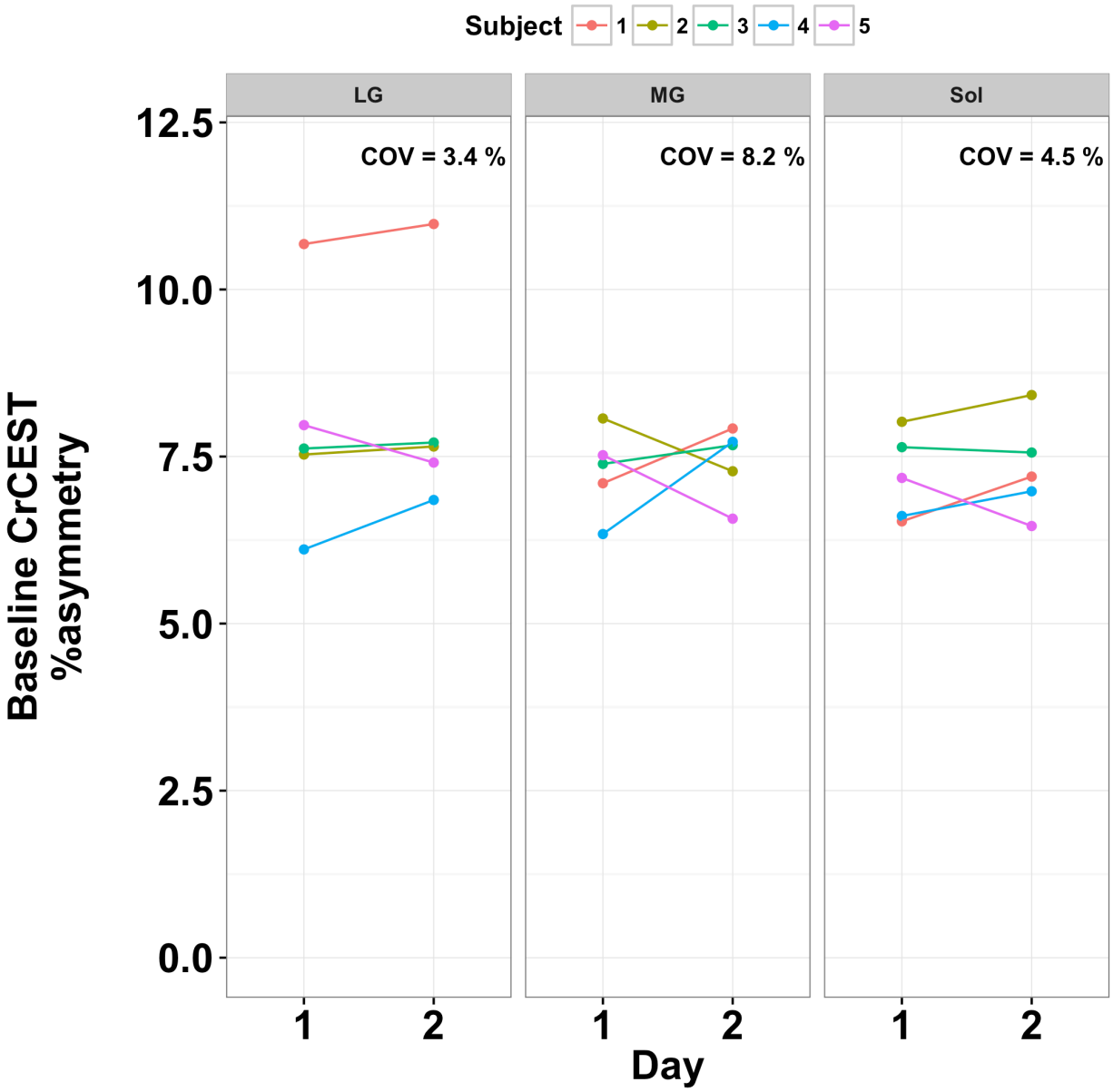
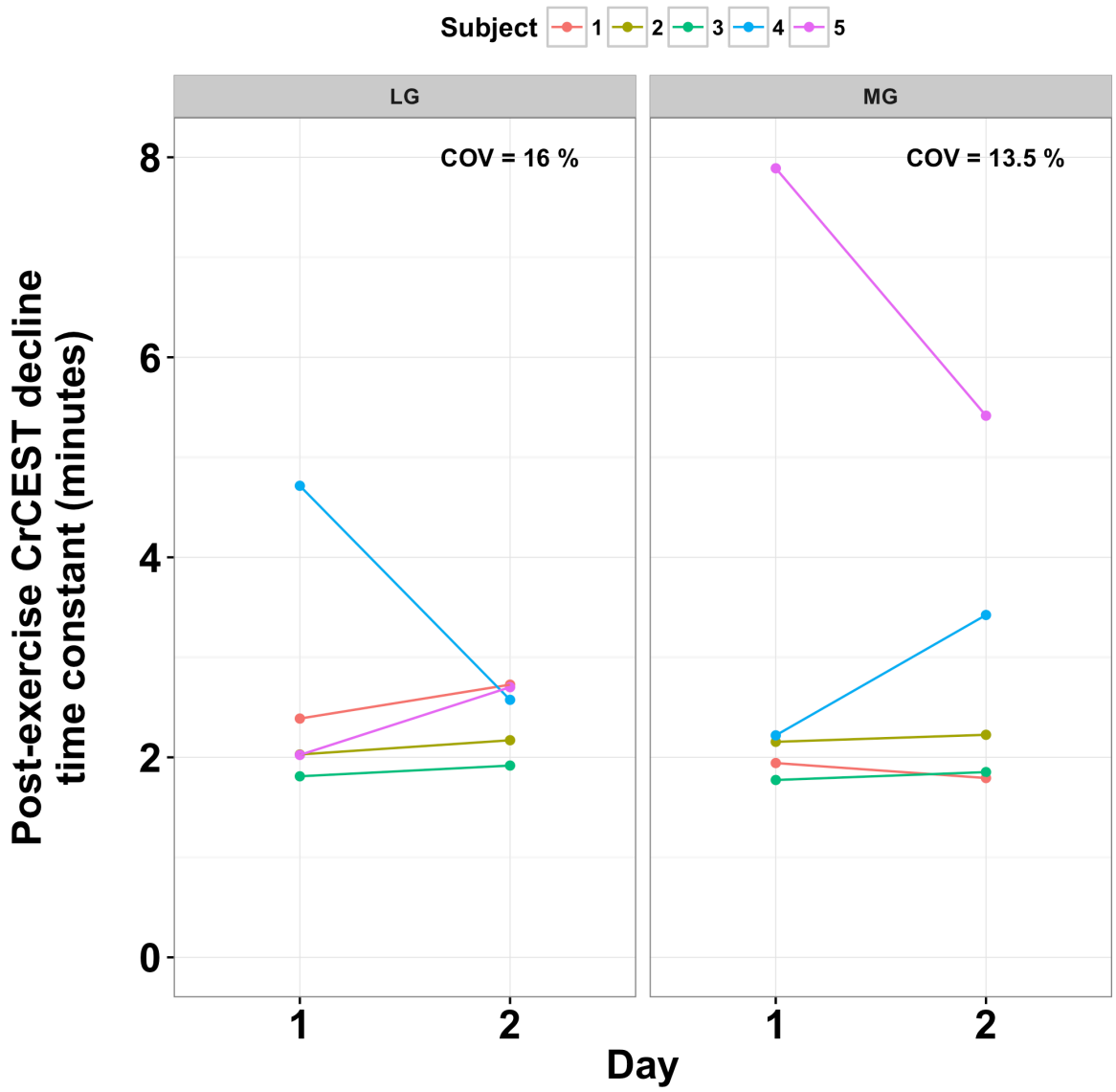
SUPPLMENTARY



Supplementary Figure 1. Reproducibility of baseline CrCEST % asymmetry, an index of free creatine concentration. For each of five subjects (shown in different colors), CrCEST measurements were obtained on a 3T MRI scanner on each of two different days, separated by less than one week. The degree of agreement between individual measurements and summary within-participant coefficient of variation (COV) estimates for these measurements are shown. LG = lateral gastrocenmius; MG = medial gastrocnemius; Sol = soleus.

SUPPLEMENTARY FIGURES (continued)



Supplementary Figure 2. Reproducibility of post-exercise CrCEST decline exponential time constant (τCr), an index of free creatine concentration. For each of five subjects (shown in different colors), CrCEST measurements were obtained on a 3T MRI scanner on each of two different days, separated by less than one week. The degree of agreement between individual measurements and summary within-participant coefficient of variation (COV) estimates for these measurements are shown. LG = lateral gastrocenmius; MG = medial gastrocnemius; Sol = soleus.

Supplemental Table 1. Mixed effects regression models including the association of intentional exercise with (Model 1) log-transformed post-exercise CrCEST decline time constant (τCr, in minutes), an index of skeletal muscle OXPHOS capacity, where prolonged τCr suggests lower OXPHOS capacity and (Model 2) log-transformed resting CrCEST (% asymmetry), an index of free creatine concentration, where higher CrCEST may reflect greater bioenergetic capacity at rest.

	Model 1 standardized β (p-value)	**Model 2 standardized β (p-value)**
Outcome	**τCr**	**CrCEST**
Mitochondrial disease status	**0.32 (0.027)**	-0.08 (NS)
Muscle group		
Lateral gastrocnemius (reference)	-	-
Medial gastrocnemius	0.05 (NS)	0.06 (NS)
Soleus	0.14 (NS)	**0.35 (0.0027)**
Intentional Exercise (MET-hours/wk)	-0.004 (NS)	0.23 (0.064)

Each of the models include the subject from which the measurement was obtained (as a random effect) and the clinical covariates shown (as fixed effects). For Model 1, n=26 subjects contributing a total of 74 muscle-specific post-exercise CrCEST recovery estimates were included (i.e., if subjects exercised more than one muscle group, then more than one post-exercise recovery time constant could be calculated); the mixed effects modeling strategy accounts statistically for the effects of obtaining multiple measurements per subject. For Model 2, n=27 subjects contributing a total of 84 muscle-specific CrCEST measurements were included; the mixed effects modeling strategy accounts statistically for the effects of obtaining multiple measurements per subject. Coefficients are represented as standardized β values, with their corresponding p values; statistically significant results are shown in bold text. NS = not significant; AIC = Aikaike Information Criterion; BIC = Bayesian Information Criterion.