**Heterogeneity of phosphorus-containing compounds across gray and white matter in the human brain**

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Target Audience: This work is of interest to researchers studying brain bioenergetics under normal or pathological conditions.

Purpose: $^{1}$H and $^{31}$P MRS have demonstrated the heterogeneity of glucose, ATP, and PCr between gray (GM) and white matter (WM) in the human brain.[1,2] However, no studies have investigated this characteristic for other bioenergetically relevant parameters that can be measured with $^{31}$P MRS. The purpose of this study is to investigate the distribution in the brain of these bioenergetic species by performing tissue regression analysis on $^{31}$P MRSI data to estimate the concentrations of all phosphorus-containing metabolites as well as the intracellular pH ($pH_i$) in pure GM and WM.

Methods: Thirty-six healthy volunteers (17M/19F age 20 yrs ± 8) were scanned using a $^{31}$P-$^{1}$H dual tuned TEM head coil on a 4T whole-body MR system. Spectroscopic and anatomic data were acquired using a one-pulse 3D MRSI sequence and a 3D MDEFT sequence, respectively. Spectra were processed using jMRUI's AMARES algorithm; the resulting resonance areas were corrected for $T_1$ relaxation and converted to concentrations (mM) via a phantom replacement method.[3] Chemical shift values were used for the indirect determination of $pH_i$. MDEFT images were analyzed by SPM5 to determine percent GM, WM, and cerebrospinal fluid (CSF) for volumes corresponding to the spatial location of each of the extracted voxels. Linear regression was performed on the results from each subject to determine the theoretical values of the parameters in homogeneous GM and WM.

Results: Two-tailed, unpaired, heteroscedastic Student's t-tests showed [PCr] ($p = 3.5 \times 10^{-12}$) , [PME] ($p = 2.9 \times 10^{-5}$), and $pH_i$ ($p = 1.7 \times 10^{-17}$) to be significantly higher in GM compared to WM while [ATP] ($p = 3.4 \times 10^{-9}$), [PDE] ($p = 2.1 \times 10^{-11}$), and [Pi] ($p = 1.1 \times 10^{-6}$) were significantly lower in GM compared to WM.

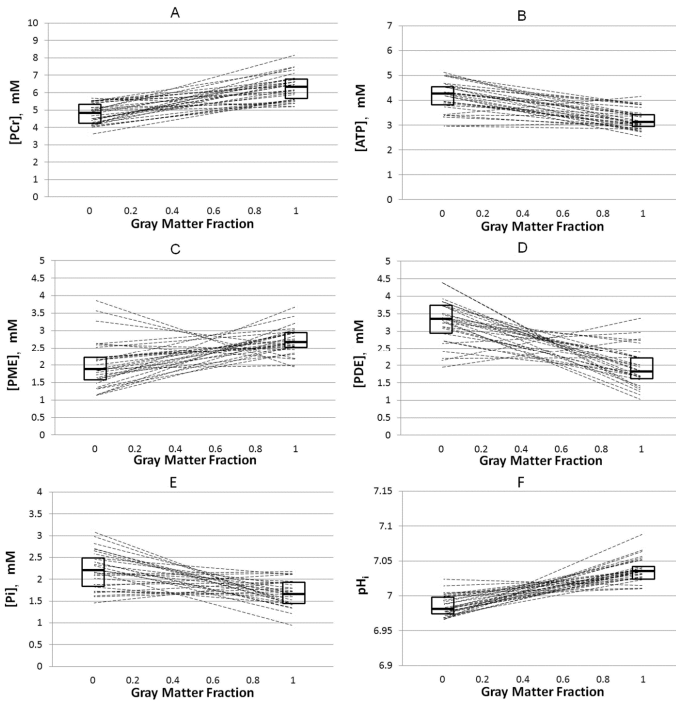


Figure 1: Correlations of PCr (A), ATP (B), PME (C), PDE (D), Pi (E), and $pH_i$ (F) with GM fraction. 1st, 2nd, and 3rd quartile estimated metabolite concentrations are shown for homogeneous WM and GM from the entire subject group.

Discussion: We demonstrated that [PME], [PDE], [$P_i$], and $pH_i$ were significantly different between GM and WM. These correlations with GM fraction indicate substantial differences in bioenergetics and phospholipid metabolism between the tissue types. In addition, our observed differences in [PCr] and [ATP] between GM and WM were consistent with previous studies.[1,2] We hypothesize these differences are partially the result of a pH-driven change in the forward flux of the creatine kinase equilibrium.

Conclusion: These findings may partially elucidate various results from previous studies of certain diseases such as altered PME and PDE levels observed in schizophrenia and Alzheimer's disease.[4,5] Additionally, our results suggest that tissue types in a given voxel should be taken into account in study design.

References

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