Examining Changes in Microbiota Over the Course of PTSD Treatment

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Data analysis

We utilized Bayesian longitudinal mixed models to examine change over the course of 1-week massed virtual CPT. The use of mixed-effects models is particularly appropriate for longitudinal analysis due to their ability to account for within-subject clustering and correlations in individual change across measurements. The Bayesian approach also allows for the incorporation of prior knowledge and results as well as for the intuitive and substantive assessment of uncertainty. Additionally, as has been noted with regularity elsewhere, Bayesian methods may be uniquely suited to estimation with small sample sizes (Depaoli & van de Schoot, **2017**; Dunson, **2001**), such as the present study, although this benefit may be contingent upon careful selection of informative priors (McNeish, **2016**). Here, weakly informative priors for time parameters were based on our prior treatment outcomes in both 3-week and 2-week CPT-based ITPs (Held et al., in press), though sensitivity analyses were conducted to examine the robustness of outcomes relative to various prior selections. Models initially examined the effects of time, as well as age and sex, which were given very vague priors (e.g., $N \sim [0, 5]$) for age) due to past massed-treatment results indicating a lack of association with ITP outcomes (Held et al., in press). Small cell sizes obviated the examination of other covariates, such as race and ethnicity, although these variables have not been shown to predict treatment outcomes in prior studies. Simulation-based power analyses based on prior effect sizes for PTSD and depression reduction (Held et al., in press) suggested that over 90% power for detecting changes in these outcomes should be attainable with over 15 participants.

To ensure the viability of priors, prior predictive checks were conducted across 1,000 simulated datasets to ensure the alignment of priors with appropriate values. Hamiltonian Markov chain Monte Carlo (MCMC) was utilized for sampling from the posterior via the No-U-Turn Sampler algorithm (NUTS). We utilized five chains, each with 1,000 burn-in iterations and 5,000 inference iterations. Posterior distributions were summarized via 94% highest density intervals (HDIs), which report the most credible values from the posterior distribution, as well as medians and means. Model checking involved the examination of trace, autocorrelation, and divergence plots assessing the posterior, as well as visual posterior predictive checks of mean, median, variance, and skewness parameters.

We also explored maintenance of gains by comparing 1-week posttreatment symptom severity (i.e., CAPS-5, PCL-5, and PHQ-9) to both 1- and 3-month follow-up time points. We utilized noninferiority tests to assess the probability that 1- and 3-month follow-up severity scores were not inferior to those recorded at 1-week

posttreatment. A recently developed Bayes actor approach (van Ravenzwaaij et al., **2019**) was utilized here, which allowed for intuitive interpretations of noninferiority by assessing the probability that the follow-up severity measurement can be considered noninferior to the posttreatment measurement relative to the probability that the initial postprogram measurement is superior. This approach was modified to accommodate the repeated-measures structure of the comparisons of interest. We chose conservative noninferiority intervals of 5 points for the PCL-5 and CAPS-5 and 3 points for the PHQ-9.

Bayesian linear mixed models were also explored, including follow-up timepoints. As expected, the linear, PCL-5: $B = -0.37$, HDI [−0.72, −0.01]; PHQ: $B = -0.18$, HDI [−0.34, −0.02], and quadratic slope components, PCL-5: $B = 0.004$, HDI [0.0004, 0.007]; PHQ-9: $B = 0.001$, HDI [0.003, 0.002], were clear given the deceleration of outcome reduction over follow-up time points. These results are not reported here in detail due to consistency with reported results as well as our interest in modeling the degree of massed CPT change and post hoc illustrations of noninferiority of follow-up points compared to outcomes immediately following the treatment. Bayesian linear mixed models and model checks were explored using PYMC3 in Python (Version 3.9.), and noninferiority tests and figures were conducted using R (Version 4.1.1.)