Neuro-affective Response to Light in Depressed Adolescents and Young Adults

NCT Number: NCT05712772

STATISTICAL DESIGN & POWER

Design: We will recruit 80 participants with unipolar depression -- 40 adolescents (12-17yr) and 40 adults (18-30yr) -- to participate in a neuroimaging pilot study investigating age-related differences in neuro-affective brain response to therapeutically-active (blue) versus inactive (red) wavelength light.

Randomization: Randomization (counterbalancing) of the order of blue versus red light during the MRI scan will be accomplished using a stratified permuted block randomization design (block size = 4). We will stratify by age and sex. Participants will be randomized at Visit 2, prior to the neuroimaging protocol.

Main Analysis Overview: Numerical summaries and graphical displays will be used to check distributional assumptions, outliers, and missing data. **Missing data** mechanisms will be explored. Given **sex differences** in light sensitivity, brain function, and affect in depression[88,131-134], interaction terms will explore moderation effects of sex; stratified analyses will probe significant interactions. Our set of ***primary* outcomes** for main analyses are in **Table 3**. A priori baseline **covariates** include sex; depression severity; SSRI use; season; sleep midpoint; actigraphy-based light history; and blue/red light order and pupil size during MRI. We estimate there will be a maximum of 7 IVs per model, after to excluding variables that do not meet collinearity and model fit assumptions.

Aim 1: Evaluate the effect of blue vs. red light exposures on tonic and threat-related amygdala activity in adolescents versus adults with depression. Hypothesis 1: Across all participants, blue light (vs red light) will be associated with *lower* (1.1) amygdala cerebral blood flow and (1.2) threat-related amygdala activity. (1.3) During blue light only, the effects observed in 1.1 and 1.2 will be *greater* in adolescents versus adults. Hypothesis 1 Testing: **H1.1, 1.2**: A repeated-measures mixed-effects model will test effects of *light condition* (blue light vs red light vs dark) on amygdala cerebral blood flow (1.1) and amygdala reactivity to punishment (threat) (1.2). Participant will be included as a random effect and light condition as a fixed within-subjects effect. We expect to observe lower tonic and threat-related amygdala activity in blue light relative to red light. **H1.3**. A repeated-measures mixed-effects model will test interactive effects of *age group* (adolescent vs adult) and *light condition* (blue light vs red light) on Aim 1 neural outcomes. Participant will be included as a random effect, light condition as a fixed within-subjects effect, and age group as a fixed between-subjects effect. We expect to observe an age group x light interaction, such that effects of blue light (but not red light) will be stronger in adolescents versus young adults (e.g., lower amygdala cerebral blood flow and threat-related amygdala activity).

AIM 2: Evaluate the effect of blue vs. red light exposures on tonic and reward-related striatal activity in adolescents versus adults with depression. Hypothesis 2: Across all participants, blue light (vs red light) will be associated with *higher* (2.1) striatal cerebral blood flow and (2.2) reward-related striatal activity. (2.3) During blue light (but not red light), the effects observed in 2.1 and 2.2 will be *greater* in adolescents versus adults.
Hypothesis 2 Testing: **H2.1, 2.2**: A repeated-measures mixed-effects model will test effects of *light condition* (blue light vs red light vs dark) on ventral striatum cerebral blood flow (1.1) and striatal reactivity to wins (reward) (1.2). Participant will be included as a random effect and light condition as a fixed within-subjects effect. We expect to observe lower tonic and reward-related striatal activity in blue light relative to red light. **H2.3**. A repeated-measures mixed-effects model will test interactive effects of *age group* (adolescent vs adult) and *light condition* (blue light vs red light) on Aim 2 neural outcomes. Participant will be included as a random effect, light condition as a fixed within-subjects effect, and age group as a fixed between-subjects effect. We expect to observe an age group x light interaction, such that of blue light (but not red light) will be stronger in adolescents versus young adults (e.g., greater striatal cerebral blood flow and reward-related striatal activity).

Power and Sample Size: This study is designed to provide pilot data to seed a well-powered grant. Effects of light on cerebral blood flow[84] (**H1.1, 2.1)** and threat and reward-related brain activity[80,81] (**H1.2, 2.2**), and age differences[136,137]**(H1.3, 2.3)** in young vs older adults show medium-large effects (Cohen's f=0.17-0.40). Detectible effect size was estimated assuming N=72 (~10% MRI data loss) participants in a repeated-measures ANOVA model including a within-person effect and within-between interaction (2-tailed, α=0.05 tests)[138]. After multiple comparison adjustment (α=0.05/4 tests per aim), we are powered to detect medium effects (f=0.21-0.25).