Brain Serotonin 1A Receptor Binding as a Predictor of Treatment Outcome in Major Depressive Disorder

Supplemental Information

Bootstrap Errors

To increase precision of estimation and power for comparisons, we have developed a method for weighting observations according to the standard errors estimated by a bootstrapping algorithm (1). The bootstrap algorithm takes into consideration errors associated with fitting the metabolite curve, input function and time activity curve (TAC) for each region of interest. Incorporating standard errors significantly impacts PET-based contrasts and inferences. The raphe uptake of a serotonin 1A receptor radiotracer is very susceptible to noise. We re-modeled the data presented in our previous publication regarding baseline [^{11}C]WAY-100635 BP_F and treatment outcome with naturalistic treatment for major depressive disorder (2), this time using estimates of the bootstrap errors. As can be seen in Figure S1, the raphe time activity curve for this subject is well described by a two compartment kinetic model, and the resulting bootstrap-based standard error is low, 3.3 ml/cc^3. In contrast, the TAC for the subject in Figure S2 is quite noisy, and the standard error is naturally higher, 162 ml/cc^3. Figure S3 compares the raphe 5-HT$_{1A}$ binding estimates of remitters and non-remitters. If the BP_F estimates are not weighted according to the bootstrap errors, the non-remitters have a higher mean than the remitters (black lines), but when these weights are incorporated, the direction of the estimated difference is reversed (yellow lines). The effect of one of the poorest single-subject fits is reduced by weighting the means based on errors. This improved quantification reverses our published findings in raphe nuclei, but not in any other cortical or subcortical region of interest examined, emphasizing the susceptibility of raphe nuclei quantification to sources of error.

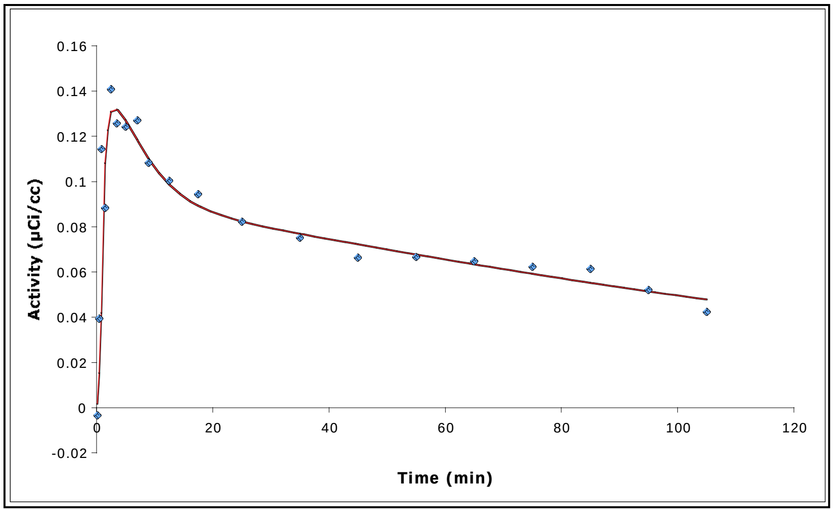

Figure S1. Good fit: binding = 21 ± 3.3 ml/cc^3

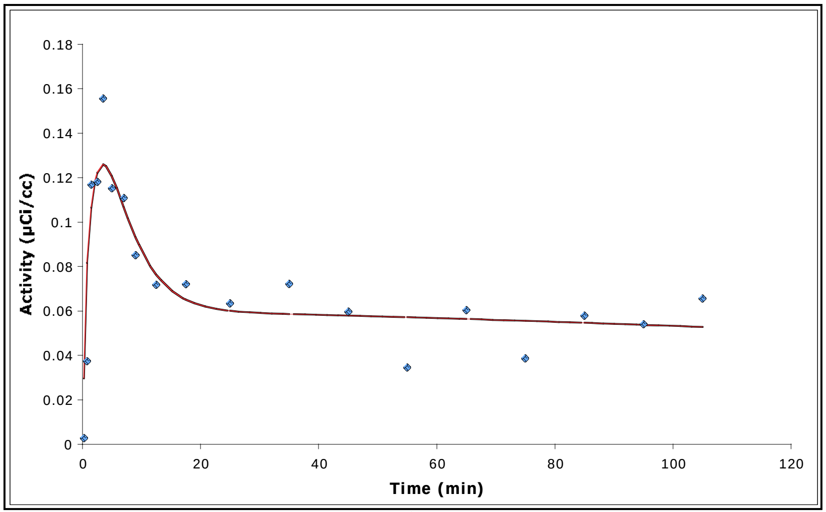

Figure S2. Poor fit: binding = 151 ± 161.7 ml/cc^3

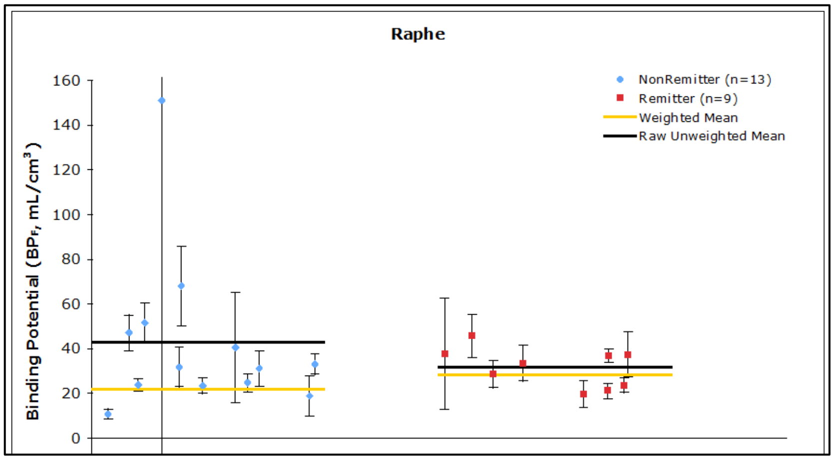

Figure S3. Bootstrap errors significantly affect contrasts and inferences. The effect of one of the poorest single-subject fits is reduced by weighting the means based on errors

Supplemental References

1. Ogden RT, Tarpey T (2006): Estimation in regression models with externally estimated parameters. *Biostatistics* 7(1): 115-129.

2. Parsey RV, Olvet DM, Oquendo MA, Huang YY, Ogden RT, Mann JJ (2006): Higher 5-HT1A receptor binding potential during a major depressive episode predicts poor treatment response: preliminary data from a naturalistic study. *Neuropsychopharmacology* 31(8): 1745-1749.