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Response to “On the Correction of effects of flip angle in 1H MRS signal acquired using STEAM sequence” by Zhengchao Dong, PhD

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Dear Editor

In a Correspondence by Dr. Zhengchao Dong, he indicated that in our recent paper “Chronic Cigarette Smoking in Healthy Middle-Aged Individuals Is Associated with Decreased Regional Brain N-acetylaspartate and Glutamate Levels” published in *Biological Psychiatry* 76 (6), the formula we used for a correction factor employed for the calculation of absolute metabolite concentrations derived from STEAM (stimulated echo acquisition mode) magnetic resonance spectra is incorrect. Dr. Dong’s mathematical treatment of the topic (calibration for different flip angles used for the metabolite and water spectra) appears to be correct; however, his assumptions and conclusions about the experimental conditions and accuracy of the spectroscopy data used in our report are not correct.

We agree with Dr. Dong that when the flip angles for metabolite spectra and water spectra “are severely different from each other”, proper corrections are required. Accordingly, we applied the appropriate corrections in our calculation of metabolite concentrations, as indicated in the supplement accompanying the original paper. In the derivation of his equation 5, Dr. Dong further states that “both metabolite and water signals need to be corrected individually for flip angle deviations before metabolite signal is calibrated by water signal”. We agree that this is correct, if the flip angles for both the water and metabolite spectra deviate from 90 degrees. However, for our study, the experimental conditions were such that the metabolite spectra were always obtained with a 90 degree pulse, while in about 10% of cases, the corresponding water spectrum was obtained erroneously with a slightly different flip angle. Specifically, 4 of 120 spectra were corrected by <2%, 8 of 120 spectra had peak area corrections between 2.5 and 10%, and 1 of 120

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spectra were corrected by 15%. Therefore, the correction factor described in our supplement was different from 1 only in the above cases, and, more importantly, it was properly applied only to the water the signal. We apologize if it was not clear in the supplementary materials that only the water spectrum flip angle deviated from 90 degrees in a few cases.

We further agree with Dr. Dong that “when the metabolite signal and water signal are acquired from different locations ... also the effects of transmitter gains should be corrected for”. Accordingly, in our STEAM experiments, the spectrometer frequency was always set half-way between the myo-inositol and NAA frequencies for acquisition of the metabolite spectra, and on the water resonance for acquisition of the corresponding water spectra.

Respectfully,

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