Habenular connectivity as a possible biomarker of substance use, depressive, and anxiety disorders

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\textbf{Background:} The habenula is a small and understudied brain region that activates upon negative events. It has been implicated in several psychiatric illnesses such as major depressive disorder (MDD), anxiety disorders (ANX), and substance use disorders (SUD). However, data on human habenular function and connectivity is scant.

\textbf{Methods:} We used resting state functional MRI (rsfMRI) and diffusion tensor imaging (DTI) to study habenular connectivity in a large sample of psychiatric patients with diverse diagnoses (MDD, ANX, SUD, personality disorders, bipolar disorder, with many patients showing co-morbid illnesses).

\textbf{Results:} We found that: a) Patients who abuse opioids showed increased habenula/striatum connectivity, b) Mood disorder patients (MDD and bipolar) showed an asymmetric decrease in habenula-associated white matter fractional anisotropy, c) Post-traumatic stress disorder patients showed decreased habenula/striatum connectivity, and d) Suicidal patients showed increased habenula/striatal connectivity.

\textbf{Conclusions:} The habenula is connected to the dopaminergic, serotonergic, noradrenergic and cholinergic systems through connections to the ventral tegmental area, raphe, locus coeruleus, and interpeduncular nucleus, respectively. Thus, it is not surprising that habenular connectivity is altered in several psychiatric illnesses. We showed that depression, anxiety, and substance abuse may impact habenular connectivity (or vice-versa) in specific ways. More research is necessary to understand the habenular role in those illnesses, and whether treatment can be impacted by habenular function modulation.