

# Enhanced Functional Connectivity of the Precuneus in Propofol Sedation

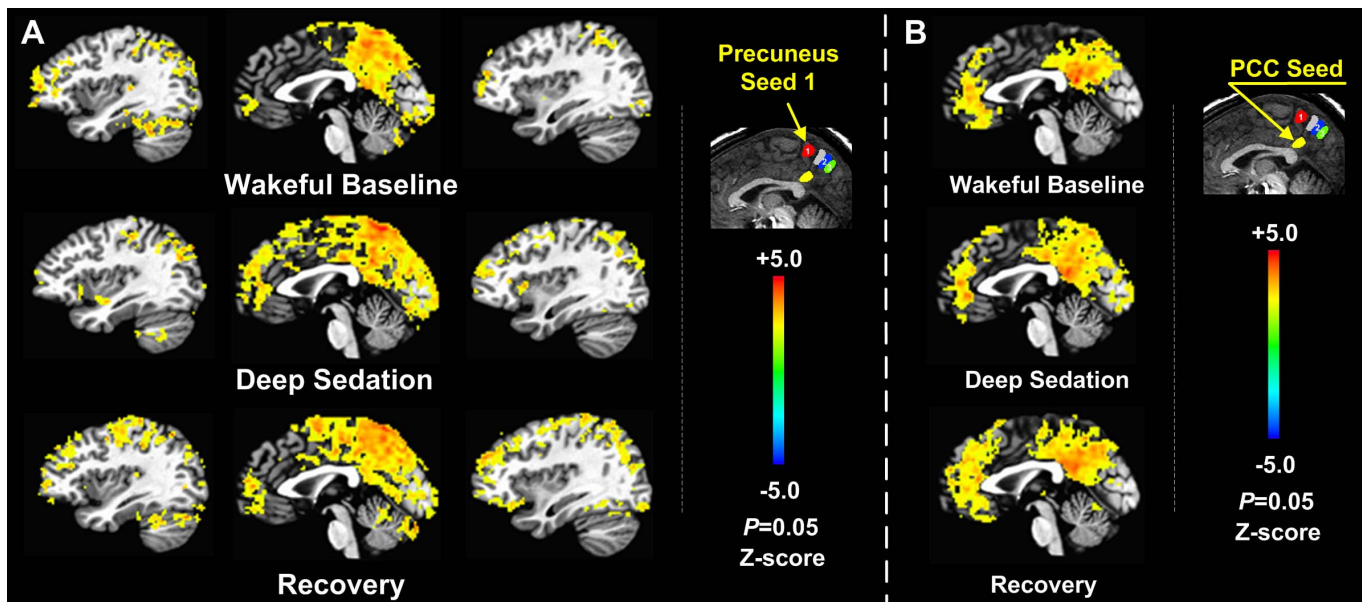
Xiaolin Liu<sup>1</sup>, Shi-Jiang Li<sup>1</sup>, and Anthony G. Hudetz<sup>2</sup>

<sup>1</sup>Biophysics, Medical College of Wisconsin, Milwaukee, Wisconsin, United States, <sup>2</sup>Anesthesiology, Medical College of Wisconsin, Milwaukee, Wisconsin, United States

**Introduction:** The precuneus, along with the adjacent posterior cingulate and retrosplenial cortices, is among the most metabolically active regions of the brain's default mode network (DMN) in the conscious resting state<sup>1</sup>. The involvement of the precuneus and associative posteromedial parietal structures in memory and consciousness has been supported by a variety of studies<sup>2-4</sup>. Specifically, the metabolic rate of the precuneus is significantly reduced in suppressed or altered states of consciousness, such as sleep, vegetative state, anesthesia, epilepsy, Alzheimer's disease, and schizophrenia<sup>2</sup>. Under normal conditions, the precuneus has been proposed to act as a well-connected small-world network hub that functionally links the frontal and parietal regions<sup>5</sup>. However, there has been a lack of understanding of how functional interaction of the precuneus with other regions of the brain is altered during reduced states of consciousness, such as general anesthesia. Given the presumed importance of the precuneus in information integration across the cerebral cortex, here we tested the hypothesis that functional connectivity of the precuneus with the rest of the cortex would be disrupted during anesthetic sedation with propofol. We report that, contrary to our expectation, propofol sedation produced a significant increase in precuneus connectivity with various cortical areas, most prominently with the dorsal prefrontal and visual cortices. These results imply a need for rethinking the functional role of the precuneus in modulating the state of consciousness. An interpretation of the results in the context of a recent proposition for the uncoupling of consciousness, connectedness, and responsiveness in general anesthesia is suggested<sup>6</sup>.

**Methods:** Blood oxygen level-dependent (BOLD) signals at 1.5 Tesla (repetition time, 2s; in-plane resolution, 3.75 x 3.75 mm; thickness, 6 mm) were collected from eight healthy volunteers (four men and four women; ages 24 to 42) who performed a verbal memory task in the scanner during each of the three 6-minute-long functional magnetic resonance imaging (fMRI) runs in wakeful baseline, propofol-induced sedation, and recovery. The propofol dose was titrated to the point just beyond the loss of responsiveness to verbal commands. Functional connectivity was determined using seed-based analysis. A recent study identified three subdivisions of the precuneus in the resting state, including the sensorimotor anterior region, cognitive/associative central region, and visual posterior region<sup>7</sup>. Accordingly, we manually defined three precuneus seeds based on the separating landmarks of the cingulate gyrus, precuneal sulcus, and parietooccipital fissure in each participant's medial sagittal anatomical images. For a comparison with the well-defined DMN connectivity, we also defined an additional nearby seed region in the posterior cingulate cortex (PCC).

**Results and Conclusions:** Compared with wakeful baseline, deep sedation at the point of unresponsiveness was marked by an increase in precuneus connectivity, particularly in the dorsal medial prefrontal and visual cortices (**Fig. 1A**). These changes were reversed upon recovery of consciousness, reestablishing a connectivity pattern similar to that observed at wakefulness. In contrast, connectivity of the PCC seed, which demonstrated the typical pattern of DMN connectivity during wakefulness, showed minimal changes in deep sedation and recovery (**Fig. 1B**). The dissociation of PCC and precuneus functional connectivities during sedation suggests different functional attributes of the two regions. Though unexpected, the increased precuneus connectivity during propofol sedation does not contradict its reduced neuronal or metabolic activity. For example, reduced activation and increased connectivity of the hypothalamus has previously been observed in slow-wave sleep<sup>8</sup>. According to a recent proposition to differentiate the states of consciousness, connectedness, and responsiveness in anesthesia<sup>6</sup>, enhanced cortical connectivity of the precuneus may reflect disconnected endogenous mentation or dreaming that continues at a lower rate of energy consumption during the unresponsive state of propofol sedation.



**Figure 1.** (A) Functional connectivity of the precuneus seed 1 in wakeful baseline, deep sedation, and recovery in eight participants. Functional connectivity patterns of all three precuneus seeds showed the same trend of increase in the dorsal medial prefrontal and visual cortices. (B) PCC connectivity showed minimal changes during propofol sedation.

## References:

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