INTRODUCTION: The creatine kinase (CK) reaction plays an important role in ATP metabolism, which is crucial for neuronal activity and cell functioning. The CK forward reaction rate constant ($k_1$) (i.e. unidirectional PCr->ATP rate) can be measured in vivo using $^{31}$P MRS with magnetisation transfer (MT) techniques. Unlike fMRI and PET, $^{31}$P MRS MT provides a direct measure of neuronal activity at the metabolic level. Previously, a 34% increase in $k_1$ has been found during visual stimulation with an 8 Hz flashing photic stimulus. Aim: to measure the change of CK activity to a visual stimulation paradigm at 3 Tesla using an optimised protocol.

METHODS: 1) RF pulses for MT saturation were optimised to reduce RF bleed-over effects and keep within SAR limits. 2) TR, number of averages (NSA) and voxel size were adjusted to minimise acquisition time (5mins/scan) while providing acceptable signal-to-noise ratio (SNR) (250 in lowest PCr peak). 3) Monte Carlo simulation was performed to determine the scan time required to measure a change in $k_1$ with sufficient power to detect a 10% change in PCr (this showed that there was not sufficient SNR to estimate the constant rates of the ATPase reaction due to the low SNR of the Pi peak).

MR measurements: 9 healthy subjects (age 22-27 yrs) were recruited and participated in two in vivo $^{31}$P MT experiments: 1) Progressive saturation transfer experiment (N=6) to saturate $\gamma$-ATP to determine $T_1$ of PCr at baseline; 2) Steady-state saturation experiment (N=9) to quantify the apparent CK forward rate constant ($k_1$) in the visual cortex at rest and on visual stimulation. Data was collected on a Philips Achieva 3T scanner. A $^1$H image localizer was acquired using the body coil. $^{31}$P spectra were acquired from a localized volume (5x9x7 cm$^3$) encompassing the occipital lobe using a $^{31}$P transmit-receive coil and an ISIS sequence (TR = 12000 ms, samples = 4096, BW = 3000 Hz, NSA = 24, phase cycles = 8). The MT saturation sequence optimized to selectively irradiate only the $\gamma$-ATP peak comprised multiple HYSPER (Philips) RF pulses of constant amplitude and length (2 $\mu$s, 114 ms) interleaved with crusher gradients (4 ms, 10 mT/m, bandwidth = 140 Hz). Progressive Saturation of $\gamma$-ATP: Seven $^{31}$P spectra with varying MT saturation time ($t_{sat}$ = 0, 493, 987, 1974, 2961, 4934, 8224 s) were obtained by varying the number of RF pulses in the train. Steady-State Saturation of $\gamma$-ATP: Two cycles of 10-min rest period followed by 10-min visual stimulation period were applied. The visual stimulation comprised contrast-defined wedges moving towards or away from a fixation cross, which was presented through goggles (NordicNeuroLab, NNL). This paradigm has been shown to induce large increases in energy metabolism.

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RESULTS AND DISCUSSION: The intrinsic $T_1$ of PCr ($T_1^{int}$) for each subject was estimated by fitting the progressive saturation data to Eq. [1]. The forward rate constant during the rest ($k_{1,rest}$) and visual stimulation ($k_{1,stim}$) periods were calculated using Eq. [2], where $M_{PCR}$ is the steady-state magnetization of PCr in the presence of $\gamma$-ATP saturation and $T_1^{int}$ is the mean of the estimated intrinsic $T_1$ of PCr at rest. Previous animal studies have shown that $T_1^{int}$ is insensitive to physiology and can be treated as constant. Paired t-tests were used to test for the significant difference in $k_1$ between visual and rest periods.

CONCLUSION: This study showed that the CK forward reaction rate constant ($k_1$) increased by 17±12% over the voxel studied, during a relatively long visual stimulation. As predicted, it was not possible to detect a significant change in the forward rate constant of ATPase reaction due to the limited SNR of the Pi peak. In future work, $k_1$ will be corrected for active grey matter volume based on BOLD fMRI data, and the correlation between the BOLD signal change and % change in $k_1$ will be assessed for visual stimulation of varying intensity.