

Done By: Moath Darweesh

## Introduction

Neurochemistry is the study of inter neuronal communication. One example of neuronal communication is what happens in a behavioral action. For occurrence of behavioral action, one neuron transmits its signal to another neuron and so on. But here the question is, how these neurons communicate or talk?

Neurons communicate through what we call neurotransmitters, which are chemical substances that transmit the signal through neuronal pathways.

Regardless of the type of neurotransmitter involved, several common steps comprise the process of transmission at a chemical synapse. The first steps are the synthesis of the neurotransmitter usually within the nerve terminal and its storage within synaptic vesicles. This is followed by release of the chemical into the synaptic cleft in response to nerve impulses (action potential). The secreted neurotransmitter can then act on receptors on the membrane of the postsynaptic neuron. The final steps in the process lead to termination of the actions of the neurotransmitter and include reuptake into the nerve terminal, and enzymatic degradation.

-Keep in mind that in order to have good perceptions, your neurotransmitters have to be in their normal level. It was found that the availability of specific neurotransmitter is associated with the etiology of many psychiatric conditions.

Note: the doctor talked about how action potential generates from resting potential to depolarization and then repolarization. Also, he talked about how each neurotransmitter acts specifically on its receptor.

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**Classification**: the three major classes of neurotransmitters are biogenic amines, amino acids and peptides.

Biogenic amines:  
further subdivided into

### A) Catecholamine or monoamines.

This category consist of Norepinephrine, Epinephrine and Dopamine.

#### 1) Epinephrine and norepinephrine

Epinephrine is called so because in Latin Epi means above or on, and nephron means kidney. And as we know, epinephrine is mainly synthesized in adrenal glands which are above the kidney.

Epinephrine and norepinephrine are secreted when we are scared or excited. For example, you were walking in a dark street, and suddenly, someone attacked you with a knife. Not surprisingly, you have either to fight him, or to fly and escape. That's why it's called fight or flight response.

What happens during fight or flight situation is the following

- 1) Pale face because of vasoconstriction of skin arteriole.
- 2) Dilated pupil
- 3) Tachycardia and increased stroke volume, which result in increased blood pressure.
- 4) Hyperventilation.
- 5) Vasoconstriction of GIT
- 6) Hyperglycemia, because of catabolism of glycogen.

Also, we use adrenaline in the following situations

- 1) Cardiac arrest
- 2) Anaphylactic shock
- 3) Patient with severe asthma and didn't respond to bronchodilators.
- 4) Superficial bleeding.

Note: adrenaline is available in all formulations, like inhalation, IV, Intramuscular or subcutaneous.

Now, let's start discussion our important topics.

### Theory of depression:

the lower the concentration of neurotransmitters (norepinephrine and serotonin) in the brain, the more likely to develop depression. That's because serotonin is responsible for happiness. Also, dopamine plays a major in reward circuit.

-Extra: depression is not always associated with lack of belief in God. Recently, Chromosome 3 specifically 3p21.1 was identified as a locus for increased risk for depression.

- Tricyclic antidepressants was the most popular antidepressants in 1970s. Currently, SSRI (serotonin specific reuptake inhibitor) replaced Tricyclic antidepressants. Unlike SSRI, tricyclic antidepressants inhibit reuptake of norepinephrine more than serotonin. Neurologists still use tricyclic antidepressants like amitriptyline not to treat depression, instead, they use them to treat intractable pain.

-MAO inhibitors are still used drugs to treat depression, but there are certain foods patient should avoid while taking MAO inhibitors. Because tyramine is a compound that's found in certain foods, beverages, and other substances and has an effect on your blood pressure. Tyramine is regulated by the MAO enzyme, which helps break it down. MAOIs work by restricting the MAO enzyme, which usually results in reducing the symptoms of depression and anxiety. However, when the MAO enzyme is inhibited, such as when you're taking an MAOI, tyramine can reach dangerously high levels, causing your blood vessels to narrow and resulting in critically high blood pressure.

-SSRI could increase serotonin level too much and this carry risk of inducing mania, making it essential to monitor of signs of excess energy and elevated mood in patient.

## 2) Dopamine

-Dopamine is derived from Phenylalanine. Which is converted into tyrosine by hydroxylation. Tyrosine is converted into L-DOPA by hydroxylation too. DOPA is converted into dopamine by decarboxylation. Doctors advise patients who suffer from mild depression to eat tyrosine rich diet like dairy products and fish, to increase the synthesis of Dopamine and norepinephrine in their brains. Also, a recent study reveals that people who eat Mediterranean diet ( vegetables and fish ) are less likely to develop depression.

-There are 5 receptors of dopamine. D2 and D4 receptors which are found in the striatum are the most important, because all of antipsychotic drugs inhibit mainly these two receptors.

### Theory of schizophrenia :

more level of dopamine is associated with schizophrenia.

-What the antipsychotic do is they inhibit dopaminergic receptors, which results in decreasing in the effect of dopamine, and so we treat the condition. But low dopamine level also might result in symptoms of parkinsonism. ( remember that parkinsonism is associated with low dopamine level).

### Symptoms of schizophrenia

There are positive symptoms of schizophrenia, and negative symptoms.

-Positive symptoms include

1) Hallucination, which means false perception with the

absence of stimulus. People with schizophrenia hear, see, smell or feel things no one else does. These hallucinations could be in form of tactile hallucinations which create a feeling of things moving on your body like insects.

Note: Cocaine addiction could lead to tactile hallucination too.

2) Delusions, which means false beliefs, like when a patient thinks that people conspire against him because he's intelligent. One type of delusions is Erotomanic delusions, which occur when a patient might be convinced a celebrity is in love with him, and the celebrity is cheating his/her partner.

-Negative symptoms means absence or lack of normal mental function involving thinking and behavior. Bleuler summarized them in 5 A's

1) Affective flattening: terrible case of blahs, when they talk their voice can sound flat, with no emotion. Also, they are neither happy nor sad.

2) Anhedonia: lack of pleasure. The person may not seem to enjoy anything anymore even when going to gym or hanging out with friends.

3) Apathy : patients stop taking care of what is happening , even if a disaster is happening in his/her country, he/she might not care anymore.

4) Alogia: they might not talk much. Schizophrenic patients can feel like pulling teeth when talking with people. That's because they have no thoughts to share with. Also, they could suffer from sleep pattern reversal.

5) Was not mentioned by the doctor, but for your information, it's attention. Schizophrenic patients might develop loss or absence of attention.

-Before 1984-1986, antipsychotics was working just on positive symptoms. That's because D4 receptor which is implicated in the negative symptoms, was not targeted by any drug.

Amisulpride(Solyan, Amex), a new drug, targets D4 receptor, and because of that, it could treat negative symptoms of schizophrenia.

Please here note, newer drugs like amisulpride are amazing, but one of their disadvantages is they increase the appetite for eating, so please take care when giving these drugs to obese patients especially if there is a history of diabetes in the family. These drugs also could cause diabetes even in non-obese patients.

Extra: Don't think schizophrenic patients are extremely pathetic, I know it's a dangerous disease, but around 80% of patients respond well to antipsychotics. As well as, they usually have high IQ, one example is John Nash, who made fundamental contributions of game theory and differential geometry. Also, John Nash is the only person to be awarded both the Nobel Memorial Prize in Economic Sciences and the Abel Prize.

## B) Indolamine

one example of this category is serotonin, which is derived from tryptophan. Tryptophan is converted to tryptamine, and then to 5-hydroxytryptamine (5-HT). There is 7 types of serotonin receptors, 5HT1 to 5HT7. Also these receptors have subtypes.

The most important receptors are 5HT2 and 5HT7.

5HT2 is the target of Clozapine (colzaril, leponex ) which is the only available drug to treat drugs resistance schizophrenia.

5HT7 is the target of Lorasedom, which treat depression associated schizophrenia. Patient with this illness suffer from

loss of concentration and memory as well as schizophrenic symptoms.

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2) Acetyl choline : AC has two receptors. Muscarinic receptor, which could be blocked by atropine and cause dry mouth, constipation and double vision, and nicotinic receptors.

Misem, a popular psychiatrist, thought that acetylcholine plays a role in mood regulation. According to his thought, Misem used to give Acetylcholine IV to treat depressed and anxious patients. But unfortunately, it did not work.

As we know, dementia is associated with low acetylcholine concentration. So one approach to treat dementia is giving acetylcholine esterase inhibitors. Another approach is by working through nicotinic and NMDA (glutamic ) receptors. Memantine, a drug work through NMDA and nicotinic receptors, and used to treat severe dementia.

-11 years ago, a journal published that high activity of nicotinic receptors is associated with low chance of developing dementia. According to this thought, many people started smoking. But it's was found out that the journal was cheating because it was sponsored by a smoke company.

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3) Histamine.

-Histamine Has 3 receptors H1, H2 and H3.

-Drugs which are used to treat allergy target H1 receptor.

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## Amino Acid neurotransmitters :

1)glutamate : one of the excitatory neurotransmitters in the brain. Since schizophrenia is associated with high level of glutamate ,new drugs now act by blocking glutamate receptors to treat schizophrenia.

2) GABA: it's the major inhibitory neurotransmitter in the brain. Benzodiazepines drugs act by increasing the effect of GABA.

-Zalopidem, zaleplon and zopiclone ( Z drugs) are hypnotic drugs work also in GABA receptors.

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## Peptides.

are short chains of amino acids

THE END

