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Neuroimaging in Psychiatry: A Review of the Background and Current Trends

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ABSTRACT

This paper offers a selective literature review of neuroimaging in psychiatry, with the goal of offering a background and a summary of current trends. While not exhaustive, numerous publications are cited in an attempt to provide a reasonable cross-section of research activity in the field of brain imaging in psychiatry and how to overcome the challenges in our setting. There are two different types of neuroimaging of value in clinical psychiatry, namely: structural neuroimaging techniques (e.g., CT, MRI) which provide static images of the skull, and brain, and functional neuroimaging techniques (e.g., single photon emission CT [SPECT], positron emission tomography [PET], functional MRI [fMRI], electroencephalography [EEG], magnetoencephalography [MEG]) which provide measures that are directly (MEG, EEG) or indirectly (SPECT, PET, fMRI) related to brain activity. Although neuroimaging is making increasing contributions to multiple aspects of clinical psychiatry, including differential diagnosis, prognosis, clinical management, and development of new interventions, it still remains largely a research tool and is of limited use in clinical psychiatry.

INTRODUCTION

Psychiatrists have known for at least 100 years that mental illness must be fundamentally due to perturbations of normal neural activity in the brain (Andreasen, 1988). Emil Kraepelin a founding father of modern psychiatry in his work with a group of distinguished brain scientists which included Alzheimer, Nissi, Brodmann and Gaupp working in the psychiatric clinic of Munich University could not demonstrate those perturbations with naked eye or microscope and this led some psychiatrists to conclude that there were no specific neural abnormalities (Andreasen, 1988). However, it is now clear that these psychiatrist-neuroscientists were on the right track but lacked sufficiently sensitive tools to map and measure the complex aberrations of cognitive, perceptual, emotional and motor functions that characterize major mental illnesses such as schizophrenia or the affective disorders (Andreasen, 1988).

Modern neuroimaging techniques demonstrate that there is substantial localization of many functions in the neural tissue of the brain (Daliri and Behroozi, 2012).

Some research findings have shown that advances in brain imaging techniques have made it possible to identify the anatomic, metabolic and neuro-chemical substrates of mental illnesses (Malhi & Lagopoulos, 2007; Davoren et al, 2009). These advances have also been applied to treatment options and drug development, making it possible to predict the therapeutic response (Fu & McGuire, 1999; Tamminga & Conley, 1997).

The available brain imaging techniques applied in psychiatry are classified into two types, namely: structural and functional imaging methods.

Structural Imaging Methods

The structural neuroimaging methods include Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) which provide static images of the skull and brain.

Computed Tomography (CT)

Computed tomography (CT) is the earliest structural imaging technique to be applied to psychiatry being the oldest brain imaging technique developed in the early 1970s. Remarkable structural abnormalities have been reported over the years on CT of the brain in various psychiatric disorders. For example Johnstone et al. reported in 1976 that patients suffering from schizophrenia tended to have a significantly greater degree of enlargement in the ventricular system than did a matched control group (Johnstone et al., 1976). There are also several reports of gross focal brain lesions on CT and MRI in schizophrenia which are clinically unsuspected; such findings include aqueductal stenosis (Tamminga & Conley, 1997), arachnoid and septal cysts (Kuhnley, 1980; Lewis and Mezey, 1985) and agenesis of the corpus callosum(Lewis et al, 1988). Marchie et al in southern Nigeria also reported a case of frontal lobe lesion on CT presenting with psychiatric disorder (Marchie et al, 2002).

CT scans use multiple x-ray sources and detectors to provide cross-sectional images of the brain. On CT films, areas of increased beam attenuation, like the skull, and calcifications appear white; areas of low attenuation such as gas appear black, while those of intermediate attenuation such as soft tissues appear in shades of gray. The use of

intravenous radio-opaque contrast significantly improves the ability of CT to visualize certain normal and abnormal structures. Contrast highlights vascular structures as well as lesions that lead to compromise of the blood–brain barrier. As a result, vascular abnormalities such as aneurysms, dissections, and arteriovenous malformations will be more easily visualized. Contrast will also highlight lesions that lead to gross disruption of the blood–brain barrier. Such lesions include inflammatory processes of the brain (e.g., infection) and tumors (Park & Gonzalez, 2004). However, up to 5% of patients can develop idiosyncratic reactions to contrast media, manifested by hypotension, nausea, flushing, urticaria, and anaphylaxis. (Roffman et al, 2010).

Computed Tomography also has some functional imaging applications, such as Xenon-enhanced computed tomography and dynamic perfusion-computed tomography.

Magnetic Resonance Imaging (MRI)

Magnetic resonance imaging (MRI) is used for both structural and functional imaging techniques with a lot of advantages over CT. Unlike CT which involves the use of ionizing radiation for imaging, MRI uses high magnetic field for imaging and this makes it safer especially for follow-up imaging and human research studies. MRI has multiplanar capabilities unlike CT where brain imaging is limited to transverse plane, except reformatted images which usually results in compromise of the structural details. The ability of MRI to image in all planes, including coronal plane, which is particularly useful for visualizing frontal and limbic regions as well as superb grey-white resolution (Andreasen, 1988), has made it a preferred brain imaging modality. The major drawback so far against the use of MRI is cost and availability, most especially in developing countries like Nigeria and most African countries. In Nigeria there are limited numbers of MRI scanners compared with the population and the highest MRI field strength available at the time of this review is 0.5 tesla (T), and it has limited application. For routine MRI imaging, 1.5 to 3T super-conducting systems are used for general clinical imaging with field strengths of 1T and below being applied in niche situations and few very high field systems of 7 to 9T are available worldwide. Neurological applications like MR spectroscopy (MRS), functional MRI (fMRI) and spin-tagging perfusion imaging (also called Arterial Spin Labelling, ASL) which fall under functional assessment of the brain, are possible with an optimized 3T system (Jones and Jenkins, 2003).

Functional imaging methods

These imaging methods are based on the following parameters: 1) Regional cerebral blood flow (rCBF) and brain perfusion studies; 2) Cerebral glucose metabolism; 3) Oxygen consumption in the brain and 4) Neurotransmitter functions and occupancy.

Imaging techniques which determine regional cerebral energy metabolism and blood flow, including oxygen consumption are normally regarded as regional cerebral function tests, while the techniques for studying cerebral neurotransmitter functions in man are used to delineate the mechanisms of action of antipsychotic and antidepressant drugs, as well as the diagnosis and progression of Parkinson's disease and to evaluate neuroprotective drugs (Kessler, 2003).

Functional imaging methods include the following:

1. Positron emission tomography (PET) including Amyloid PET imaging
2. Single photon emission computed tomography (SPECT).
3. Xenon-enhanced computed tomography (XeCT),
4. Dynamic perfusion-computed tomography (PCT).
5. Functional magnetic resonance imaging (fMRI).
6. Magnetic resonance spectroscopy (MRS)
7. Magnetic resonance imaging dynamic susceptibility contrast (DSC).
8. Arterial spin-labeling (ASL).
9. Doppler ultrasound (Transcranial Doppler).

All of the above listed imaging methods are used for brain perfusion studies and they give similar information about brain hemodynamics in the form of parameters such as cerebral blood flow (CBF) or volume (CBV) but each technique has its advantages and drawbacks (Wintermark et al., 2005)

The MRI based methods are functional MRI, (fMRI), and magnetic resonance spectroscopy (MRS). In general terms, MRI provides exquisitely detailed images of brain structure; fMRI provides images of local neuronal activity with high spatial and temporal resolution; and MRS provides measurements of the concentrations of numerous chemicals in the brain without the radiation exposure of PET and SPECT but with much lower sensitivity (Malison and Innis, 1999).

The oxygen consumption as a parameter in brain functional assessment is possible using the ability to detect in vivo blood oxygenation changes with MRI. During changes in neuronal activity there are local changes in the amount of oxygen in the tissue which can be monitored with the **b**lood-**o**xygen-**l**evel-**d**ependent or BOLD signals in fMRI ((Fox and Raichle 1986; Fox et al., 1988). When a BOLD signal is detected, blood flow to a region of brain has changed out of proportion to the change in oxygen consumption (Kim and Ugurbil,1997). BOLD signals on MRI

are indicators of both increases and decreases in oxygen consumption in normal human brain.

The two radiotracer methods of neuroimaging, positron emission tomography (PET) and single photon emission computed tomography (SPECT) entail the injection of radioactively labeled drugs. The imaging and measurement over time of the distribution of these radiotracers is used to assess the neurochemistry, blood flow, or metabolism of the brain. For SPECT it involves the use of tracers, like xenon-133 and (123)I-labeled iodoamphetamine(123 I-IMP) . With these techniques, cerebral perfusion is assumed to provide an indication of metabolic activity, with areas of hyperfusion reflecting an increase in cerebral metabolic activity (Andreasen, 1988). Tracers for dopamine and acetylcholine receptors are available and increased dopamine receptors in the basal ganglia have been observed with SPECT (Eckelman et al., 1984; Crawley et al.,1986). SPECT has been applied in the study of Alzheimers disease. Both SPECT and PET have shown a pattern of hypo-perfusion in posterior temporo-parietal regions which appear to be specific to and characteristic of this disease (Bonte et al., 1986; Rezaie et al.,1985; McGeer et al.,1986). Flow pattern differences between Alzheimer's disease and depression could be useful in differentiating these disorders, which is often a difficult differential in psychiatry (Rush et al., 1982; Post et al,1987).

Positron Emission Tomography (PET)

Positron Emission Tomography (PET) has been reported as the most elegant of the available brain imaging techniques giving better resolution images (Andreasen, 1988), but it is more expensive to acquire and to operate. It is used for assessment of metabolic activity and measurement of neurotransmitter function. Cerebral metabolic activity is measured with deoxyglucose labeled isotopes, using the following isotopes; Fluorine-18 (^{18}FDG) Carobon-11 (^{11}C), and Oxygen-15 (^{15}O). These isotopes have short half-life, with ^{15}O having the shortest half-life of 2 minutes, thereby allowing a rapid comparison of cerebral metabolic activity in a variety of conditions (Andreasen, 1988). The study of neurotransmitters using PET has been possible using various ligands.

Ligands are currently available for the study of D1 and D2 dopamine receptors and for serotonin, benzodiazepine, opiate, and muscarinic receptors (Sedvall et al., 1986). PET imaging of neurotransmitter systems permit direct measurement of receptor occupancy as direct brain assessment of drug activity instead of peripheral method of assessment using serum blood levels as indicators of the presence of drugs in the brain. PET application in the study of dopamine D2 receptor has contributed to the understanding of the pathophysiology of schizophrenia and the mechanism of action of neuroleptic drugs (Sedvall et al., 1986). Early studies demonstrated that D2 receptors could indeed be labeled, as evidenced by clear areas of uptake in the caudate and putamen (Sedvall et al., 1986; Wagner et al., 1983).

Compared with other functional imaging techniques, PET has several advantages. Compared with SPECT and MRS, PET is more sensitive in detecting processes that occur in minute concentrations (such as neurotransmitter and neuroreceptor processes). Compared with SPECT, PET also has the potential to measure a wider range of biochemical and physiological processes (partly because the positron-emitting radiosotopes ^{15}O, ^{11}C, ^{13}N, and ^{18}F which can be incorporated into physiological and pharmacological compounds without affecting their behavior in the body) and has fewer artifacts from radiation scatter and attenuation (because of the current availability of attenuation-correction procedures) (Reiman, 1999).

Compared with fMRI, advantages of PET include a better-established role in comparing images acquired in the resting state during different scanning sessions (e.g., in patients versus controls, before and after treatment, and in longitudinal studies of aging and age-related disorders); less-severe artifacts from head movement, claustrophobic anxiety, and ambient noise; the absence of signal dropout in brain regions in close proximity to sinuses (e.g., the hippocampus); the ease with which one can provide sensory stimuli and acquire ancillary measurements during the imaging session; and the ability to characterize a wide range of neurochemical processes (Reiman, 1999).

Disadvantages of PET include its relatively low spatial resolution (limiting its ability to characterize changes in extremely small regions, such as brainstem nuclei), the time required to acquire an image (requiring behavioral and baseline tasks to be studied in blocks), radiation exposure (limiting the number of scans that can be acquired in normal volunteers), expense, and limited availability (Reiman, 1999).

Single Photon Emission Computed Tomography (SPECT)

Like PET, SPECT is an imaging technique that provides information about biochemical and physiological processes. This technique capitalizes on radiosotopes (e.g., ^{123}I, ^{99}mTc, ^{133}Xe) with longer radioactive half-lives than those used in PET studies. SPECT is commonly used to provide measurements of cerebral blood flow (e.g., using the radiotracer ^{99}mTc-hexamethylpropyleneamine oxime [HMPAO]). SPECT also has

the potential to measure neuroreceptor processes. Techniques have been developed for estimating the density of acetylcholine presynaptic and muscarinic receptors and dopamine type 1 (D1), D2, and transporter receptors (Reiman, 1999). Compared with PET, SPECT studies are less expensive and more widely available. However, SPECT provides a smaller range of biochemical and physiological measurements; current imaging systems have a slightly lower spatial resolution, have lower sensitivity for detecting processes that occur in minute concentrations, and cannot acquire transmission images for the correction of radiation attenuation.

The longer-lived radioisotopes tend to be associated with slightly higher levels of radiation exposure. PET and SPECT are presently not available in Nigeria.

Magnetic Resonance Spectroscopy (MRS)

MR spectroscopy has been practiced across a wide variety of neuropathological conditions, including traumatic brain injury, neonatal hypoxic ischaemic brain injury, epilepsy, multiple sclerosis, infection and metabolic disorders. Arguably, the two conditions for which it has shown its greatest clinical potential are brain tumours and Alzheimer's disease (Currie et al., 2013). In psychiatry, the best-known application of proton MR spectroscopy for the measurement of psychoactive drugs in humans is the quantification of brain lithium (Komoroski, 1993), Gonzalez et al haven developed a method using proton MR spectroscopy that provides adequate measurement of brain lithium in humans (Gonzalez et al, 1993).

Transcranial Doppler (TCD) Ultrasound

Brain perfusion can also be studied using the transcranial Doppler (TCD) ultrasound. TCD can detect intracranial arterial stenoses and occlusions, as well as aneurysms (Arger and Debarilyoob, 2004). This imaging modality is useful in cases of vascular depression or late-life depression (McDonald et al., 2006).

Specific Imaging Findings in Major Psychiatric Disorders

The major drawback in the utilization of imaging modalities in psychiatric diagnosis has been from the reported inconsistent imaging findings from various studies and the small population studies (Amen & Flaherty, 2006, Andreasen, 1988). Yet it is a well-known fact that there is lack of coherence in the diagnostic criteria in psychiatry and efforts have been made over the last 2 decades to bring reliability and validity to psychiatric diagnosis. There is nonetheless a growing dissatisfaction with current diagnostic systems in psychiatry as Linden (2011) asserts that although the authors of the Diagnostic and Statistical Manual of Mental Disorders (DSM) (American Psychiatric Association, 2000) and the International Classification of Disease (World Health Organisation, 1992) were guided by the aim to make the diagnostic criteria more reliable, these criteria are still largely based on clinicians' assessments. Thus, patients whose symptoms are caused by very different biological processes may be subsumed under the same category, and some of them may receive inappropriate treatment as a consequence (Linden, 2012). There are as yet no reliable etiological models and biomarkers that are currently available for most psychiatric disorders (Linden, 2012).

Psychiatric diagnosis will thus continue to be based on descriptive criteria for the foreseeable future (First, 2010).

However with further studies more consistent imaging findings are emerging in the major psychiatric disorders in the last decade, especially as a result of the technological advances. The use of imaging in psychiatry has also been seen as a possible anti-stigma tool which may enhance the appreciation of mental illness as a real medical problem (Amen & Flaherty, 2006).

In psychiatry, fMRI has led to an improved understanding of the cerebral correlates of psychopathological phenomena, cognitive disorders, and genetic risk factors. Functional neuroimaging has been used to study the effects of treatment, not just with medications of different kinds, but also with electroconvulsive therapy, vagus nerve stimulation, and various types of psychotherapy. This use of psychological techniques (psychometry and psychotherapy) in combination with biological techniques (functional neuroimaging) typifies the trend in modern psychiatry toward the integration of these two approaches to mental illness, which were once widely held to be incompatible (Linden, 2006).

Possible clinical applications of functional neuroimaging in psychiatry include

1. Assessment of the effects of treatment,
2. Determination of differential indications for treatment,
3. Identification of target areas for neurophysiological treatment methods, either invasive (deep brain stimulation) or noninvasive (transcranial magnetic stimulation),
4. Development of neurobiologically inspired treatments such as neuropsychotherapy and neurofeedback (Linden, 2006).

Imaging Findings in Schizophrenia and Affective Disorders

Structural Imaging Methods

On structural imaging methods, which include CT and MRI, the following abnormalities have been consistently found in series of studies in **schizophrenia.**

1. Enlargement of the ventricles, the lateral ventricles most prominently.
2. Cortical atrophy as evidenced by sulci widening.
3. Reduction in cerebral cortical grey matter volume.
4. Cerebellar atrophy.
5. Reduction in volume of the hippocampal-amygdala complex.
6. Increased CSF in the ventricles

Dilatation of the lateral and third ventricles was one of the first and consistent neuroimaging findings in schizophrenia and a recent study confirmed the specificity of ventricular enlargement in schizophrenia compared to affective psychosis (Vu and Aizenstein, 2013).

Patients with schizophrenia as a group also show loss of local brain volume in numerous areas, including the language and auditory areas of the temporal lobe, the attention and visuomotor integration areas of the parietal lobe, the memory and executive areas of the frontal lobe and parts of the limbic system and the basal ganglia. Such volume loss has been reported in adolescent schizophrenics and found to progress at a rate of up to 4% per year (Vu and Aizenstein, 2013).

Several reports of gross unsuspected brain lesions on CT and MRI in patients presenting with schizophrenia abound in the literature. Three of such studies gave a prevalence of unsuspected focal abnormality on CT of between 6-9%.(Owens et al.,1980;Brugha et al., 1988)

The study of identical twins discordant for schizophrenia by Suddath et al (Suddath et al.,1990) also reported lateral and third ventricular enlargement as well as reduced volume of temporal lobe grey matter including hippocampus when compared with the unaffected co-twin.

Harvey et al and Zipursky et al showed similar findings of a small (6%) but significant reduction in diffuse cerebral cortical grey matter volume but not white matter volume in schizophrenic patients compared to controls taking into account all anthropometric and demographic variables (Harvey et al.,1993; Zipurski et al., 1994).

The grey matter volume reduction has been found to be specific to schizophrenia rather than psychosis in general and in two studies this finding was reported in schizophrenics but not in bipolar patients, compared with controls (Zipurski et al., 1994;Schlaepfer et al., 1994).

Reduced volume of the hippocampus-amygdala complex and para-hippocampal gyrus is now a fairly well replicated finding in schizophrenia compared to healthy volunteer controls and some studies claimed that this reduction is more pronounced on the left than the right side in schizophrenia (Suddath et al.,1990; Barta et al.1990;), but bilateral finding is more consistent. Reduced superior temporal gyrus volume on the left was found to be associated with auditory hallucinations and thought disorders (Barta et al.1990; Shenton et al.,1992).

At the presently time, MR neuroimaging is used in schizophrenia research as a tool to assess the anatomic manifestations of the psychiatric pathophysiologic processes underlying the disorder. Thus, structural brain imaging though non-diagnostic for schizophrenia, it is proving helpful in correlating physiologic changes to patient self-reported experiences of symptoms of the disease.

The structural imaging findings in affective disorders have not been as consistent as in schizophrenia. In late life depression, appearances of atrophy as well as an increased rate of subcortical white matter lesions have been shown (Rabins et al.,1991; Figiel et al.,1991). Lateral ventricular enlargement in depression is usually found in chronic cases and elderly patients as well as correlation with psychotic symptoms (Lewis, 1996; Beyer and Krishnan, 2002). Enlargement of the third ventricle in bipolar affective disorders has been linked to volume losses in the medial thalamic or hypothalamic areas that form the walls of the third ventricle (Strasser et al., 2005). Hypothalamic volume loss is of particular interest because of its possible implication in the prominent somatic and autonomic symptoms such as disturbed circadian clock present during both depressed and manic episodes.

Depressive symptoms occur frequently (in up to a third of cases) in stroke, traumatic brain injury or brain tumours, particularly those affecting the frontal lobe and basal ganglia (Linden and Fallgatter, 2009). Other brain disorders which commonly present with depression include multiple sclerosis and some systemic illnesses affecting the brain such as acquired immunodeficiency syndromes, thyroid disease or even heart failure (Angermann et al., 2007).

The following structural imaging findings have also been reported in affective disorders; reduced basal ganglia volumes, basal ganglia hyperintensities on MRI in depression as well as increased rates of sub-cortical hyperintensities in several studies of bipolar disorders, compared with controls (Krishnan et al. 1992; Dupont et al. 1990; Swayze et al.,1990).

Functional imaging findings

Functional magnetic resonance imaging (fMRI) neuroimaging investigations in schizophrenia have been used for a variety of purposes. These include shedding light on the underlying pathophysiology of the illness, understanding the neural basis of characteristic symptoms, aiding with diagnostic classification, predicting treatment outcome, and

understanding the effects of risk genes for the disorder (Pearlson, 2011).

The studies by Ingvar and Franzen observed abnormalities in blood flow in patients with schizophrenia, referred to as hypofrontality and this finding has been replicated by a number of investigators, but not by all (Ingvar and Franzen, 1974; Mathew et al., 1982; Gur et al.,1985; Weinberger et al., 1988).

The use of some frontal lobes challenging tests like continuous performance test and Wisconsin card sorting tests show increased blood flow in the frontal cortex in normal individuals as assessment of frontal lobe function, but non-response to challenging tests is noted in schizophrenics. Left hemispheric abnormaiities have also been observed which is consistent with the language and auditory abnormalities observed in schizophrenia (Berman et al., 1993).

Neuroreceptor imaging using PET and SPECT have shown higher dopamine level in schizophrenia (Sedvall et al., 1986; Wagner Jr et al.,1983; Farde et al.,1985; Wong et al.,1986; Amen & Flaherty, 2006).

Mechanism of action of various antipsychotic drugs in schizophrenia have been studied with the dopamine D2 receptor occupancy using PET. D2 receptor blockage was demonstrated at clinical dosages of antipsychotic drugs (Farde et al., 1988).

As hippocampal volume reduction has also become a consistent structural abnormality in schizophrenia; abnormal hippocampal activity at rest, during experience of auditory hallucinations and during performance of memory retrieval tasks have been demonstrated (Heckers, 2001). Studies by Todtenkopf and Benes show more pronounced increase in hippocampal regional cerebral blood flow (rCBF) during a tone-recognition task in patients off antipsychotic medication, which confirms previous evidence that antipsychotic drugs normalize hippocampal dysfunction in schizophrenia (Todrenkopf and Benes, 1998).

Studies by Weinberger has also linked schizophrenia with genetic problem involved in the development and maintenance of hippocampal circuitry (Weinberger, 1999).

Dementia

This refers to disorders with cognitive impairment which consist of mild cognitive impairment (MCI), non-Alzheimer's and Alzheimer's dementia (AD).

Structural imaging

Dementia is the commonest area of application of structural brain imaging in psychiatry.

CT or MRI is usually requested in cases of pre-senile dementia to exclude focal organic brain disorders such as slow growing tumours, chronic subdural haemorrhage and normal pressure hydrocephalus.

Normal aging is accompanied with brain volume reduction of 5-10% by the age of 80 years, and associated lateral and third ventricular dilatation as well as cortical cerebral sulci enlargement. Therefore signs of cerebral atrophy alone without clinical features of dementia and other neuropsychological evaluation as well as EEG features is not diagnostic but follow-up scans showing progressive change is more diagnostic (Lewis,1996; Burns and Pearlson, 1994).

Structural imaging In Alzheimer's disease (AD) has shown progressive enlargement of lateral and third ventricles and cortical sulci, which is most marked in medial temporal lobe regions (Todrenkopf and Benes, 1998). Another promising distinguishing feature between elderly controls or depressives from Alzheimer's disease, is hippocampal atrophy on MRI , which was positive in 90% of cases studied (Heckers, 2001).

Functional imaging

The application of functional imaging in dementia has made it possible to differentiate AD from other types of dementia; AD being a more severe form of the disease.

Amyloid PET imaging is the most prominent among the functional imaging methods and it has been found useful in differentiating MCI from AD and predicting future outcomes of MCI as a possible early form of AD.

However amyloid PET positivity has been found to be age related and can also be seen in dementia with Lewy bodies and few other medical conditions such as amyloid angiopathy (Rowe et al., 2010; Morris et al., 2010; Gomperts et al., 2008; Edison et al., 2008). Therefore interpretation of amyloid PET positivity is expected to be in conjunction with proper psychiatric clinical evaluation and to follow the appropriate use criteria for amyloid PET imaging. (Keith et al., 2013)

Mild cognitive impairment (MCI) is believed to be a transitional phase before progression to Alzheimer's disease (AD), and this offers a window for therapeutic intervention to slow or halt disease progression (Pauwels et al., 2009).

The use of biomarkers in CSF such as beta amyloid (AB1-42) and phosphorylated tau (t Tau and pTau) has been reported to provide a sensitivity and specificity of > 80% in AD (Pauwels et al., 2009). The use of CSF and MRI biomarkers have also been shown to have prognostic value in predicting which MCI patient will develop AD in other studies (Vos et al., 2012; Andreasen and Blennow, 2005)

Amyloid imaging also has significant application in drug development for the treatment of AD (Mathis et al., 2007; Blennow et al., 2014).

There are several attempts on new treatment strategies of AD

based on the amyloid hypotheses (Shimada, 2014) one of such drugs is phenserine which is aiming to lower beta amyloid (AB) production (Greig et al., 2005; Thatte, 2000).

Recent study on effect of phenserine and other cholinesterase inhibitors on AD patients showed positive effects on cognition as well as changes in brain amyloid levels (Lahiri et al., 2000)

Multi-infarct dementia is another disorder which shows generalized cortical atrophy and radiological features of lacunar infarcts in about 70% of cases, which is similar to the findings in AD (Weinberger, 1999). However, location of the atrophic changes and other functional imaging findings as discussed above will differentiate this from AD

Current trends

In several articles, Amen and co-authors have argued for the value of SPECT in psychiatry, emphasizing its usefulness in complex and treatment-refractory cases (Amen et al. 2011; Amen, Willeumier & Johnson 2012). Amen (2006) asserts that brain imaging technology has already reached the point that is useful for making clinical diagnosis and help in treatment selection, adding that psychiatry remains the only medical specialty that rarely looks at the organ it treats (Amen, 2001; Amen, 2006; Amen & Flaherty, 2006). Neuroimaging has indeed been found most useful in neurological conditions like stroke, seizure disorders, tumours and head trauma, but is still a developing field in the diagnosis and management of psychiatric illnesses (Gupta et al. 2004). The Consensus Report of the APA Work Group on Neuroimaging Markers of Psychiatric Disorders stated that "there are currently no brain imaging biomarkers that are currently clinically useful for any diagnostic category in psychiatry" (First et al. 2012). The Work group concluded that "despite the invaluable leads that the neuroimaging studies have provided regarding the neurobiological bases for psychiatric disorders, they have yet to impact significantly the diagnosis or treatment of individual patients" (First et al. 2012).

Given all the work remaining to be done, the claims of clinics that they can reliably use structural or functional brain scans such as MRI, PET, SPECT, diffusion tensor imaging (DTI), or fMRI to help diagnose and choose treatment for a range of psychiatric disorders is without medical or scientific support (First et al.,2012; Farah and Gillihan, 2012). The APA Council on Children, Adolescents, and their Families asserts further that, "Although knowledge is increasing regarding specific pathways and specific brain areas involved in mental disease states, at present the use of brain imaging to study psychiatric disorders is still considered a research tool." and, "Specifically, no published investigation in the field has determined that any structural or functional brain abnormality is specific to a single psychiatric disorder. Additionally, imaging studies examine groups of patients and groups of healthy controls; therefore, findings may not apply to all individuals with a given disorder." (APA 2005). Mayberg (2012) added that "Such claims are beyond the scope of current research and give false hope to patients and their families dealing with a condition that is difficult to diagnose or treat".

Which Categories of Psychiatric Patient May Benefit From Imaging?

Definitely not all psychiatric patients will need to be imaged like in other medical conditions. Just like one of the advocates of imaging in psychiatry said; on a clear day radar is not necessary to land a plane, but radar is needed when there is trouble seeing the airport (Amen & Flaherty, 2006). In unclear cases, poor or non-response to treatment and those who can afford the available imaging modalities in our setting, imaging will definitely add to the patient's treatment in many ways. If a treatable organic cause is found, definitive treatment may result in cure and finding a structural abnormality may help with compliance. In AD early diagnosis has been linked with better outcome with therapy and possibility of planning for the future before the patient becomes completely incapacitated is also an advantage.

At the present time, it is only structural neuroimaging methods that are available in our setting. This is as a result of the high equipment cost of functional neuroimaging.

Indications for structural neuroimaging in patients with psychiatric symptoms include the following:

- New or first-onset psychiatric illness
- Recent or advancing cognitive dysfunction
- New or worsening instances of syncope, vertigo, loss of consciousness, etc.
- New-onset dementia
- Onset of any psychiatric problem (psychosis, affective disorder, personality change) in a patient > 50 years old
- A history of head trauma
- New, worsening, or altered pattern headaches
- New signs of brain pathology, e.g., seizure, paresis, or brain-related visual alteration
- Concerns about intracranial infection, inflammation, metastases, or increased pressure
- During an initial work-up for ECT (Park and Gonzalez, 2004).

CONCLUSION

The science of using neuroimaging techniques to diagnose psychiatric conditions is in a nascent stage (MacQueen, 2010). It must however be admitted that neuroimaging is making increasing contributions to multiple aspects of

clinical psychiatry, including differential diagnosis, prognosis, clinical management, and development of new interventions (Osuch and Williamson, 2006).

At the present, neuroimaging can contribute to psychiatric practice in the following ways:

- To exclude other causes that may lead to similar symptoms, such as space occupying lesions, cerebrovascular or inflammatory diseases.
- Improvement in therapy and more objective follow-up of patients.
- Consistent use of neuroimaging may eventually improve diagnosis in psychiatry and nosology of psychiatric disorders.
- Consistent use of neuroimaging and research may eventually lead to genetic markers and preventive treatment options.

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