10. SPECIFIC AIMS

The public health burden of depression\textsuperscript{33} combined with the limited accessibility and effectiveness of current treatments\textsuperscript{34} highlight the need for implementation of strategies to prevent depression. Prior selective prevention interventions in depression have targeted medically ill populations, such as post-stroke\textsuperscript{35} and macular degeneration patients.\textsuperscript{36} The proposed research involves a selective preventive intervention aimed at reducing depression among Hepatitis C (HPC) patients receiving Interferon-\(\alpha\) (IFN-\(\alpha\)) treatment.

IFN-\(\alpha\) treatment is an efficacious treatment for HPC; however, IFN-\(\alpha\) treatment results in a significant increase in depressive symptoms.\textsuperscript{37,39} This increased depressive symptomatology is associated with significantly impaired quality of life,\textsuperscript{40,41} reduced IFN-\(\alpha\) treatment adherence\textsuperscript{42} and poorer IFN-\(\alpha\) treatment outcomes.\textsuperscript{43} The increase in depressive symptoms and the associated effects highlight the need for effective strategies aimed at the prevention of IFN-\(\alpha\)-induced depression. Research examining the prophylactic use of SSRIs to prevent IFN-\(\alpha\)-induced depression has failed to demonstrate a preventative effect\textsuperscript{44-46} and highlights the need for alternative strategies for the prevention of IFN-\(\alpha\)-induced depression.

One potential prevention strategy is exercise. Exercise is efficacious as a stand-alone or augmentative treatment for major depressive disorder (MDD)\textsuperscript{2,7,47} and epidemiological evidence suggests physical activity is protective against the future incidence of MDD.\textsuperscript{48,49} The mechanisms for development of IFN-\(\alpha\)-induced MDD further support the potential for prevention using exercise. IFN-\(\alpha\) treatment increases peripheral levels of interleukin-6 (IL-6)\textsuperscript{50,51} and decreases in sleep quality.\textsuperscript{52} These changes have been shown to mediate the increase in depressive symptoms during IFN-\(\alpha\)-treatment.\textsuperscript{53} Conversely, higher levels of physical activity and physical fitness are associated with lower levels of IL-6,\textsuperscript{5,54} while exercise interventions have been shown to reduce IL-6.\textsuperscript{55,56} Similarly, exercise improves various aspects of sleep quality in individuals with sleep complaints\textsuperscript{57,58} and in individuals with MDD.\textsuperscript{59,60} Taken as a whole, previous research supports the plausibility of exercise in the prevention of IFN-\(\alpha\)-induced MDD.

The purpose of the proposed project is to conduct a pilot study of an exercise intervention to prevent IFN-\(\alpha\)-induced MDD in HPC patients. Participants will be recruited from the UT Southwestern Clinical Center for Liver Disease and randomized to 26 weeks of either aerobic exercise (EX) or a health education (HE) group. Based on the recommendation of Leon et al.\textsuperscript{61}, the primary aims of the pilot study will be to determine the feasibility of conducting an RCT examining the efficacy of an exercise intervention to prevent depression in HPC patients receiving IFN-\(\alpha\) treatment. Secondary aims will be to assess the effects of the exercise intervention on depressive symptoms and proposed mediators (inflammatory cytokines and sleep quality).

Specific Aims

Specific Aim 1. Examine the feasibility of recruitment and randomization of eligible HPC patients into a RCT examining the efficacy of exercise in the prevention of IFN-\(\alpha\)-induced depression.

\textit{Aim 1A.} Assess the number of participants screened for participation per month.

\textit{Aim 1B.} Assess the percentage of screened eligible participants that are randomized.

Specific Aim 2. Examine the feasibility of maintaining participant engagement throughout the trial.

\textit{Aim 2A.} Assess intervention adherence – defined as percentage of weekly intervention sessions attended.

\textit{Aim 2B.} Assess participant retention – defined as percentage of assessments completed


\textit{Hypothesis:} Participants in the exercise intervention will have lower depressive symptoms compared to the HE group at the end of the 26-week study.


\textit{Hypothesis:} Participants in the EX group will have lower levels of inflammatory cytokines (IL-1beta, IL-6, IL-10 and TNF-alpha) compared to the HE group at the end of the 26-week study.

\textit{Hypothesis:} Participants in the EX group will have higher sleep quality compared to the HE group at the end of the 26-week study.

The successful completion of the proposed research and training plan will provide the knowledge and experience necessary to progress toward becoming an independent investigator examining the role of physical activity in the treatment and prevention of mental illness. Specifically, the data from the proposed study will serve as the basis for an R01 application to be submitted during the final year of the K01 award. The R01 will propose an RCT sufficiently powered to examine the efficacy of an exercise intervention in the prevention of IFN-\(\alpha\)-induced depression.