

INTRODUCTION

- Adolescent depression is a public health crisis, with rates | increased to 20.1% in 2021.
- Current treatments for depression (i.e Selective Serotonin Reuptake Inhibitors [SSRIs]) have shown limited success in achieving clinical remission and undesirable side-effects.
- Gut microbiota differences, such as decreased Bifidobacterium and imbalances in Firmicutes, ar Bacteroides, in adolescents with high stress and emotional problems suggest a connection between the gut microbior adolescent mental health.
- Several studies suggest that higher levels of the the bacter Lactobacillus and Bifidobacterium commonly found in many probiotics may help protect against adult depression.
- In our adult pilot randomized controlled trial (RCT), the prob Visbiome[®] had a large effect on the left hippocampus-prec resting state functional connectivity (HP RSFC) of the brain increase in Lactobacillus, and improved depression scores.
- No studies have examined the effects of probiotics on adolescent depression, and limited research exists on its in on the adolescent gut-brain axis.



- Aim 2: To study whether and how the composition and structure of the gut microbiome are modified by the probiot treatment.
- Aim 3: To study whether microbiota changes are associated with changes in left HP RSFC.

Probiotic Administration for Depressed Adolescents: Protocol for a Double-Blinded Randomized Controlled Trial

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ria			Plac n =
biotic	Figure 1: Simp inclusion criter under the care 8 weeks.	lified timeline of ia include (1) ag of a primary car	participant activities one ed 15-24, (2) have a clini e or mental health provid
cuneus	Sample collect	ion includes (1)	MRI scans for left HP RS
n,	information, (3) saliva samples for cortisol and cotinine Beck's Depression Inventory-II, Columbia Suicide Severi [*]		
mpact	Participants in probiotic group receive pills containing 4 <i>Bifidobacterium,</i> and <i>Streptococcus</i> bacteria. All particip to confirm treatment adherence and questionnaire com		
		S	TATISTICALA
	Figure 2: Once statistician.	processed all re	esults will be analyzed ac
			Aim 1: Mixed linear mo RSFC & 3 (test relation microbiome changes)
ents			• Aim 2: Generalized mix differences in test for a diversity, representation abundance.
otic			• Aim 3: Mixed linear mo between left HP RSFC
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ce they screen into the study. Major ical diagnosis of a depression disorder, (3) der, and (4) currently taking SSRI for at least

SFC, (2) stool samples for gut microbiota levels, and (4) questionnaires including ity Rating Scale, and more.

450 billion CFUs of Lactobacillus, pants will have zoom visits every two weeks npletion.

NALYSIS

ccording to our three aims with our in house

odels to see any increase in left HP ships between left HP RSFC and gut

xed linear models for testing differences in beta diversity, alpha on of functional genes, and relative

odels to test the relationships and the gut microbiome



We are in the middle of participant recruitment and enrollment. By the end of the study we aim to have 58 participants after accounting for a 25% dropout from the 77 total enrolled. Stool and saliva samples will be processed in one batch at the Benioff Center for Microbiome Medicine (BCMM) at UCSF to ensure batch variability is minimized. MRI imaging data will be coded and analyzed by the Yang lab group.

EXPECTED IMPACT/INNOVATION

This current R61 phase is not a fully-powered efficacy trial. Significant results meeting the Go/No-Go Criteria below will allow us to move to the R33 trial phase to (1) replicate the impact of the probiotic on the brain and microbiota and (2) to determine the optimal dose of probiotics (450 vs. 900 billion CFUs) for a future fully-powered efficacy trial (R01).

- RSFC: np2≥0.06 (p<0.05)
- diversity: ηp2≥0.06 (p<0.05)

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TIMELINE

Complete Data Analysis

• Go/No-Go Criteria 1: The probiotic group vs. placebo group must meet the following medium effect size threshold for the left HP

• Go/No-Go Criteria 2: The probiotic group vs. placebo group must meet the following medium effect size threshold for beta