SPRING/SUMMER 2023

UNIVERSITY OF LOUISVILLE DEPRESSION CENTER NEWSLETTER

Catch an Evening of Entertainment to Benefit the UofL Depression Center

The Jazz Birds present "It's Wonderful, It's Marvelous"

The University of Louisville Depression Center is excited to resume our in-person benefit events after a three year hiatus because of the COVID-19 pandemic. The program for our 2023 benefit event will be a sure-fire mood lifter!

The evening will begin at 6:00 p.m. with a cocktail hour, followed by dinner, and a performance by the Jazz Birds, a group of singers who will take everyone on a romp through the music of George Gershwin, Cole Porter, and many Broadway show tunes. The benefit event will be held at the University of Louisville ShelbyHurst Conference Center, Thursday, April 13, 2023 from 6:00 - 9:00 p.m.

The 2023 benefit event will provide an opportunity to support the essential work of the UofL Depression Center in providing much needed treatment services; educating students, residents, and practicing clinicians; and performing fundamental research.

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Save the Date: 17th Annual Depression and Mood Disorders Conference Nov. 16-17, 2023

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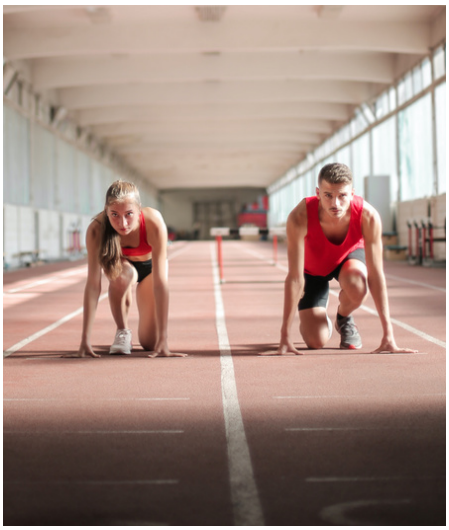
UofL Researchers Examine "The Emerging Adult Triad"

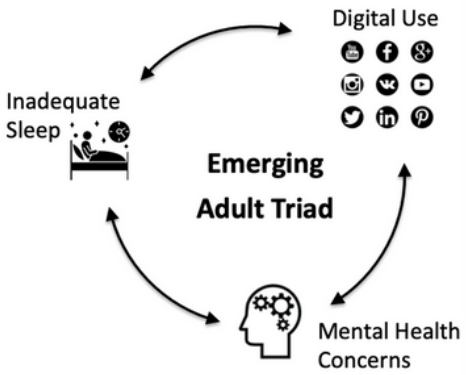
By Ernie Rimer, Ph.D. and Becky Antle, Ph.D., MSSW, LMFT

The 2022-23 Wright Endowment for Mood Disorders Research Endowment has awarded a grant to University of Louisville researchers Drs. Becky Antle and Ernie Rimer to study what they have coined, "The Emerging Adult Triad," which is the three-way interaction between technology use, sleep behavior, and mental health among emerging adults. The study seeks to understand the prevalence and consequences of the three issues affecting emerging adults through a systematic review of the literature and a study of 200 UofL students and student-athletes. This study will test the hypothesis that there are positive correlations between technology use, sleep behaviors, and mental health symptoms, and that those relationships will be multi-directional. It is also hypothesized that collegiate student-athletes have higher than normal rates and impact of technology use, sleep behaviors, and mental health symptoms compared to other college students.



Finally, the lived experiences of collegiate student-athletes will confirm that technology use, sleep behaviors, and mental health symptoms have escalated during the emerging adulthood stage and are influenced by their unique experiences and stressors associated with playing collegiate sports.

For this study, 100 UofL students and 100 UofL student-athletes will be



recruited. Participants will use validated surveys to report their digital use, sleep behaviors, and mental health. A sub-set of 20 participants who provided survey data will be recruited for an interview, which will explore their experiences of technology use (motivating factors, frequency, attempted limits, impact), sleep disruption (sleep hygiene, sleep history), and mental health (history, current symptoms, and treatment) as well as their perspectives on the role each of these play in the life of a college student and athlete.

This research has the potential to lead to the development of effective interventions that can support the well-being of both students and athletes in the collegiate setting.

Dr. Ernie Rimer is the Director of Sport Science for University of Louisville Athletics. Dr. Becky Antle is a Professor & University Scholar for the Kent School of Social Work at the University of Louisville.

Novel Study of Ouabain in Pregnant Women with Bipolar Disorder

By Rif S. El-Mallakh, M.D., Audrey Summers, M.D., Jacqueline Young, M.D.

Bipolar disorder (BD) is a severe psychiatric illness that manifests as extreme variations in mood and energy, usually labeled as mania and depression, occurring between periods of normal functioning. Although the disorder is widespread and effective treatments are available, many sufferers have ongoing symptoms that don't respond well to treatment or have unpleasant side effects from medications and other therapies. Despite over sixty years of concentrated effort, the causes of the illness remain largely unknown. However, multiple clues have emerged that are stimulating research with great potential for improving treatments.

Among the most reproducible findings in bipolar illness have been alterations of movement of important ions such as sodium, potassium, hydrogen, and calcium across the cell membrane and inside the cells. One of the chemicals that controls movement of these

ions is a newly discovered hormone called endogenous ouabain (EO). EO production by individuals with bipolar illness who are manic appears to be reduced compared to normal controls. Furthermore, persons with bipolar illness are unable to increase EO production when they are exposed to stresses that are known to do so, like intense exercise or seasonal variation.

Pregnancy is associated with elevations of EO which decline immediately after delivery. Experiments in laboratory animals suggest that pregnancy is an ouabain-resistant state associated with elevated circulating levels of EO. The frequency of bipolar disorders is either lower or not different between pregnant and nonpregnant women. But episodes of mania or depression are thought to occur in 25%–30% of women with bipolar disorder during pregnancy and are dramatically elevated in the immediate postpartum period.

EO levels have never been measured in pregnant women with bipolar illness. In a study at the University of Louisville Depression Center, we plan to collect exploratory data regarding EO production in pregnant women with and without bipolar disorder. Women with bipolar disorder are predicted to have lower EO levels throughout the pregnancy and significantly lower levels immediately after delivery. The findings of the study may help improve the understanding of the course of bipolar disorder during pregnancy and generate new theories on the role of EO in mood disorders.

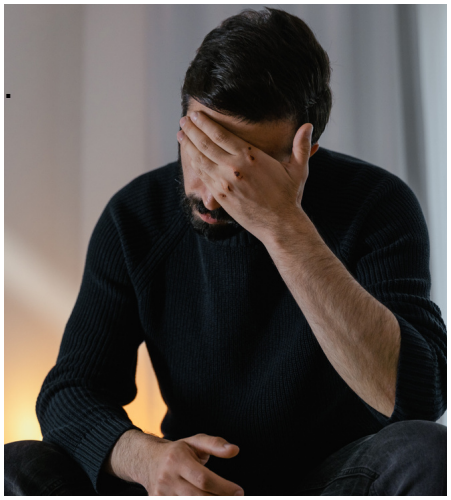
This investigation is supported by a grant from the Jesse H. Wright, M.D., Ph.D., Research Endowment.

Dr. Rif El-Mallakh is a Professor and Director of the Mood Disorders Research Program at the University of Louisville. Drs. Audrey Summers and Jacqueline Young are residents in Psychiatry at the University of Louisville.

Ketamine for the Treatment of Depression

By Ali A. Farooqui, M.D. and G. Randolph Schrodt Jr., M.D.

Since the 1950s, the biological treatment of depression has focused on modulation of brain neurotransmitters with antidepressants and other medications that act on serotonin, dopamine, and norepinephrine. These medications typically take weeks to show improvements in depressive symptoms. Despite advances in antidepressant therapies, at least a third of depressed patients fail to achieve remission. Transcranial magnetic stimulation (TMS), although effective and durable, also does not have immediate effects. Other treatments, such as electroconvulsive therapy, are limited by their availability and invasive nature. There is a need for treatments that have proven efficacy and fast effects, particularly with treatment-resistant depression.



The NMDA and glutamatergic systems were hypothesized to be involved in antidepressant effects in the 1990s, and since then the role of ketamine in the treatment of depression has been explored in multiple research studies. In addition to acting on NMDA receptors, ketamine impacts many other receptors and processes that are important for brain health.

Ketamine also has been found to be a mild hallucinogen at doses used in psychiatric treatment and to have some potential for dependence. So, caution is required in prescribing this medication.

Intravenous Ketamine and Intranasal Esketamine for Depression: Key Research Findings

Doses of intravenous ketamine that are below the usual dose for anesthesia resulted in a significant reduction of depression symptoms in a placebo controlled double blind study. 71% of patients responded to IV Ketamine and 29% met remission criteria the day following the infusion. Thirty-five percent of subjects maintained the positive response for at least one week. Meta-analyses of placebo-

controlled studies have confirmed the rapid onset of action with antidepressant effects measured as early as 40 minutes post-infusion. The rapid effects of IV ketamine are an advantage of this form of treatment, but lack of sustained benefit is a concern.

Despite the robust effects of IV ketamine, it is not currently approved by the FDA for the treatment of depression. Esketamine (Spravato) is chemically related to ketamine and has been studied in industry funded trials with an intranasal application. These trials showed that intranasal esketamine plus an oral antidepressant are superior to oral antidepressant alone. These trials resulted in FDA approval of Spravato for treatment resistant depression.

A systematic review comparing the two treatments, conducted by the National Institute of Mental Health, revealed that IV ketamine demonstrated greater response rates, remission rates, and fewer dropouts compared to intranasal esketamine.

Treating Depression with IV Ketamine

Careful screening is required by a psychiatric provider to determine if ketamine is appropriate and safe for each patient. Because ketamine can have anesthetic effects, vital signs must be monitored throughout the infusion, and a qualified provider be available on site to manage any issues such as nausea and changes in blood pressure. Nevertheless, the treatments are usually well tolerated. Most patients require infusions over a 3-to-6-week period in the acute phase of the treatment, while some patients require maintenance infusions that are tailored to each individual. The patient experience is highly variable, but it usually involves some mild degree of alteration in senses. Thus, it is important for the treatment environment to be peaceful and calm, and the treatment team to be knowledgeable in guiding patients through the therapy.

As detailed in a recent New York Times report, the promise of ketamine for the treatment of depression (and perhaps other psychiatric illnesses) has lead to a surge of popular interest, the emergence of a relatively unregulated market, including online prescribers, and an increasing incidence of abuse and dependence. Besides the inherent risks of a less-than-thorough medical and psychiatric evaluation, the administration of ketamine outside of a clinic setting may result in people taking the drug at higher doses than prescribed and a greater risk of serious medical complications, including difficulties with bladder functioning.

Conclusion

Ketamine has emerged as a valuable treatment option for depression, especially for patients with inadequate response to standard therapies. It is unique in its rapid onset of antidepressant effect. Although the durability of the antidepressant response to ketamine alone is generally short-term, there is growing evidence that sustained response and remission may be achieved in combination with maintenance ketamine infusions and other treatments.

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Doctors Farooqui and Schrodt are in private practice with Integrative Psychiatry, PLLC and are clinical faculty members of the Department of Psychiatry and Behavioral Sciences at the University of Louisville.