





Understanding Schizophrenia: An Integrative Perspective

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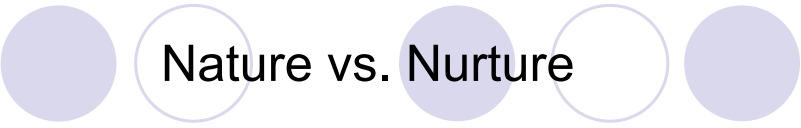
Introduction

- Much attention has been devoted to understanding the positive and negative symptoms of schizophrenia
- Cognitive symptoms and the biological components of schizophrenia need to be better understood in order to provide the best possible treatment



Overview

- Etiology
- Biological Components
- Cognitive Components
- Treatment Options



Nature vs. Nurture

- Strong genetic component
 - Heritability estimates as high as 80-85%
- Environment also plays an important role
 - Adoption studies provide evidence that genetics alone do not determine the development of schizophrenia



Onset of Schizophrenia

- Typically develops in early adulthood between the ages of 16-25
- Onset is very unpredictable
 - It can take years for schizophrenia to develop or only a matter of weeks



Symptom Presentation

- Positive: symptoms of excess such as hallucinations and delusions
- Negative: symptoms of diminution such as flat affect and poverty of speech
- Cognitive: impairments in areas such as memory and executive function



Prognosis

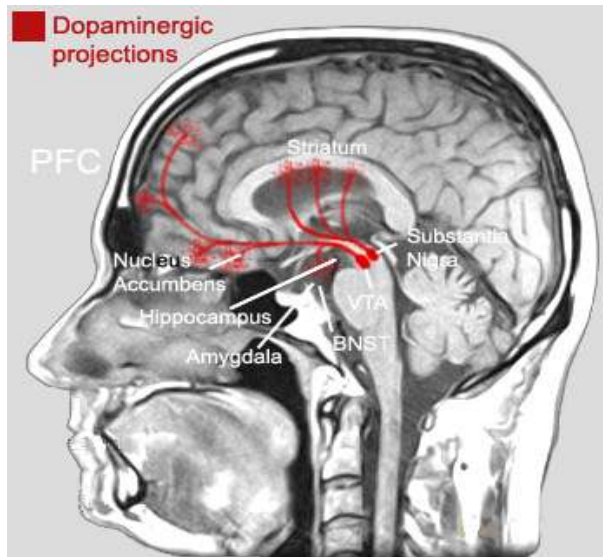
- Individuals with positive symptoms have the best prognosis
 - Symptoms fluctuate in severity
 - Good response to antipsychotic medication
- Negative and cognitive symptoms are the most difficult to treat
 - Symptoms are stable over time
 - Poor response to antipsychotic medication



The Role of Dopamine

- Dopamine hypothesis: positive symptoms of schizophrenia are the result of overactive dopaminergic neurons in the mesolimbic pathway

Dopamine and the Mesolimbic Pathway

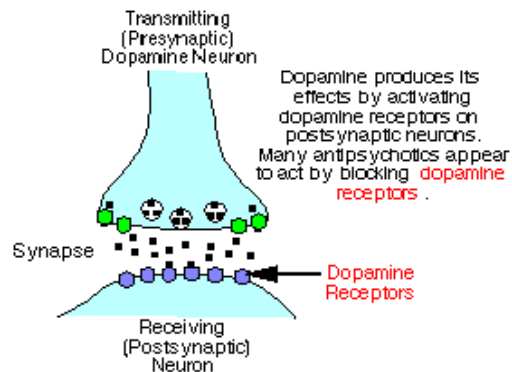


Dopamine and the Nucleus Accumbens

- The nucleus accumbens (NA) plays a role in reinforcement
- Overactive dopamine stimulates the NA and creates a feeling of euphoria that gets paired with the positive symptoms
- This reinforcement of the positive symptoms increases their frequency

The Use of Antipsychotic Medication

- Antipsychotic medication decreases positive symptoms by blocking dopamine receptors and decreasing the activity level of dopamine

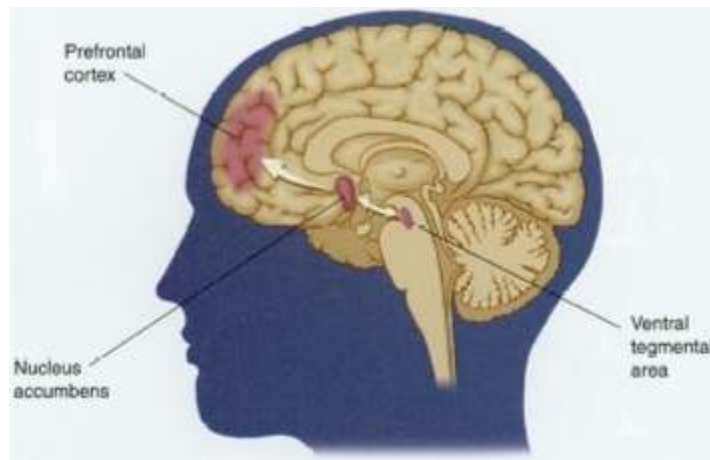


Dopamine and Negative Symptoms

- Hypofrontality theory: a lack of dopamine in the dorsolateral prefrontal cortex (DLPRC) decreases the metabolic activity of that part of the brain
- This theory contradicts evidence of dopaminergic neurons being hyperactive in the NA and producing positive symptoms

Dopamine and the DLPFC

- There is an inverse relationship between the DLPFC and the NA
- A decrease in dopamine in the DLPFC triggers an increase in dopamine in the NA



The Use of Atypical Antipsychotics

- Atypical antipsychotics may target the prefrontal cortex and increase dopamine levels
- Atypical antipsychotics have been successful in treating both negative and positive symptoms

Brain Abnormalities

- Brain abnormalities in the prefrontal cortex have been associated with negative symptomology
- Abnormalities found in the prefrontal cortex include deficits in volume and thickness of specific areas



Prefrontal Cortex Deficits

- Deficits in volume of the bilateral pars triangularis
 - This is a crucial component of the DLPFC
- Deficits in volume and thickness in the orbitofrontal cortices
 - These are essential components of social functioning
 - Integrate self-monitoring and emotional valence



Areas of Cognitive Impairment

- Declarative memory
- Working memory
- Executive Functioning

Declarative Memory

- Includes episodic and semantic memory
- Episodic memory deficits may be due to an inability to encode new information
- There is some debate over the source of semantic memory impairment
 - Inability to organize information into a network of associated concepts
 - Inability to inhibit the activation of irrelevant associations

Working Memory

- Working memory is comprised of three components which all show deficits
- The central executive system has impaired maintenance and retrieval
- The visual and verbal systems display impairments with encoding



Executive Functioning (EF)

- Includes abilities such as planning, problem solving, and set shifting which all show impairment
- Abnormalities found in the prefrontal cortex are believed to be the root of EF impairment



Treatment Options

- The traditional approach to treating cognitive symptoms is through the use of medication
 - Atypical antipsychotics are used due to the similar nature of cognitive and negative symptoms
 - Alternative options such as the acetylcholinesterase inhibitor galantamine are being explored

Therapeutic Options

- Neurocognitive Enhancement Therapy (NET) and Work Therapy have been studied to determine their impact on improving cognitive functioning

NET and Work Therapy

- NET
 - Up to 5 hours of cognitive exercises per week for 26 weeks
 - Rating of work related cognition in the support group
 - Weekly social information processing groups
- Work Therapy
 - Paid work activities in job placements at a medical center

How Effective Are They?

- Individuals who participated in both NET and work therapy displayed the greatest cognitive improvement six months after therapy ended
- Individuals who just had work therapy also showed some improvement
 - The opportunity to practice cognitive skills in a real world setting is important

Conclusion

- Cognitive symptoms are just as devastating as positive and negative symptoms
- There is still much to learn about the biological components of schizophrenia and how they relate to the cognitive deficits that are being observed



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