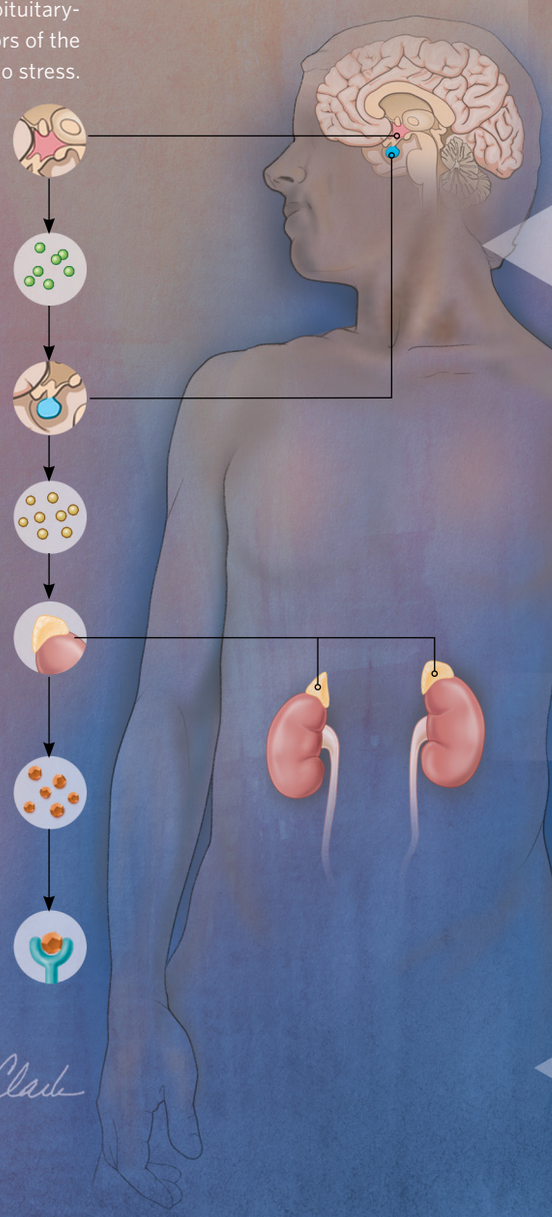
NEUROBIOLOGICAL PATHWAYS LINKED TO SUICIDE RISK

Scientists have identified several key neurobiological pathways with ties to suicidal behaviors. Research in the field addresses only a fraction of the complexity of this serious public health problem, and the literature on the topic is complicated by variation in study design, but the clues point to several interacting moderators of suicide risk. Three of the systems best-studied in relation to suicide are depicted below.

NOTE: The findings shown in this graphic come from studies with very different approaches to investigating suicide. Some studies control for psychiatric disorders, others don't; different studies focus on different brain areas; and many of the findings are preliminary.

STRESS RESPONSES

Many studies have linked suicidal behaviors to dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis and other mediators of the body's responses to stress.



CRH
Corticotropin-releasing hormone (CRH) has been found in higher concentrations in the brains of people who die by suicide.

ADRENAL GLANDS
People who die by suicide, and particularly those who die by violent means, may have enlarged adrenal glands.

CORTISOL
Basal cortisol levels have been found to be both higher and lower than normal in people who have attempted suicide. The reactivity of cortisol to stress may also be dysfunctional in people with suicidal behaviors.

NR3C1
NR3C1, also known as the glucocorticoid receptor, may be in lower abundance in people who die by suicide, particularly those with a history of childhood abuse.

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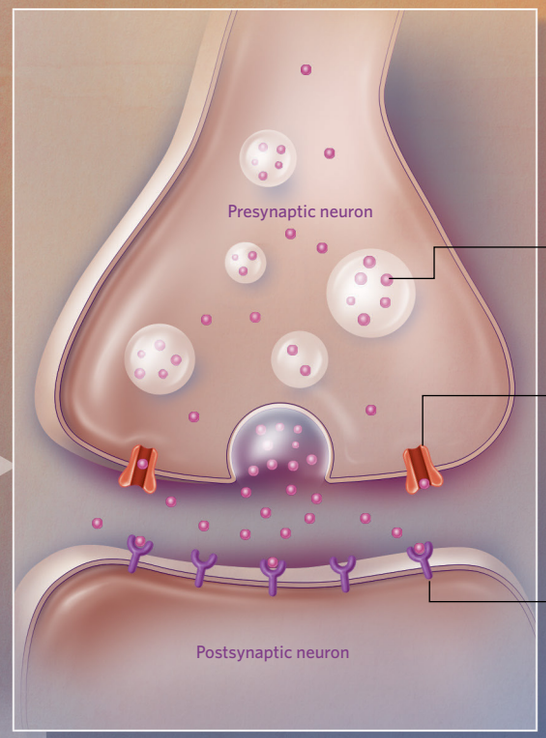
Cortisol levels appear to be correlated with levels of certain serotonin receptors, and increases in CRH may boost serotonergic activity in some brain areas.

POSSIBLE CONNECTIONS

Serotonergic neurons influence the release of HPA components such as CRH, and drugs that target serotonin receptors have been shown to affect HPA-axis function.



NEURAL TRANSMISSION

Neural communication via serotonin and other neurotransmitters such as glutamate often shows signs of dysregulation in people who die by suicide.

SEROTONIN
Disruption of serotonin signaling has repeatedly been found in the brains of people who die by suicide.

SERT
Levels of the serotonin transporter SERT, which shuttles serotonin back into the presynaptic neuron, may be lower in people who die by suicide.

5-HT$_{1A}$ AND 5-HT$_{2A}$
Levels of the serotonin receptors 5-HT$_{1A}$ and 5-HT$_{2A}$ may be higher in people who attempt or die by suicide.

Inflammation may dysregulate the serotonin system via several pathways.

POSSIBLE CONNECTIONS

Serotonin may be involved in directing immune cells to sites of inflammation.

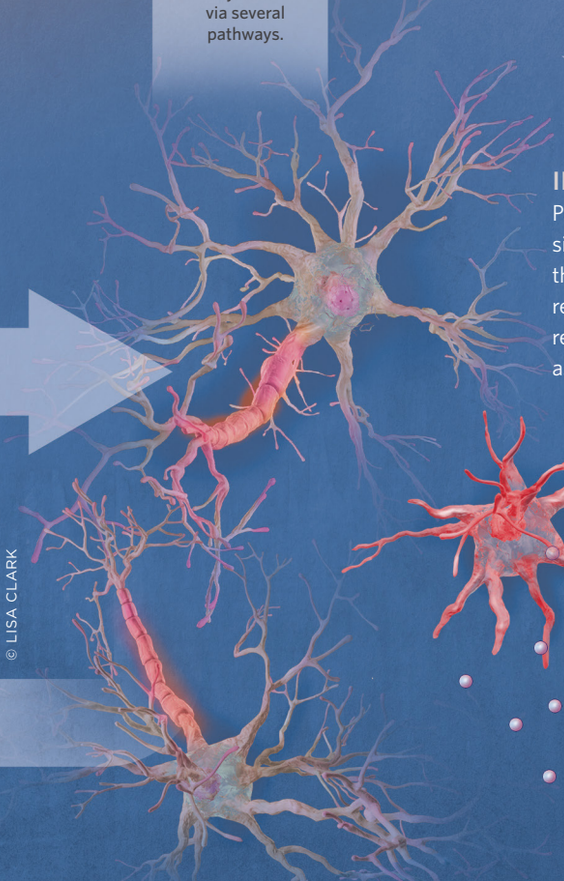
INFLAMMATION

People who die by suicide show signs of increased inflammation in the brain while epidemiological data reveal that some inflammation-related health conditions are associated with higher suicide risk.

Cortisol released as part of a stress response can help suppress inflammation.

POSSIBLE CONNECTIONS

The release of certain cytokines can stimulate HPA axis activity.



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MICROGLIA
The brains of people who die by suicide show higher levels of microglia activation.

CYTOKINES
Blood levels of inflammatory cytokines, particularly some types of interleukins, have been found at higher levels in people who attempt suicide.