Two anesthetics, two completely different connectivity results

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TARGET AUDIENCE: connectivity under anesthaesia and animal connectivity researchers

PURPOSE: Studies of functional connectivity in humans and animals during anesthesia have shown the presence of modulated resting-state networks (RSNs)[1-3]. These studies have been performed with a range of anesthetics and all conclude the details of the anesthetic are important in obtaining results. There appears to be a trend towards using propofol as an anesthetic, and this may be due to the steadily increasing association of propofol as the general-purpose anesthetic of choice for uncomplicated subjects. Here we report on a rhesus macaque that was scanned once under propofol and once under ketamine. We found reasonable connectivity patterns visible under ketamine, but observed a complete lack of connectivity patterns (apart from noise) under propofol, even with scan time of an hour and low levels of propofol. This suggests it is inadvisable to design a study involving anesthesia around propofol.

METHODS: A rhesus macaque was scanned on two separate dates a few months apart under an IRB and IACUC-approved protocol. All scans acquired on a 3T Trio using a home-built transmit-receive loop coil optimized for macaque head size. On each session, a T1-weighted anatomic scan with 1mm isotropic voxels and two BOLD-weighted EPI scans were acquired. EPI scan protocol: 128x128 matrix, 31 axial 2mm-thick slices, 256x256mm FOV, 250-600 reps, TE/TR/FA/BW=29/2800msec/80/1954Hz/pix (second EPI scan used 4mm thick slices to increase SNR). For the first session, the animal was anesthetized prior to scanning with propofol (Session 1) and two 30 minute EPI scans acquired; for the second session, animal was anesthetized prior to scanning with ketamine (Session 2; only one anesthetic used on each date) and due to time constraints two 20 minute EPI scans acquired. On both dates an experienced anesthesiologist was present and administered and monitored dosages throughout. Animal was placed in the sphinx position with the loop coil positioned above the top of the head (in the brain's axial plane). Pulse and oxygen saturation were monitored using an MR-compatible plethysmograph/oximeter for the duration of anesthesia.Data was analyzed using motion correction and AFNI's InstaCorr tool. Seeds were placed over the left primary motor cortex, posterior cingulate and visual cortex and correlation maps auto-generated.

RESULTS

Surprisingly, no connectivity patterns were observed in the Session 1 data acquired under propofol anesthesia, while robust connectivity patterns were easily seen in the Session 2 data, acquired under ketamine anesthesia. The Session 1 connectivity maps appeared to be noise and blood vessels when lowering the statistical thresholds and searching for seed regions, while the Session 2 data did not require much searching, and other searched seeds produced maps that appeared similar to those seen in humans when adjusting seed locations.

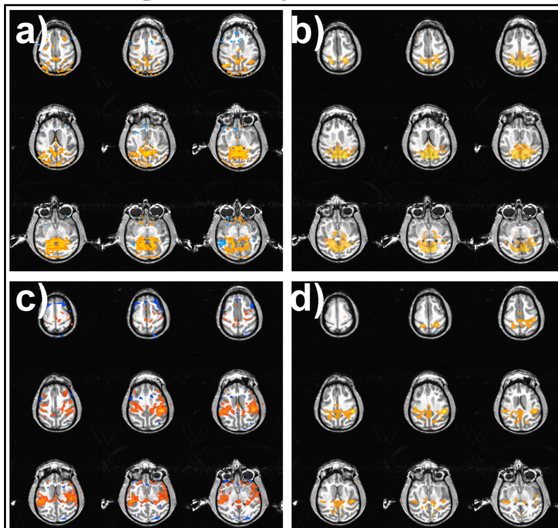

Fig 1: Session 2 (ketamine) connectivity maps for posterior cingulate seed in a) low-res and b) high-res data, and c,d) left primary motor seed.

DISCUSSION

We have shown that the type of anesthetic can dramatically affect the connectivity maps on one animal. When anesthetized using propofol, we observed no functional connectivity, even after scanning for two thirty minute sessions. During the first session, the level of propofol used was reduced to the lowest level considered necessary to retain consciousness due to our concern at not finding connectivity in a pilot 10 minute scan (previous separate session occurring several months prior to Session 1). At one point during later diffusion imaging the subject began to move, necessitating a small increase in anesthetic level. When using ketamine as the sole anesthetic, we observed typical connectivity patterns in two scans with different voxel sizes. Even with long scan times and with a relatively low level of propofol we failed to observe connectivity patterns, but under ketamine reasonable connectivity patterns did emerge in repeated scans despite shorter scan times.

These findings are troubling as there appears to be a general tendency of increased use of propofol in anesthesthetised human and animal connectivity studies. We suggest that researchers designing new anesthetized connectivity studies take care when choosing the anesthetic.

References: 1)) Kiviniemi V et al, 2000, Magn. Reson. Med. 44:378–383., 2) Peltier S, et al, 2007, Neuropsychologia, 45:476-83., 3) Vincent JL, et al, 2007, Nature, 447(7140):83-6.