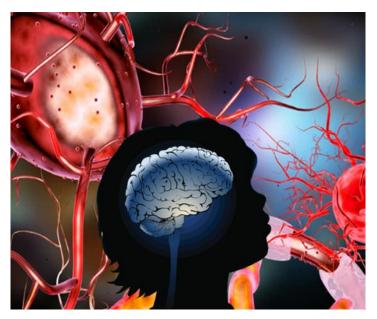


DNA DILIGENCE

PANS - PANDAS Biohack

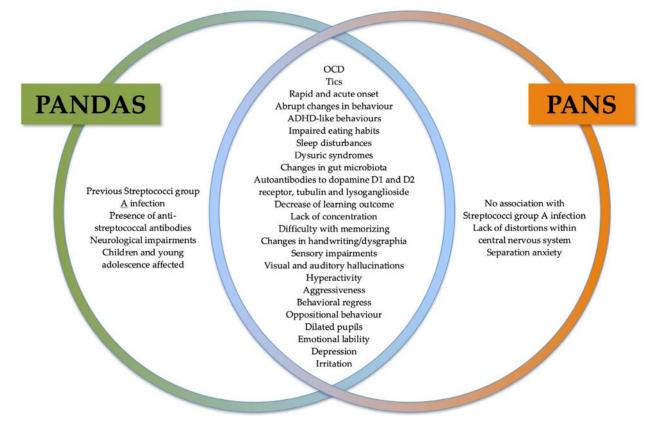
[SAMPLE REPORT]

Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS) & Pediatric Autoimmune Neuropsychiatric Disorders associated with Streptococcus infections (PANDAS) BioHack



Pediatric Acute-onset Neuropsychiatric Syndrome (PANS) is a clinical diagnosis given to children who have a dramatic – **sometimes overnight** – onset of neuropsychiatric symptoms including obsessions/compulsions or food restriction. They are often diagnosed with **obsessive-compulsive disorder (OCD) or an eating disorder**, but the **sudden onset of symptoms** separates PANS from these other disorders. In addition, they may have symptoms of depression, irritability, anxiety, and have difficulty with schoolwork.

Like PANS, children with Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infections (PANDAS) have an acute onset – within 2 to 3 days – of neuropsychiatric symptoms, specifically OCD or tics (involuntary, purposeless movements).



The proposed link between infection and these disorders is that an autoimmune reaction to infection produces antibodies that interfere with **basal ganglia function**, causing symptom **exacerbations**, and this autoimmune response results in a broad range of neuropsychiatric symptoms.

PANDAS patients test positive for a recent streptococcal infection, such as strep throat, perianal strep or scarlet fever. Like PANS patients, they also may suffer from **uncontrollable emotions, irritability, anxiety** and loss of academic ability and handwriting skills. Although PANDAS was identified as a medical syndrome more than a decade before PANS, it has been classified as a subset of PANS. To date, PANDAS is the only known subset of PANS. Treatment for children suspected of PANDAS is generally the same as the standard treatments for **Tourette syndrome (TS) and OCD**.

Therefore, for the purposes of PANS/PANDAS we will dissect primarily three maladies including:

- Obsessive-Compulsive Disorder (OCD)
- Tic Disorder (TICS)
- Gilles De La Tourette Syndrome (GTS) Tic Disorder

Sources:

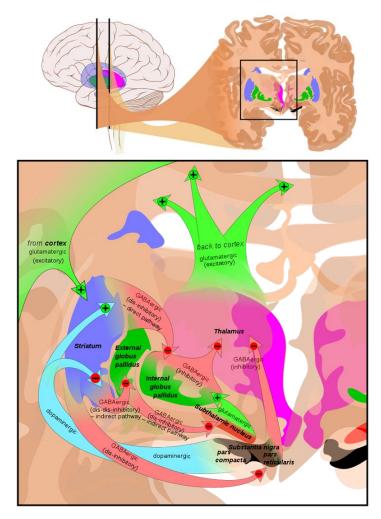
https://med.stanford.edu/pans.html https://www.stanfordchildrens.org/en/service/pans-pandas/what-are-pans-pandas

Basal ganglia

Basal ganglia disease is a group of physical problems that occur when the group of nuclei in the brain known as the **basal ganglia fail to properly suppress unwanted movements** or to properly prime upper motor neuron circuits to initiate motor function. a disorder leading to abnormally low output of the basal ganglia leads to reduced inhibition, and thus excitation, of the thalamocortical projection neurons (VA and VL) which synapse onto the cortex. This situation leads to an inability to suppress unwanted movements. These disorders are known as <u>hyperkinetic</u> disorders. Recent research shows that basal ganglia disorders can lead to other dysfunctions such as <u>obsessive-compulsive disorder</u> (OCD) and <u>Tourette syndrome</u>.

Basal ganglia circuits

Of all the circuits, the motor circuit is the most studied due its importance to motor disorders. The basal ganglia is able to initiate voluntary movements by disinhibiting thalamic neurons that drive upper motor neurons. This process is **regulated by dopamine** secreted by the striatum onto the **D1 dopamine receptor**. Dopamine excites striatal neurons in the direct pathway. The indirect pathway inhibits unwanted movements by simultaneous increase in excitatory input. Similar to the direct pathway, the indirect pathway is regulated by striatal dopamine. **D2 dopamine receptors inhibit transmission** via the indirect pathway. D2 receptors inhibit striatal neurons in the indirect, inhibitory pathway. This inhibitory effect of dopamine on the indirect pathway serves the same function as its excitatory effects in the direct pathway in that it reduces basal ganglia output, leading to the disinhibition of motor neurons.



Circuits of the Basal Ganglia

https://en.wikipedia.org/wiki/Hyperkinesia#/media/File:Basal ganglia circuits.svg

Hyperkinetic disorder

Hyperkinetic disorders are movement disorders characterized by **increased uncontrollable motor function**. They are caused by **reduced basal ganglia output**, which causes increased thalamocortical function which leads to the **inability to stop unwanted movement**.

Tourette syndrome/obsessive-compulsive disorder

Tourette syndrome is a disorder that is characterized by behavioral and motor tics, OCD and attention deficit hyperactivity disorder (ADHD). For this reason, it is commonly believed that pathologies involving limbic, **associative and motor circuits of the basal ganglia** are likely. Since the realization that syndromes such as Tourette syndrome and OCD are caused by **dysfunction of the non-motor loops of basal ganglia circuits**, new treatments for these disorders, based on treatments originally designed to treat movement disorders are being developed.

PANDAS

PANDAS is a controversial hypothesis that there exists a subset of children with rapid onset of obsessive–compulsive disorder (OCD) or tic disorders and that these symptoms are caused by group A β -hemolytic streptococcal (GABHS) infections. The proposed link between infection and these disorders is that an initial autoimmune reaction to a GABHS infection produces **antibodies that interfere with basal ganglia function**, causing symptom exacerbations. It has been proposed that this autoimmune response can result in a broad range of neuropsychiatric symptoms.

DRD1 Gene - Dopamine Receptor D1

The D1 subtype is the most abundant dopamine receptor in the central nervous system. This G-protein coupled receptor **stimulates adenylyl cyclase and activates cyclic AMP-dependent protein kinases**. D1 receptors regulate neuronal growth and development, mediate some behavioral responses, and **modulate dopamine receptor D2-mediated events**.

Therapeutics for DRD1 Gene

Ergothioneine (Bolete, Oyster, and Shiitake mushrooms), Mucuna pruriens (Dopamine), Serotonin (Griffonia simplicifolia), Spermidine, Vinpocetine, Yohimbine, Quercetin, Genistein, ATP (D-Ribose), GABA, Phosphatidylcholine (PC), Nitric Oxide (Arginine, Citrulline), Butyric acid [R]