

BOLD fMRI in Infants under Sedation: Comparing the Impact of Pentobarbital and Propofol on Auditory and Language Activation and Connectivity

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Target Audience: radiologists, anesthesiologists, language researchers, and investigators of consciousness mechanisms.

Purpose: Recently, the utility of fMRI has been extended to the radiology clinic where it is applied to map eloquent cortex for presurgical planning. For the youngest patients referred for imaging assessment, however, sedation is routinely administered to maintain compliance. Sedation incurs challenges for interpretation of fMRI as mechanisms of altering consciousness are not well understood. Recent investigations suggest a disintegration of meaningful information transfer [1] within and between brain networks. Confident interpretation of fMRI from birth to preschool age requires understanding activation signatures in the context of the applied sedation protocol. This work compares two standard pediatric radiology sedation protocols based on Propofol and Nembutal in regards to their impact on brain activation in infants subjected to auditory stimulation. Story listening elicits language processing at multiple levels with temporal hierarchy. An intermittent event-related imaging protocol³² was utilized with which the temporal evolution of language processing was explored. (Supported by NIH R01-DC07186)

Methods: Twenty infants participated after referral to Radiology for non-hearing-related issues. Normal hearing was confirmed by otoacoustic emissions testing. Eleven subjects (mean±sd age=12±3 mos., 7 F) were sedated by Nembutal bolus while 9 subjects (mean±sd age=12±3 mos., 8 F) had Propofol i.v. sedation. Post-hoc, images were read as normal by a certified neuroradiologist. Immediately following the prescribed clinical protocol, subjects participated in fMRI using a silent interval clustered acquisition protocol designed to permit auditory stimulation without gradient noise. Stimulation cycled through 20 epochs, each including 3 stimulus conditions: Tones, Silence, and Stories, each presented during 5s periods with no gradients followed by 3 EPI T2*-weighted acquisitions at TR=2s to capture BOLD response (180 volumes total). Following realignment and spatial normalization of imaging data using infant templates [2] in SPM8, statistical parametric maps were generated for each session by pairwise comparison, by epoch, of BOLD signal changes between conditions. We calculated the effect of sedation method on 1) average language activation and 2) the temporal change of language activation over time (slope) represented by the 3 image volumes. Random-effects composites of Nembutal and Propofol groups were compared. Comparisons were also made in select anatomical ROIs pertaining to language and default-mode networks. Intrinsic connectivity, in select networks assessed by ICA, was also compared between sedation groups.

Results: Voxel-wise activation is greatly diminished under Propofol compared to Nembutal. Activation under Nembutal is predominantly in auditory cortices. Aggregate ROI responses for the Stories vs. Silence contrast indicate auditory activation and thalamic deactivation commonly for Nembutal and Propofol groups, but activation of higher language areas such as the inferior parietal lobule only persists under Propofol. For Nembutal brain activation decreased with time after the stimulus in the selected ROIs while the temporal slope under Propofol was positive in most regions. In the thalamus slope was negative for both sedatives. Group ICA identified plausible language networks. Back-projections of these components differed between sedation protocols.

Discussion: While Propofol results in diminished activation overall, it preserves activity high-level language regions better than Nembutal. Listening to a story narrative engages a sequence of language processing over time. Positive slope of cortical response under Propofol may suggest more engagement of language areas toward the end of the story-listening period when narrative comprehension is required. Negative slopes of response under Nembutal may indicate a deeper deactivation of default mode regions as story stimuli develop over time. Back-projection of a group ICA component describing an auditory network suggests distinctions between sedation groups with respect to connectivity between parietal and thalamic regions. Differences were also found in connectivity between a component containing parietal elements and frontal regions. Other investigators [3], using a resting-state connectivity model including parietal, frontal, and thalamic nodes, report a breakdown of backward connectivity between frontal and parietal regions under Propofol with preservation of thalamo-cortical connections. Together, these observations tentatively support a model in which Propofol induces a breakdown of top-down feedback while Nembutal diminishes bottom-up processing.

Conclusion: Language activation and connectivity profiles were found to differ in infants under sedation using Nembutal vs. Propofol. Distinctions such as these may impact clinical interpretation of fMRI of sedated children and the choice of drug protocol.

- References:**
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