request in the management of neuropsychiatric disorders in a Teaching Hospital. African Health Sciences, 17(3), 852-858.

xvi. Tunde-Ayinmode MF, Abiodun OA, Ajiboye PO, Buhari OIN, Sanya EO (2014) Prevalence and clinical implication of psychopathology in adults with Epilepsy seen in an outpatient clinic in Nigeria. General Hospital Psychiatry, 36, 703-708.

xvii. E. Obayiuwana, O. E. Falowo and A. Periola "Wireless Networks Performance Enhancement Via Buffered Cooperative Communications" *Institute of Engineering and Technology (IET) Communications*, 12pp DOI: 10.1049/iet-com.2019.0589 , Print ISSN 1751-8628, Online ISSN 1751-8636 Available online: 23 August 2019

xviii. E. Obayiuwana and O. E. Falowo, "Network Selection in Heterogeneous Wireless Networks using Multi-Criteria Decision-Making Algorithms: a Review" *Springer Journal of Wireless Networks* (WINE), pages: 1-33, Vol. 22, Issue 6. 07, June 2016.

xix. E. Obayiuwana and Joseph Orimolade "The Effect of Decision-Criteria Dynamics on Network Selection for Group Calls in Heterogeneous Wireless Networks " International Journal of Computer Applications, vol. 177, Issue,31. , 16, January, 2020

Ongoing research work include:

S/N	Title	Researcher
1	Effect of micronutrient abnormality among patients with schizophrenia	Prof S.K Mosaku
2	Development of EEG-based brain-machine interfaces using continuous-decoding algorithm	Dr. K.P. Ayodele
3	Development of a mental health intervention program for health care workers following COVID-19	Dr. A Akinsulore

3:3. Previous Research Grant [Provide short summary of grants won and managed in the last five years]

Grants won in the last five years

Dr Akinsulore a co-researcher in this project recently won the grant on the development and pilot ting of a mental health intervention to reduce COVID 19 associated psychosocial distress among gerian Health among Nigerian healthcare workers. This is part of the Global effort on COVID-19 ECO) Health Research grant. The grant is worth £171,719 pounds. He is the principal investigator

Dr. K. P. Ayodele is the head of the engineering subteam of a TETFund National Research Fund project. The project titled "A Robotic Platform for Upper Limb Rehabilitation for Improved Post-Stroke Functional Outcomes" is worth ₦ 28,316,000, and is ongoing.

Dr. Ayodele is the Principal Investigator of a TETFund Institution Based Research Project titled "Development of a Robotic Orthosis for Hand Rehabilitation after Stroke". The project is worth ₦2,000,000 and scheduled for successful completion in December 2020.

Dr. Ayodele won an OpenBCI hardware grant in May 2020 for brain-machine interfacing for rehabilitation robotics. The grant was worth $5000, and the project is ongoing.

Dr K.P. Ayodele is a member of the research team that won a grant to extend the World Bank-funded, and NUC-administered OAU ICT-Driven Knowledge Park project in 2019. The project is ongoing, and is worth one million, fifty-five thousand dollars ($1,055,000).

Dr. Ayodele won (along with Prof. K.A. A. Makinwa of the Delft University of Technology, The Netherlands, as the principal investigator) a T.U. Delft research grant with a proposal titled "Towards

Robust Low-Cost Environmental Sensors for Africa" in 2018. The grant is ongoing, and is worth fifteen thousand euros (€ 15, 000).

Dr. Ayodele jointly won (with Prof. P. Ogunbona) an Nvidia Corporation hardware grant for research on epileptic seizure detection in 2017. The grant was an in-kind donation of a graphical processing unit (GPU) and embedded device hardware worth two thousand dollars ($2000). The project is ongoing.

Previously, Dr. Ayodele was the software and instrumentation lead on the "Realizing the Potential of Ilabs in Sub-Saharan Africa" grants by Carnegie Corporation. The multi-year contract was renewed annually between 2006 and 2012, and was worth a total of $355,000. The project was successfully completed with an evaluation report submitted to Carnegie Corporation by an independent international assessor. He also won (as the sole investigator) an "iLab Junior Fellowship" research grant for the development of remote and distributed instrumentation systems in 2011. The grant, worth $12,500, was funded by the Carnegie Corporation of New York, through an MIT subcontract. The project has been concluded.

3:4. Group Research

Previous working relationship as a group [For group research, applicants are encouraged to consider gender, age and discipline. They should also provide details about roles and responsibilities of each member.]

Members of the Computational Psychiatry research group have previous research experience in various relevant disciplines covering mental health, neurology, bioinstrumentation, and signal processing. There is a female researcher in the group. There is also a good spread in terms of the age and academic maturity of group members. The membership of the group - with the respective responsibilities of members indicated - is as follows:

S/N	Name	Designation	Responsibilities
1	Prof.. K.S. Mosaku	Principal Researcher	Overall coordination of the project, including study design and clinical matters; coordination of participating mental-health personnel and facilities.
2	Dr. K.P. Ayodele	Research Partner	Coordination of engineering (instrumentation, general electrical, and fabrication) aspects of the main study; overall coordination of algorithm design and software development.
3	Dr. A. Akinsulore	Research Partner	Direct supervision of participating personnel from mental health clinic, and of all categories of medical research assistants; coordination of interaction between psychiatry, and engineering constituencies.
4	Prof. P.O Ajiboye	Research Partner	Direct supervision of participating personnel in the mental health clinic, and of all categories of medical research assistants; coordination of interaction between psychiatry, and EEG technician at the University of Ilorin Teaching Hospital arm of the project.
5	Dr E Obayiuwana	Research Partner	Assist in the overall coordination of engineering aspects; lead the implementation of signal processing components.
6	Dr O. Akinwale	Mentee	Assist in the overall coordination of engineering aspects; direct supervision of engineering research assistants, software developers and artisans.

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