

Disorders of the Brain Systems

I. INTRODUCTION

As was shown in Part II, the brain can be divided into systems. These brain systems consist of separate cortical and subcortical anatomical structures and play different functions in processing sensory information and organizing actions. The systems we have analyzed in the previous part are: sensory systems, attentional networks, executive system, affective system, and memory systems. We presume that dysfunctioning of a separate brain system is associated with a separate class of brain disorders.

However brain disorders are classified not on the basis of neurophysiological data but on the basis of behavior. There are two main classification manuals: DSM-IV and

ICD-10¹. The two manuals rely only on behavioral symptoms. Although research is advancing and several objective diagnostic parameters² have been suggested for specific disorders, no reliable biological markers or endophenotypes of distinct disorders are accepted so far. This part of the book holds the following closely related goals: (1) analyzing dysfunctions of the above mentioned systems in connection with known psychiatric and neurological disorders, (2) associating the dysfunctions of the brain systems with QEEG/ERP markers described in Parts I and II of this book, (3) suggesting an appropriate neurotherapy for correcting dysfunctions of the brain systems.

From Part II we have learnt that distinct brain systems are controlled by separate neuromodulators in the brainstem. Consequently, the brain systems can be corrected by pharmacological³ interventions on these mediators. The interventions include increasing or decreasing the action of neuromodulators (1) by feeding the brain with biochemical precursors of mediators (such as with L-dopa – a precursor of dopamine), (2) by blocking the postsynaptic receptors (such as with antipsychotic drugs that have affinity to dopamine receptors), (3) by blocking the reuptake mechanisms (such as with Ritalin that suppresses the dopamine reuptake mechanisms), or changing the cellular mechanisms of neurotransmission in other ways⁴.

It should be noted here that before 1950s, scientists tried several non-pharmacological interventions such as electrical invasive and non-invasive

¹The Diagnostic and Statistical Manual of Mental Disorders (DSM) is a handbook that lists different categories of mental disorder and the criteria for diagnosing them, according to the American Psychiatric Association. It is used worldwide by clinicians and researchers. The DSM has gone through several revisions since 1952. The last major revision was the DSM-IV published in 1994. The DSM-V is currently in preparation, due for publication in approximately 2011. The mental disorders section of the International Statistical Classification of Diseases and Related Health Problems (ICD) is another commonly used guide, and the two classifications use similar diagnostic codes.

²Such as the inattention index (theta beta ratio) in EEG spectra for diagnosis of attentional dysfunctions.

³Pharmacology (from Greek *pharmakon* - drug and *lego* – to tell about) studies effects of different biochemical substances on function in the leaving organs. If substances have medical properties, they are called pharmaceuticals. The field includes composing drugs, studying their properties, and observing their medical applications. *Neuro-* and *psychopharmacology* (effects of medication on behavior and nervous system functioning) are considered as sub-fields of pharmacology.

⁴Although different plants were the source of medication for centuries, modern western medicine utilizes purified bioactive compounds, rather than an entire sample of plant matter. The real breakthrough period in psychopharmacology started in 1950s by introduction of the first set of psychotropics and new methodological approaches in pharmacology. Treatment of heterogeneous disorders such as mania, schizophrenia, depression, bipolar disorder, became available.

intrusions, as well as anatomical destructions including neurosurgical and stereotactic operations. Most of the attempts were abandoned after the revolutionary events in psycho-pharmacology. However, 50 years of using psycho-pharmacology brought some dissatisfaction and controversy. One part of this controversy is associated with a failure to find a certain genotype as a pathological mechanism for a certain disease⁵. Recent attempts of medical genetics have indicated that most of psychiatric disorders do not follow a simple Mendelian rule and that no single gene could be attributed to a single disorder. This led some scientists to introduce the concept of endophenotypes as biological markers of disease that are non-molecular but closer to the genotype than behaviorally defined classification of diseases. Some QEEG parameters and ERP components have been suggested as candidates for endophenotypes of at least some of brain diseases.

Renaissance of non-pharmacological methods of treatment started recently as a rebound effect of exponentially increasing use of pharmacological substances to treat various brain diseases. The non-pharmacological methods include neurofeedback and electromagnetic stimulation methods such as transcranial direct current stimulation (tDCS), transcranial magnetic stimulation (TMS), deep brain stimulation (DBS), and electroconvulsive therapy (ECT). They are united under a common name “neurotherapy.”

So, in this part of the book we are going to present the most common brain diseases in association with QEEG and ERP indexes of the brain systems that are supposed to be involved in pathogenesis of the diseases. The diseases we are going to discuss in this part of the book are listed in Table PIII.1. The brain systems that are associated with these dysfunctions are marked. The table simplifies the reality. It does not show complex interactions between systems⁶ and heterogeneity of distinct diseases. Still, the concept depicted in the table may serve as a starting point for presenting

⁵The other part of controversy is associated with more practical issues. First of all, pharmacotherapy does not help everyone: some patients remain unresponsive to the pharmacological interventions. Moreover, selection of the appropriate medication (especially in depression) is a matter of trial and error. Because the effect of some substances needs few weeks to be exhibited and there are many potential drugs that might treat the disease, the trial and error procedure could last for many months and is very expensive both in monetary expression and in human resources. On the top of that most of the drugs have undesirable side effects.

⁶In the dysfunctional brain different systems interact with each other so that dysfunction, for example, of executive system might cause the dysfunction of the affective system and vice versa. This interaction complicates the behavioral pattern of disease in a particular patient.

TABLE PIII.1 Association Between Psychiatric/Neurological Diseases and Impairments of Brain systems

Disease/System	Sensory	Affective	Memory	Executive
Dyslexia	_____			
Neglect	_____			
Depression		_____		
Anxiety		_____		
Alzheimer's			_____	
Parkinson's				_____
Schizophrenia				_____
OCD				_____
ADHD				_____
Addiction		_____	_____	_____

data and ideas regarding QEEG/ERP markers of brain disorders and neurotherapeutical approaches for correcting these disorders.

We have learnt in this book that operations of the brain systems are maintained by complex neuronal networks that include subcortical and cortical anatomical structures. Let us consider some generally defined neuronal network⁷. The network is characterized by two parameters: (1) by activation level of the network and (2) by response of the system to an elemental increase of the input to the system. As we have shown in Introduction to the book the relationship between the response of the network and its activation level is described by the inverted U-curve (Fig. PIII.1).

We presume that the response of the neuronal network is approximated by the corresponding ERP independent component generated in by the network in an adequate psychological condition⁸. One can see that the maximum of ERPs amplitude corresponds to the optimal level of activation of the neuronal network. From Part I we know that the increase of the optimal level of activation of the cortex is associated with the excess of beta activity in the background EEG generated by the corresponding part of the

⁷For example, the network subserving monitoring operation includes several cortical areas of the frontal cortex with the anterior cingulate cortex as a key element.

⁸For example, the response of the monitoring network is measured by the amplitude of P400 monitoring component in two stimulus GO/NOGO task.

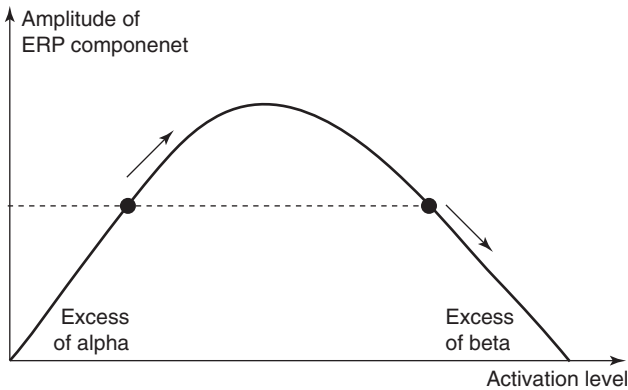


FIGURE PIII.1 Response (amplitude of ERP component) versus activation level of a hypothetical neuronal network. Horizontal axis – overall activation of neuronal network. Vertical axis – response of the system to a relevant stimulus measured in amplitude of evoked potential. Lower level of activation is characterized by excess of alpha activity while higher level of activation is characterized by excess of beta activity in the EEG.

cortex, while decrease in the level of activation is associated with the excess of alpha activity⁹. Note that both extremes are associated with decrease of amplitude of ERP components. The decrease of ERPs amplitude is associated with decrease of reactivity of the system when the system moves away from its optimal performance point¹⁰. Consequently, the excess of beta activity as well as excess of alpha activity is accompanied by low amplitude of ERP components that are associated with poor performance of the system. These theoretical considerations show necessity of simultaneous measurement of ERP components and background EEG characteristics.

II. GLOSSARY

Addiction is a compulsive, out-of-control drug use despite serious negative consequences.

⁹Recall the relationship between metabolic activity of the cortex and alpha and beta activity generated in the corresponding local cortical area (see Fig. PIII.1). According to this relationship, excessive (in comparison to norms) beta in EEG corresponds to increase of metabolic activity, while excessive alpha corresponds to decrease of metabolic activity in the local cortical area.

¹⁰For example, decrease in the monitoring component may be associated with excessive activation of the monitoring network as well as with decrease of its activation.

ADHD is the most common developmental disorder that affects 3–8 per cent of children worldwide according to conservative estimation and includes children displaying developmentally inappropriate levels of inattention, hyperactivity, and impulsivity that begin in childhood and cause impairment to school performance, intellectual functioning, social skills, driving, and occupational functioning.

Alzheimer's disease is a degenerative brain disorder that at the first stage starts with progressive memory loss and at later stages develops into a generalized dementia. The loss of cholinergic cells in the basal forebrain appears to be responsible for the first stage.

Antipsychotic drugs are pharmacological agents that are used to treat psychosis.

Anhedonia is loss of interest or pleasure in almost all activities.

Cognitive-behavioral psychotherapy is a form of psychotherapy that aims to strengthen self-esteem and provide the patient with support and understanding. Cognitive-behavioral psychotherapy emphasizes the analysis of the problems at hand, and the definition of concrete goals and solutions so that the patient can recognize progress.

Compulsions are actions repeated over and over in ritualistic, stereotyped succession.

DC (direct current) is a flow of electric charge that does not change direction and value. Applying to a cortical tissue, DC polarizes neurons, that is, changes membrane potentials of cells.

Depression (or major depression) is a disorder of the affective system characterized by low or depressed mood, anhedonia, and low energy or fatigue.

Diagnostic and Statistical Manual of Mental Disorders (DSM) is a handbook that lists different categories of mental disorder and the criteria for diagnosing them, according to the American Psychiatric Association. It is used worldwide by clinicians and researchers. The DSM has gone through several revisions since 1952. The last major revision was the DSM-IV published in 1994. In Europe, the mental disorders section of the *International Statistical Classification of Diseases and Related Health Problems (ICD)* is more often used.

Electroconvulsive therapy (ECT), also known as electroshock, is a psychiatric treatment in which seizures are induced by means of strong electrical current.

Effect size is a measure of a certain effect that is defined as the difference between the means of a measured parameter for the experimental and control groups, divided by the standard deviation of the control group or the average standard deviation of both groups. The effect size is a standardized measure and allows comparing the effects found in different studies with different parameters.

Endophenotype is a biological marker of a disease.

Monoamine oxidase is an enzyme located on the outer mitochondrial membrane, which catalyses the hydrolysis of biogenic amines such as catecholamines and serotonin.

Morbidity is the incidence or prevalence of a disease in a population.

Neurofeedback is a technique of self-regulation by means of EEG-based biofeedback. In this technique, neurofeedback parameters of EEG currently recorded from a subject's scalp (such as an EEG power in a given frequency band) are presented to the subject through visual, auditory, or tactile modality with the task to voluntarily alter these parameters in a desired (leading to a more efficient mode of brain functioning) direction.

Obsessions are thoughts that repeat over and over again, unwanted but insistent.

OCD is a disorder characterized by recurrent obsessions and compulsions causing marked distress or significant impairment.

Oppositional defiant disorder (ODD) is associated with taking unsafe risks, breaking laws, refusing to follow instructions or directions.

Psychosis includes distortions in thinking, such as delusions (false beliefs that are firmly held in the face of contradictory evidence), and perceptual disturbances, such as hallucinations. Auditory hallucinations, usually experienced as voices distinct from one's own thoughts, are most common in schizophrenia.

Psychopharmacology is a subfield of pharmacology that in particular studies effects of different biochemical substances on behavior and nervous system functioning.

Psychosurgery is a type of surgical ablation or disconnection of brain tissue with the intent to alter affective or cognitive states caused by mental illness.

Schizophrenia is a psychiatric disorder characterized by (1) impairments in the executive system such as disordered thoughts, disorganized

speech, inability to plan, initiate, and regulate goal directed behavior, as well as by (2) impairments in the sensory systems such as hallucinations, and by (3) associated symptoms of the affective system, such as blunted emotions.

Learning disability (LD) is a difficulty in mastering language, reading, or math.

tDCS – transcranial direct current stimulation – a neurotherapeutic technique of application of direct current to the brain by means of electrodes placed on the head. Because of polarizing effect on neuronal cells, tDCS in 1960–1970s was called polarization technique.

Tourette’s syndrome is associated with having tics – uncontrolled movements like eye blinks, or facial twitches, or vocal sounds.

Tricyclic drugs are molecules that inhibit biogenic amine reuptake, therefore prolonging the period during which these neurotransmitters are active at the synaptic cleft.