TARGET AUDIENCE: Researchers interested in using caffeine as a physiological challenge or investigating neural physiological effects of caffeine.

PURPOSE: Caffeine, as a common substance in beverage, effectively alters the alertness via inhibiting inhibitory neurons. There are also on-going studies of investigating therapeutic effect of caffeine on Alzheimer’s and diabetes (1,2). However, the exact effect of caffeine on neural activity and metabolism in vivo has not been examined. The primary reason is that caffeine has a vasconstriction effect on brain blood vessels, independent of its neural effect (3-5). As a result, conventional hemodynamic based method such as fMRI is not able to correctly depict the neuro-metabolic effect. Therefore, in Study 2, we used the whole-brain finding as a benchmark and examined regional heterogeneities in CBF changes following caffeine ingestion. The rationale is that, if a particular brain region manifests a CBF decrease faster than the whole-brain rate, it may indicate a neuro-metabolic effect in this region in addition to the vascular effect.

METHODS: Study 1: whole-brain CMRO2: Ten healthy caffeine naïve (not a regular caffeine beverage consumer) adults (age 28±4yrd, 5F 5M) were scanned after caffeine ingestion; another ten healthy adults (age 28±4yrd, 5F 5M) were scanned without caffeine ingestion as controls. Study was performed on a 3T Philips System. The caffeine group subject took 200mg caffeine tablet immediately before MRI scans, after he/she was positioned on the table. Following intake of caffeine tablet, the subject was quickly positioned inside the scanner and the physiological scans started promptly. A total of 40min MRI was performed, consisting of 9 continuous measurements of CMRO2. Each CMRO2 measurement consisted of a venous blood oxygenation (Yv) scan using TRUST MRI (7) and a CBF scan using phase-contrast (PC) MRI, from which CMRO2=ChxCBFxOEF, OEF=Ya - Yv. Arterial metabolism in vivo has not been examined. The primary reason is that caffeine has a vasconstriction effect on brain blood vessels, independent of its neural effect (3-5). As a result, conventional hemodynamic based method such as fMRI is not able to correctly depict the neuro-metabolic effect. Therefore, in Study 2, we used a recently developed MTRI technique to examine the effect of caffeine ingestion on whole-brain cerebral metabolic rate of oxygen (CMRO2). We are cognizant that a lack of change in whole-brain CMRO2 does not necessarily indicate the absence of regional metabolic changes (6). Therefore, in Study 2, we used the whole-brain finding as a benchmark and examined regional heterogeneities in CBF changes following caffeine ingestion. In summary, the present study revealed that, despite a pronounced CBF reduction with caffeine ingestion, oxygen extraction fraction was increased reciprocally, resulting in an unaltered whole-brain CMRO2. However, this does not rule out the possibility of regional changes in CMRO2 that could have cancelled each other out in the whole-brain measure. Indeed, voxel-by-voxel analysis of CBF changes following caffeine ingestion suggest that there exist certain degrees of heterogeneity in CBF decline rate, which may suggest differential alteration of neural activity across the brain.