

CoQ10 effect on cerebral metabolites and mood conditions in geriatric bipolar depression

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TARGET AUDIENCE – People who are interested in non-conventional treatment of psychiatric diseases.

PURPOSE – To evaluate CoQ10 effect on cerebral metabolites and mood conditions in geriatric bipolar depression.

METHODS - Ten older adults (ages ≥ 55) with bipolar disorder, current episode depressed, using the Structured Clinical Interview for DSM-IV and eight older healthy controls were recruited. The MADRS (Montgomery Asberg Depression Rating Scale), YMRS (Young Mania Rating Scale) Clinical Global Impression Scale, Geriatric Depression Scale were collected as measures of mood symptom severity. A neuropsychological battery was also administered. All bipolar depression subjects were treated with open label CoEnzyme Q10 (CoQ10) beginning at 400 mg/day and titrated up by 400 mg/day every two weeks to a maximum of 1200 mg/day. Each subject also underwent two ³¹P MRS scans at 4 T, at baseline and after eight weeks of treatment with CoQ10. The ³¹P MRS scan uses a magnetization transfer scheme to measure the rate constant (k_{for}) of the PCr to γ -ATP reaction. Steady state levels of metabolites were also collected. All MRS scans were performed using a 4T MR scanner with a ¹H/³¹P double-tuned head coil. The MT acquisition utilizes a series of long RF pulses to suppress the γ -ATP signal. Because dynamic chemical exchange occurs between γ -ATP and PCr, a portion of the saturated γ -ATP is transferred into the PCr pool, which subsequently decreases the PCr signal. An identical series of RF pulses is applied at a control frequency in order to calibrate the perturbation exerted by the γ -ATP saturating RF pulses on the PCr signal (Fig 1). By analyzing data from 4 different saturation durations at the γ -ATP and control frequencies, the k_{for} of the reaction and the intrinsic relaxation time ($T_{1\text{int}}$) of PCr can be calculated from non-linear least squared fits as detailed previously.^{1,2} Baseline and 8-week changes in k_{for} were compared between BPD and controls using the Wilcoxon rank sum test. All statistical tests were 2 sided and performed at the $\alpha = .05$ significance level.

RESULTS – The k_{for} was mildly lower for the individuals with bipolar depression (0.239 ± 0.025) than healthy controls (0.251 ± 0.013) at baseline. The k_{for} for the control group remained unchanged (0.264 ± 0.031) while the bipolar depression group had a mild elevation of k_{for} after the 8-week treatment (0.301 ± 0.098). 80% of the patients who showed a clinical improvement had an increase in k_{for} (p NS). pH and Pi/PCr ratio remained unchanged for both the patients and the controls. However, the group with bipolar disorder had a 40% increase in PME/PDE ratio ($p = 0.06$) after the treatment. Depression severity decreased with CoQ10 treatment in the patients with significant reductions in the MADRS at weeks 2 ($t_9 = -2.40$, $p = 0.04$) and 4 ($t_9 = -3.80$, $p = 0.004$) (Fig 2).

DISCUSSIONS – Recent studies suggest altered energy metabolism and mitochondrial pathology in BPD³⁻⁵ and metabolic abnormalities have been found in the frontal and temporal lobes of BPD.⁶⁻⁸ Majority of ATP is generated from mitochondrial energy-linked respiration. CoQ10 serves as an electron donor and acceptor in the electron transfer chain. CoQ10 has been shown to restore CK activity to baseline levels following metabolic challenges,^{9,10} leading to an interest in the use of CoQ10 for treating a variety of disorders, implicating mitochondrial impairment, including congestive heart failure, diabetes, and degenerative neurological conditions.¹¹⁻¹³ Among the metabolites affected by the oral CoQ10 treatment, increase of PME/PDE ratio suggests that CoQ10 improved metabolic process of cell membrane in the patients. Results of pH and Pi/PCr ratio measures suggest that the energy usage and production as well as tissue workload¹⁴ remained unchanged during the study. Creatine kinase (CK) is the enzyme responsible for the reaction from PCr and ADP to ATP while k_{for} is the rate constant of the reaction. Increases in PME/PDE ratios and k_{for} values and the decrease in MADRS scores suggest that oral CoQ10 treatment may improve the metabolic states of bipolar patients. The small sample size and heterogenous co-morbidities may have dampened the effect of the treatment. Nonetheless, the effect of CoQ10 treatment may need further investigation due to the multi-factorial nature of the coupling between the oxidative cycles of the respiratory chain and adenosine disphosphate phosphorylation.

CONCLUSIONS – This study demonstrated a reduction of depression symptom severity with high dose CoQ10 treatment and an up trend of k_{for} and PME/PDE ratio in the patients who responded to the treatment.

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