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Review article: Neural networks in psychiatry

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Abstract

Mental health is an intricate branch of medicine that involve the various brain circuits including frontal, temporal and occipital lobes, may also involve the structure and functional unit of brain. Many psychiatrist treat on the basis of subjective experience rather than implying the pathophysiology of the disease process. So in this article, we highlighted the concept of various brain circuits, role of neurochemicals and its involvement in various neuro-psychiatric illness like schizophrenia, Obsessive compulsive disorder, depression etc. Analogous to our human brain is Deep Neural Network (DNN) and Machine learning, based on "Graph Theory"(Artificial Neural Network), play a crucial role in working of Artificial Intelligence (AI) techniques. Various neuroimaging techniques like fMRI, is described in detail. Importance of AI in early diagnosis, individual treatment, counselling and research of various illness and AI based applications has been narrated.

Keywords: Artificial Intelligence; Machine Learning; Pyschiatry; Machine Learning

1. Introduction

Human Brain, the signature network system of nature, which controls the emotion and behaviour according to the crux of situation. Since ages, many scientist endeavoured to get the knowledge of human behaviour, emotion and its regulatory mechanism.

In 1878, Paul Pierre Broca, spoke about "the great limbic lobe" or "le grand lobe limbique"which means the border of cortex including cingulate, hippocampal gyri. The further accepted anatomical model of Limbic lobe was given by American physician, JamezPapez, known as the famous "Papez Circuit", in 1937. He described the harmonious relation between the hypothalamus, anterior thalamic nucleus, the hippocampus cingulate gyrusand its interconnections in describing the role inemotions, memory, affect and goal directed behaviour.[1]. And in 1952, Paul D Maclean coined the term "limbic system" (limbic lobe and its subcortical structures along with their connections) which explains various brain functions.[2]. He also put forward the "Truine Brain theory" which says that, in reality, the human brain comprises of three brains in one: the R- complex (reptilian complex), the limbic system and the neocortex[3].

Humans are different from other animals, by our ability to think. Human brain consist of frontal, parietal, temporal and occipital lobe, of which frontal lobe and its connections play a vital role in cognition, execution, personality, emotions, and motivation. The primary motor cortex (PMC), supplementary motor area (SMA), frontal eye field (FEF), oribitofrontal area (OFA), anterior cingulate gyrus are important areas of frontal lobe, connecting different parts of the brain via numerous circuits. Alexander et al. discovered five important frontal - subcortical circuits namely motor circuit; oculomotor circuit; lateral orbitofrontal circuit; dorsolateral prefrontal circuit and anterior cingulate circuit. Out

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of which two are motor circuits, rest are involved in psychosocialand executive functions[4](Fig:1).For orbitofrontal circuit, medial divison also has been described.

Each pathway originates from pre- frontal cortex, projecting to striatum- globuspallidus complex , then to thalamus and ultimately ending back infrontal lobe, thus forming close loop.In addition to this, each loop have various afferent and efferent projections which form open loop(Table:1). All these loops have both direct and indirect pathway(Fig:2) whichhave respective stimulatory and inhibitory effect on thalamus, helps in balanced and organized action. Direct pathway connects striatum , globuspallidusinternus/substantianigra complex(GPi/SN) meanwhile indirect pathway links striatum to globuspallidusexterna(GPe)then subthalamic nucleus to GPi/SN complex, ultimately both pathways reach thalamus, and finally to the cortex.

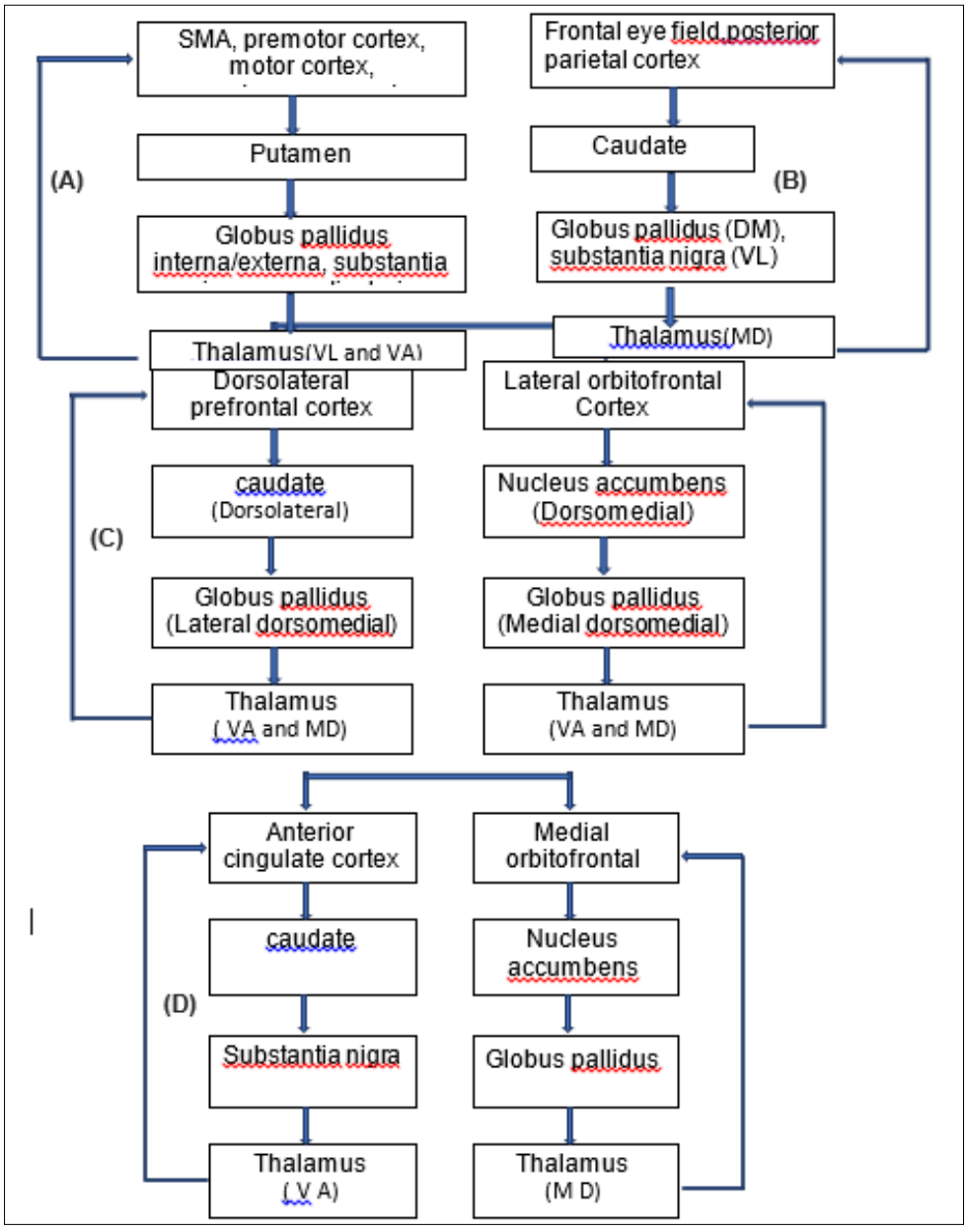

Figure 1 The basic anatomy of frontal subcortical circuits;(A)Motor(B)oculomotor (C) Dorsolateral prefrontal and lateral orbitofrontal(D) anterior cingulate circuits and medial orbitofrontal circuits. VA - ventral anterior; MD – mediodorsal

Table 1 Afferent and efferent projections [6]

Circuits	Major open afferents	Major open efferents
Dorsolateral circuit	Dorsofrontal area 46 Parietal area 7a	Dorsofrontal area 46 Anterior frontal area 8
Orbitofrontal circuit	Superior temporal area22 Orbitofrontal area 12	Orbitofrontal area 12 Mediofrontal area 25 and 32
Anterior cingulate circuit	Hippocampus Entorhinal area 28	Substantianigra pars compacta Medial subthalamic nucleus Lateral hypothalamus

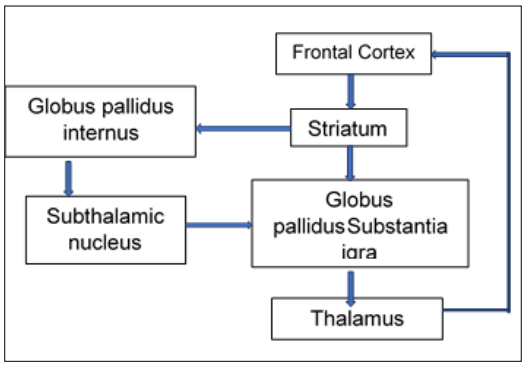

Figure 2 Direct and indirect pathway offrontal subcortical circuit

2. Neurons and neurochemicals

Brain consists of billions of neurons. Any information in brain is transferred from one neuron to another neuron with a help of chemical messengers known as neurochemicals.The neuron comprise of cell body, axons, and dendrites and the gap betweenthe two neuron is known as synaptic cleftNeurochemicals are stored in the vesicle ofpre-synaptic neuron terminal and release only when the dedicated neuron is activated.These are released and bind to the receptor on post-synaptic neuron/ cell(muscle), for its action(Fig 3). The remaining neurochemical is either destroyed by the enzymes or reuptake back.

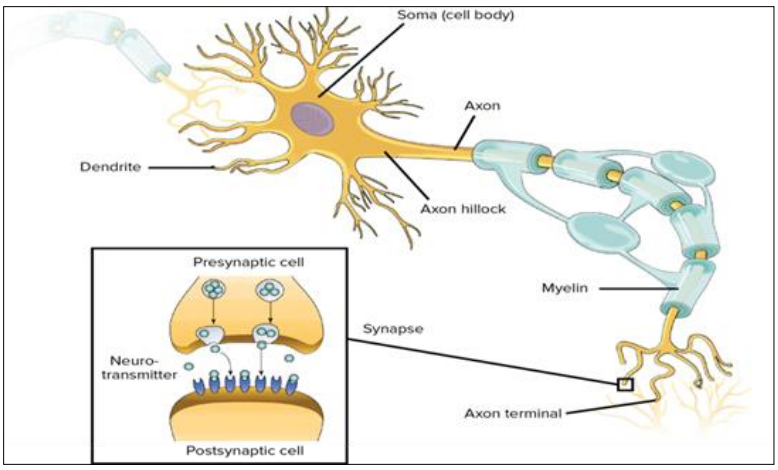

Figure 3 Neuron with synaptic cleft

Psychotic symptoms are strongly related with altered dopamine transmission. There are four dopaminergic pathways in the brain: nigrostriatal, meso-limbic, meso-cortical and tubero-infundibular of which meso-cortical and meso-limbic

pathways are more important in regulating emotions and behaviours.Excess dopamine in mesolimbic pathway cause positive symptoms of schizophrenia, while negative symptoms and cognitive deficits in schizophrenia are associated with low dopamine levels in meso-cortical pathway.[7]Nigrostriatal pathway consists of substantianigra pars compacta(SNc) which sends dopamine input to striatum, having both D1(spiny neurons)and D2 receptor. D1 activate thalamus at the same time D2 inhibit thalamus and dedicated cortical area for the particular action to occur, helping in coordination of that action and cause inhibition of any other extraneous movement/ action of body.

The Acetylcholine(Ach) in striatum,send input to the thalamus by pedunculopontine and lateral tegmentum, cause dopamine release via nicotinic and muscarinic receptor. Serotonin, the other important neurotransmitter in brain, largely present in ventral striatum, hippocampus, amygdala and septal area, offering meso-cortical and mesolimbic dopamine pathway modulation, regulates executive function, sensory gating, and social behaviour.Schizophrenia, bipolar affective disorder (BPAD), and impulsive behaviour all share common defects in these functions. Glutamate, excitatory neurotransmitter, act through NMDA receptor also activate striatum to release dopamine and its antagonism inhibit Ach release via corticostriatal and thalamocortical projection.NMDA receptor hypofunction is known to cause schizophrenic symptoms.Nucleus Accumbens, present in caudate nucleus, receives excitatory input from frontal and limbic cortex, also modulates glutamate and dopamine action.GABA, inhibitory neurotransmitter,predominant neurotransmitter in basal ganglia,enhances thalamo-cortical excitation and minimize thalamic inhibition.

Neuro-psychiatric illness is a heterogeneous group of disorder which can be due to macroscopic(structural changes- stroke, tumour) or microscopic brain changes; metabolism, blood flow, receptor-ligand binding. [4]. To identify these, there aremodalities available like to CT,MRI, fMRI, FDG PET/ SPECT, EEG(Electroencephalogram), MEG(Magnetoencephalogram)[9].MRI(sMRI) is used to rule out structural lesions of brain.Many studies done previously, showed decrease in GrayMatter Volume (GMV)of dorsal anterior cingulate gyrus and insula, by voxel based model, in illnesses like- schizophrenia, BPAD, elderly depressed patients and substance abuse while increased GMV of amygdala, hippocampus inmajor depressive disorder(MDD).[10-12]Different techniques of MRI are used 1) diffusion tensor imaging (DTI)- works on the principle of water diffusion in brain 2) magnetization transfer (MT). DTI measurement can be done by apparent diffusion coefficient(ADC) and fractional anisotropy(FA).ADC shows the amount of CSF as compared to FA, which shows the direction of flow, indirectly lining up with fibres. High FA when fibres are organized in particular direction and low when it is disorganized. MT helps in giving information about myelin sheath integrity.[13-15]As a result of this, it helps in giving information about gray and white matter of brain.

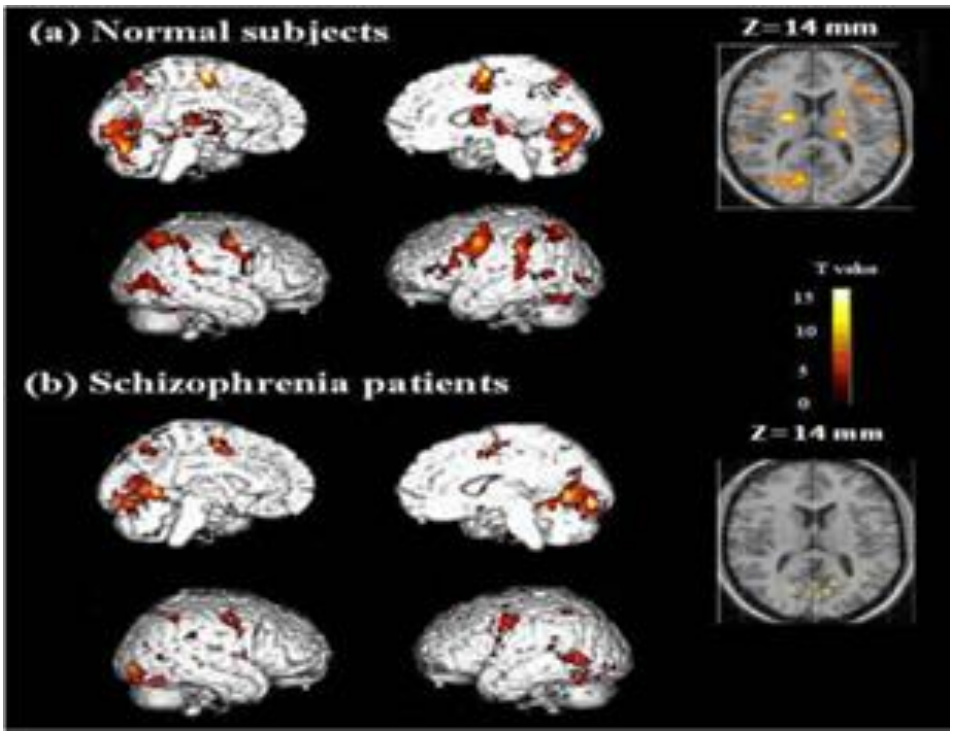

Figure 4 fMRI of of a normal and schizophrenic person

fMRI is the new springing up, non invasive, less radiation exposure causing tool, which works on the principle of BOLD-(blood oxygen level dependent) signal. It can be used to demonstrate the changes in neuronal activity with time and also the functional connectivity of neurons in particular disease. [5,6].It works on the principle that when anycells is activated by any task, there is increase activity or oxygen demand or metabolismof that cell, causing increase in blood flow and decrease in deoxyhaemoglobin(Hbr), and thus increase BOLD signal and the second mechanism is due to the paramagnetic effect of deoxygenated blood[16,17]. Scientist found out that when patient is in resting states, there is still a persistent activity going on in brain, known as "Default mode". Therefore, to see the neuronal activity during any task and in resting state, the two types of fMRI (resting state MRI (rsMRI)and task specific MRI) were discovered to monitor therapy, to see differences in brain at microscopic level in psychiatric and normal person and also as a disease biomarker. [18]For example: fMRI showshypoactivity in rostral anterior cingulate and medial prefrontal structures while abnormal activation in the prefrontal , cingulate gyrus and the medial temporal lobe in Depression[19].It act as a pre bio-marker in depression study.Following image shows the fmri difference in healthy and schizophrenic

Another frequently used is ReHo, regional homogeneity, exhibits simultaneous change in blood oxygen level in different areas of brain, aid in detecting neuronal activity in brain.[20,21]

Because imaging alone still doesn't provide the certain definitive data for diagnosis, the new popping up technology Artificial Intelligence, AI is one of the promising strategy for identifying the optimal use of different imaging metrics for diagnosing, for better treatment, therapeutic trial, to see treatment response, new drug trial or any research, to see the activities inside the brain and to differentiate it from normal person by searching for biomarkers causing mental illness.The theory put forward was "Graph Theory", which is not only used in rsMRI or task specific MRI, it is widely used to demonstrate the topography of brain network in AI. According to this, network is formed by nodes, edges, path, cluster, hub(Fig:4). Nodes which is a functional area (with single neuron) of the brain; edges i.e.connections via fibres (often white fibres);path is a connecting route, can be short path or long path, depending upon the nodes in between. Short path means efficient connection and strongly weighted (highly myelinated) and vice versa. Cluster is the density of connection between neighbouring nodes. Hub, having high number of edges connected to it, but low clustering.[22,23,24]

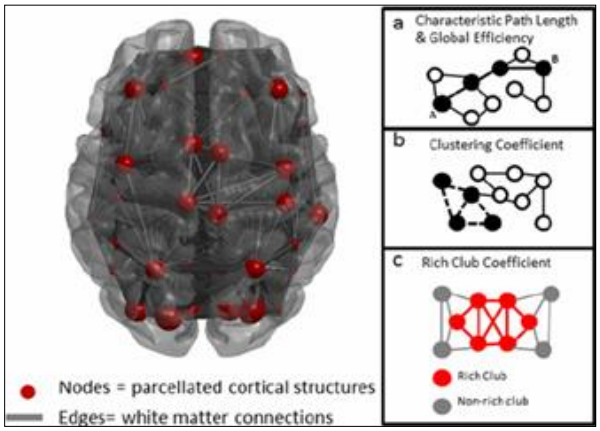

Figure 5 Graph representation of brain network

This graph theory is also used to study the surface area, cortical thickness, DWI data to know the complex brain structure, showed alteration in function and structure in ageing, mental illness, schizophrenia.AI technology is based upon the data fed to computer, processed by some pre-defined algorithm, known as Machine Learning(ML)**(Fig:5)**. The subset of ML is Deep Learning(DL).The model class use for ML is by collection of artificially made neurons, or connected units, forming a network. This network is known by the name, Artificial Neural Network(ANN) as mentioned above in graph theory[25].Machine learning works on two paradigms: supervised (SL) and unsupervised learning (USL)to analyse "big data".[26,27]

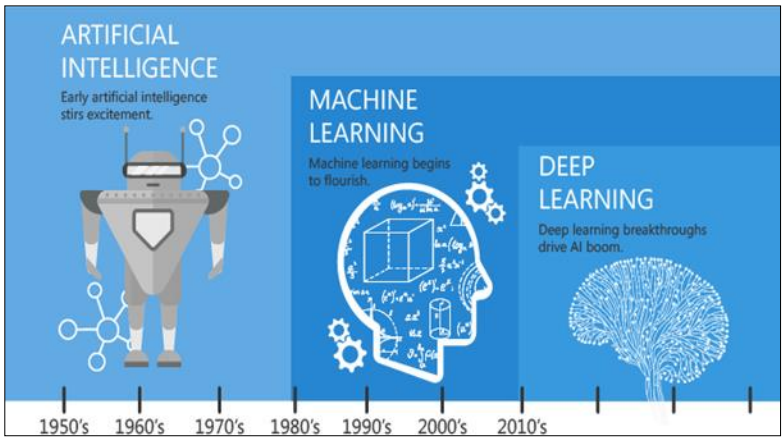

Figure 6 Machine learning

In supervised learning (SL), input and output set is to be given, accordingly we get the outcome after analysis. The purpose is to develop a model, for which predictedoutcome can be formulated in the future based on the features given. It works on the basis of predefined output. For instance task is to find out that the particular person is schizophrenic or not, based on some factors of patients.SL method try to find the outcome(i.e. schizophrenic or not) and a series of features, such as age, gender , background etc.Commonly used SL algorithm are Logistic Regression(LR)and Support Vector Machine(SVM).Lee et al developed the LR model, found the probability of suicide attempt in adolescent, used binary numbers i.e. 0 and 1, for each variables(features) (x1,x2,x3 and so on), the probability of patient committed suicide attempt is, "y". E.g.: x1= gender(if male=1, if female=0), age(continuous variable x), alcohol intake(if yes=1, no=0)[28]. In USL, no labelled outcome in contrast to SL. The machine, with the help of input data find the differences and similarities between the patients. The most common method used in USL is k-means clustering. The lack of labelled outcome make it more challenging and prevent bias. K means technique is used statistically to find the pattern of disease and its severity.Fuento-Tomas et al used cluster based Bipolar disorder classification, which helped psychiatrist for decisionmakingandpersonalised medicine.[29]

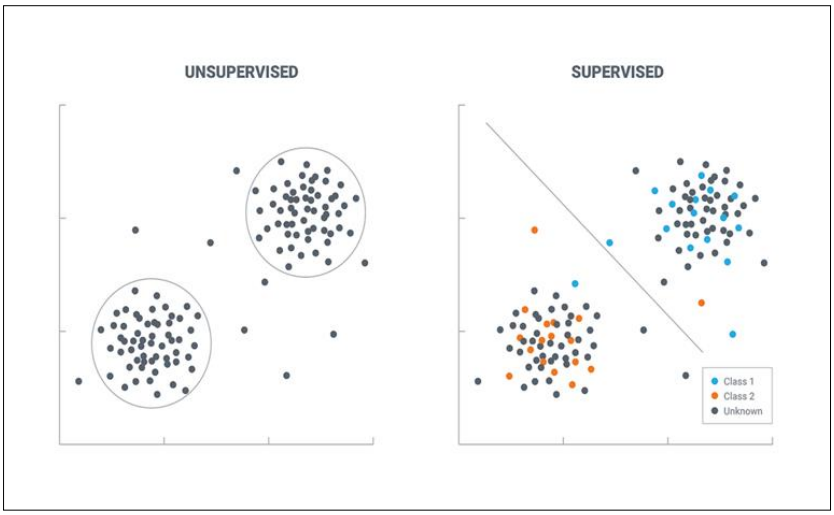

Figure 7 Supervised learning and unsupervised learning

3. Artificial neural network and deep neural network

As described earlier, ANN is an artificial brain network. It was originated in 1940s, when search for language processing and vison started by a machine.The hallmark of NN based systems is that , they consist ofnetwork mimicking brain network, process information by "artificial neurons". It works on the basis of "training algorithm" and optimization function describes the goal of machine. NNs come in a variety of designs, derived from many principles or conceived for different use.Rosenblatt, an American psychologist, designed "PERCEPTRON"(Fig:7), which was a simple model of Feed Forward NN, helped in perception[30]. It comprises of layer of input , connected to output. He also formulated various

algorithm based on the weight of input and output units. In supplementary to this, there is"hidden layer" sandwiched between input and output layer, where all the processing of information were done, based on the algorithm.

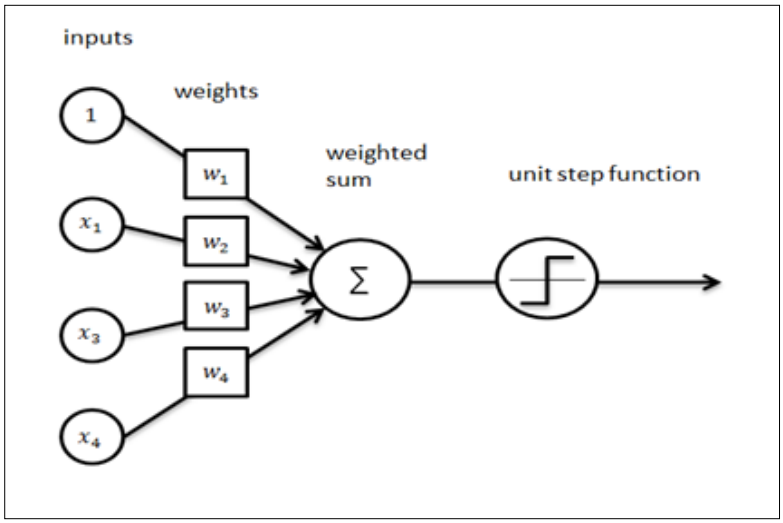

Figure 8 Perceptron

Later, it was seen that adding one to many hidden layers increase the specificity of the machine programming[31]. In Feed Forward Model, the information goes unidirectional, to give the output, in contrast to the new Back-PropagationModel,in eighties, given by David Rumehart et al, which enable information to go bidirectionally i.e. feedback connections is possible to give more relevant result and this masrked the second wave of NN[32].When the hidden layer is more than or equal to four, it is known as Deep Neural Network.Another, very commonly used model is CNN i.e.convoluted neural network or (ConvNet) foranalysing image data, social gestures , speech and pattern recognition**(Fig:8)**. It comprises of multiple hidden layers(filters), known as convoluted layer, processed by multiple feature maps. The result of the previous layer act as an element for further layer, i.e. non linear layer(rectified linear unit) to adjust the output, and then finally pass to the pooling layer, which reduces the dimension of inputs by down sampling[33,34].

The above three processing stages may be repeated multiple times.

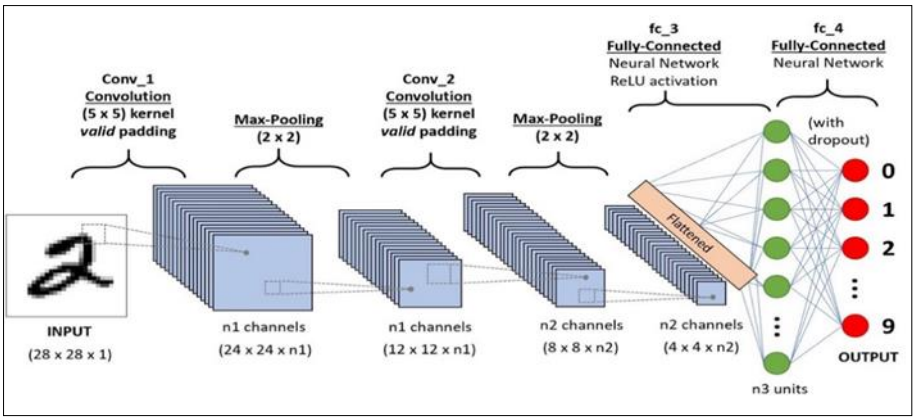

Figure 9 Convoluted neural network

4. AI in psychiatry

Many available AI based therapy in psychiatry used areComputer Assisted Therapy(CAT) (e-therapy/ Beating the Blues therapy for depression) for patients who need counselling and psychotherapy.This also provide support in the form of chat to highly skilled clinicians[35,36,37].Moderate Online Social Therapy(MOST)- provide online peer support to depressive and psychotic patient[38].AI based EEG model, depression patient were identified by 67% accuracy rates using linear discriminant analysis and 83.3% using logistic regression method[39,40].Kinesics date aid in identifying–

schizophrenia by facial expression and depression by body movements and emotional changes. Many data obtained by investigations like imaging, genetics etc are combined to provide information on etiological mechanism. Khan *et al*proposed integrated mental-disorder GEnome score or iMEGES to identify whole genome/exon sequencing data on personal genomes relating to psychiatric disorder[41,42].DNNs are used in Electronic Health Recorder(EHR) and also incorporated with social media platforms like- Reddit and Twitter for mental illness[43,44].Data obtained from wearable devices like- Health bands, sensors , mobile phones. Features like social interaction, changes in vitals, movement patterns, sleeping habit, stress can be extracted , which is also the source of prediction calculation of mental illness[46,47].>90% were correctly detected by Hamilton Depression Rating Scale asdepressed in bipolar patients by their typing speed, acceleration, and typing duration. Many people don't come out with their initial symptoms as they feel disgraceful, being treated by psychiatrist, especially in country like India, so for them AI removes stigma of this and also help to give unbiased individual treatment, cost effective, saves time and to prevent load of clinician, help in early identifying of disease, in research activities. But in spite of all the promising performances of AI, it is still lacking in human emotional behaviour, versatility to change according to the situation and decision making.

5. Conclusion

Cortical and sub cortical brain networks and its modulation via proper balance of various neurotransmitters are essential to keep up mental health in acceptable way and disturbances of this homeostasis cause numerous mental illness. AI is thus a simplified manmade version of human brain networks, which help clinicians to diagnose and treat early. In this manner, it improvise health system efficiency both in time and cost. But since it has its own demerits in terms of understanding emotions, behaviour, situational reactions and decision making, it cannot completely take over the human brain -"Humans made tachnologies not vice-versa".

Compliance with ethical standards

Disclosure of conflict of interest

Both authors do not have any conflict of interest.

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