Selective Serotonin Reuptake Inhibitors (SSRIs): Mechanism for Treatment of Depression and Relationship with Suicide Risk

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INTRODUCTION

In 2018, suicide was found to be the second leading cause of death for people aged 10 - 34 in the United States.

The monoamine hypothesis is the current leading hypothesis to explain depression on a biochemical basis. Accordingly, SSRIs are the most commonly prescribed antidepressant.

At least 90% of suicides are found to be comorbid with mental illness, most commonly depression.

SSRIs have been shown to be an effective treatment for moderate/severe depression. However in 2004 they were given a "black box" warning indicating the potential relationship between the drug and increased risk of suicidal behavior or ideation.

This thesis aims to investigate the costs and benefits of prescribing SSRIs to treat depression. I will be elucidating the mechanism of SSRIs and their highly contested relationship with suicide risk.

DEPRESSION & SUICIDE

The comorbidity of depression and suicidal ideation is generally accepted to be ubiquitous. However, many suicidal patients also suffer from other psychopathologies that complicate the relationship between the two. Recent research investigates the neurological underpinnings of both suicidal ideation and major depressive disorder (MDD) and has possibly developed a way to diagnose these disorders through brain scans. These diagnoses could lead to more accurate prescriptions of medications and a deeper understanding of exactly how SSRIs elicit their antidepressant symptoms, and possibly, an increased risk in suicidal behavior. The above image depicts the differences in fMRI activation between suicidal and non-suicidal patients. A machine-learning algorithm was successfully able to differentiate between these groups of patients; exciting implications for the future.

SSRI MECHANISM

The Monoamine Hypothesis of Depression
- Proposes depression is caused by a decrease of serotonergic and noradrenergic transmission between neurons
- Hence, this theory proposes SSRIs treat depression by increasing the concentration of these neurotransmitters in the synapses.

The BDNF Hypothesis of Depression
- Proposes that depression is related to reduced Brain Derived Neurotrophic Factor (BDNF) levels in the hippocampus
- SSRIs promote BDNF activity along with several other forms of neuroplasticity
- Suicidal people have been shown to have severe decline in neuroplasticity

SUICIDE AND SSRIS

The relationship between suicidality and SSRIs has been highly contested since they were given the "black box" warning in 2004. Research on the topic is difficult to conduct considering the many variables that contribute to suicide.

Ecological, observational, and randomized control studies have been conducted investigating the relationship between SSRIs and suicidality, but have several methodological limitations.

Evidence suggests that clinicians should not be deterred from prescribing SSRIs to patients who may benefit. Nonetheless, there is a need for increased monitoring, and frequent risk assessment (especially in adolescents).

CONCLUSIONS & FUTURE DIRECTIONS

Overall, the data indicates that caution should be used when prescribing SSRIs, but they are an effective and low-risk treatment for depression. However, there are still many unanswered questions about these drugs:
- What is the reason for the different risks for suicidality seen in adolescents and children compared to adults?
- What determines if a patient will experience increased suicidal risk after taking SSRIs?
- Do SSRIs lead to a decrease in suicidal ideation, attempts, or completion in patients if they do not lead to an increase?
- What is the exact mechanism through which SSRIs elicit their effects?
- How can physicians determine the safest, most effective method of treatment for their patients?
- How can physicians assess suicidal risk?

We can all help prevent suicide. For more information on resources visit suicidepreventionlifeline.org or call the National Suicide Prevention Lifeline at 1-800-273-8255.