**Original Paper**

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# Decreased Interhemispheric EEG Coherence during Sleep in Agenesis of the Corpus Callosum

**Key Words**
Sleep
EEG coherence
Agenesis of the corpus callosum
Posterior commissure

**Abstract**
Inter- and intrahemispheric EEG coherence was studied in 4 subjects with agenesis of the corpus callosum (ACC) and in 4 matched controls through different states of the sleep/wakefulness cycle. Interhemispheric coherence was calculated between homologous prefrontal, frontal, central, parietal and occipital electrode pairs whereas intrahemispheric coherence was calculated between all adjacent, unihemispheric electrode pairs. EEG samples were recorded from stage 2, stages 3 + 4 and stage REM sleep and the eyes closed waking state. Interhemispheric coherence measures indicated lower values for ACC subjects than for control subjects for most brain regions; the occipital cortex was least affected. These results further validate the interhemispheric coherence function as a measure of activity in the corpus callosum and suggest that occipital measures may index activity localized in the posterior commissure. Intrahemispheric coherence measures indicated very few differences between the two groups, a result consistent with the suggestion that there is no specialized intrahemispheric compensation in ACC.

## Introduction

The functional status of the corpus callosum in human sleep is still poorly understood, in part because of a lack of valid, noninvasive measures of the inter- and intrahemispheric transfer of information in the brain. The EEG coherence function is one measure which may index activity across the corpus callosum and which has been used to assess brain processes during both waking cognitive tasks [1] and sleep [2–5]. However, the assumption that EEG coherence reflects the underlying activity in the corpus callosum is one which requires further validation.

In a previous study [6] we reported the results of interhemispheric EEG coherence analyses of 2 epileptic patients who underwent partial callosotomy to alleviate intractable seizures [7, 8]. Surgical section of the corpus callosum was found to result in a lowering of coherence relative to presurgery levels. Moreover, changes in coherence levels reflected to a certain extent the underlying locus of the surgical section. On the basis of these results, we concluded that further investigation of the EEG coher-

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ence function as a noninvasive index of interhemispheric integration was warranted. In the present study, we report on a similar use of EEG coherence to measure interhemispheric activity in individuals with agenesis of the corpus callosum (ACC).

## Case Histories

Two male and 2 female subjects with total ACC (age range: 17–29, $\bar{X}$ = 23.0 years) and four age- and gender-matched controls (age range: 18–32, $\bar{X}$ = 24.5 years) were studied. Three ACC subjects (MG, LG and SG) are siblings in a French-Canadian family with 4 children. More extensive descriptions of the psychiatric, neuropsychological and cognitive status of these siblings has been described elsewhere [9–12]. Diagnoses of ACC in all cases were confirmed with computerized axial tomography scan and/or nuclear magnetic resonance imaging.

*Case 1.* MG, a 19-year-old left-handed male, is the youngest of the family. He scored a full-scale IQ of 77 (verbal: 71, performance: 87) on French versions of the WAIS-R.

*Case 2.* LG, a 27-year-old right-handed female, is the second child of the family. She has a full-scale IQ of 78 (verbal: 81, performance: 81) on the Ottawa-Wechsler.

*Case 3.* SG, a 29-year-old right-handed woman, is the second of 4 children and the sister of MG and LG described above. She has a global IQ of 84 (verbal: 88, performance: 82) on the revised WAIS.

*Case 4.* SB, a 17-year-old right-handed male, was adopted at 6 months. He scored 68 on the global IQ of the WISC-R (verbal: 58, performance: 81). He is dyslexic.

*Control Subjects.* Control subjects were persons known to members of the research team and were recruited so as to match the age, gender and hand preference of the agenesis subjects. None reported a history of neurological, psychiatric or sleep problems. Like the ACC subjects, none of the control subjects abused alcohol or took psychotropic medications. Informed consent for participation was obtained from all subjects.

## Methods

Each subject spent 2 consecutive nights in the sleep laboratory where all-night polysomnograms were recorded using the 10-20 EEG montage [13] and the standard EEG, EOG, EMG montage for sleep staging [14]. The first night was considered to be adaptation to the laboratory and was not further scored. Records for the second night were visually scored for sleep stages by an experienced polysomnographer. Subjects were also awakened from the last REM period of each night to report dream mentation. Results of analyses of sleep architecture and dream content are not reported here.

Monopolar EEG electrode pairs from left (Fp1, F3, C3, P3, O1, T3) and right (Fp2, F4, C4, P4, O2, T4) hemispheres, all referenced to a combined ear reference (A1 + A2), were digitally sampled for coherence analyses. Five-minute samples were taken from stages 2, 3 + 4 and REM sleep and the eyes closed waking state. EEG channels were amplified and low-pass filtered at 50 Hz with Grass model 7P511 amplifiers and sampled and stored on digital tape at 200 Hz by a Compaq 386 computer. Power spectral analysis and smoothing of each channel was performed for each of 4 frequency bands using a commercially available software package for EEG spectral analysis (RHYTHM software, Montréal, Que.; Systèmes Stellate Enregistré 1990). Frequency bands were defined as follows: delta (0.5–4.0 Hz), theta (4.0–8.0 Hz), alpha (8.0–13.0 Hz) and beta (13.0–22.0 Hz). Autospectra functions for each channel were calculated on 100 nonconsecutive 2.56-s epochs (total time = 5 min). Samples were all manually selected to be free from eye movement and other muscle artifact using the screen display and data selection features of the spectral analysis software.

### *Interhemispheric Coherence Values*

Interhemispheric coherence values were derived for 5 homologous channel pairs (Fp1-Fp2, F3-F4, C3-C4, P3-P4, O1-O2) for each of 4 bands (delta, theta, alpha, beta) yielding a total of 20-channel bands per sleep stage, or 80 values per subject for the 4 stages. A measure of global EEG coherence was calculated as the mean of these 80 values. Measures of coherence for the 4 sleep stages were defined as the mean of the 20 channel-band values calculated for each stage. Within stages, measures of interhemispheric coherence for each cortical region were defined as the mean of values over the 4 bands for each homologous channel pair along the midline axis.

### *Intrahemispheric Coherence Values*

Intrahemispheric coherence values were derived for 5 adjacent channel pairs for both the left (Fp1-F3, F3-C3, C3-P3, P3-O1, O1-T3) and the right (Fp2-F4, F4-C4, C4-P4, P4-O2, O2-T4) hemispheres for each of 4 bands (delta, theta, alpha, beta) yielding a total of 40-channel bands per sleep stage, or 160 values per subject. A global intrahemispheric coherence measure was defined as the mean of these 160 values. Measures of coherence for the 4 sleep stages were defined as the mean of the 40 channel-band values calculated for each stage. Within stages, measures of intrahemispheric coherence for each cortical region were defined as the mean of values over the 4 bands for each adjacent channel pair along the left and the right sides of the midline axis, separately.

Differences between group means for all global and regional coherence scores were calculated using two-tailed t tests (BMDP-3D).

## Results

### *Interhemispheric Coherence*

Overall, interhemispheric coherence was lower in ACC subjects ($\bar{X}$ = 38.7) than in control subjects ($\bar{X}$ = 52.0; p = 0.021). ACC subjects scored lower than control subjects on 78 of the coherence measures calculated for the 80 individual channel bands. By sleep stage, coherence was lower for ACC subjects during stage 2 (p = 0.021), stages 3 + 4 (p = 0.021) and stage REM (p = 0.043) sleep, but not during wakefulness (p = 0.149; fig. 1). By cortical regions, interhemispheric coherence was lower in ACC subjects for all regions except the occipital during stage 2 and stages 3 + 4 sleep, but only lower in ACC subjects for frontal and central regions during stage REM sleep and wakefulness (table 1).

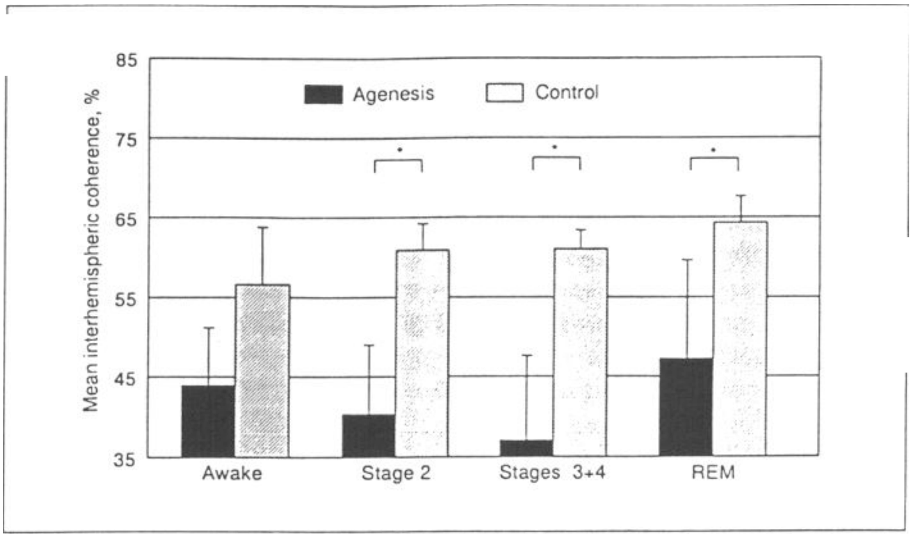

**Fig. 1.** Mean interhemispheric EEG coherence (%) by sleep stage. * $p < 0.05$.

**Table 1.** Interhemispheric EEG coherence in callosal agenesis for all bands combined as a function of brain region and sleep stage

| Region | Awake | | | | Stage 2 | | | | Stages 3 + 4 | | | | Stage REM | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | agenesis | | control | | agenesis | | control | | agenesis | | control | | agenesis | | control | |
| | mean | SD | mean | SD | mean | SD | mean | SD | mean | SD | mean | SD | mean | SD | mean | SD |
| Fp1-Fp2 | 49.3 | 15.0 | 66.9 | 15.0 | 49.8* | 7.9 | 60.9* | 3.6 | 46.4* | 10.7 | 62.3* | 5.9 | 55.0 | 16.3 | 69.3 | 7.0 |
| F3-F4 | 36.0* | 11.1 | 55.9* | 11.4 | 35.1* | 9.6 | 50.4* | 7.1 | 33.0* | 9.3 | 51.0* | 7.8 | 37.7* | 15.3 | 58.9* | 9.1 |
| C3-C4 | 23.4* | 5.8 | 34.4* | 9.9 | 23.0* | 7.0 | 38.4* | 6.4 | 23.1* | 9.2 | 38.3* | 6.8 | 30.0* | 1.5 | 42.5* | 7.4 |
| P3-P4 | 39.6 | 5.5 | 43.1 | 3.8 | 34.9* | 8.9 | 48.6* | 4.8 | 34.9* | 10.7 | 49.4* | 4.8 | 40.9 | 8.3 | 49.0 | 6.2 |
| O1-O2 | 47.9 | 5.7 | 46.3 | 9.4 | 45.3 | 14.2 | 57.2 | 13.4 | 45.1 | 18.1 | 62.2 | 13.5 | 43.2 | 26.0 | 54.8 | 11.9 |
| Mean | 39.2 | 6.9 | 49.3 | 7.5 | 37.6* | 9.0 | 51.1* | 4.3 | 36.5* | 11.1 | 52.7* | 3.5 | 41.4* | 12.0 | 54.9* | 6.0 |

* $p < 0.05$, two-tailed, agenesis and control group difference for this stage.

### *Intrahemispheric Coherence*

Overall, intrahemispheric coherence did not differentiate between ACC ($\overline{X} = 50.4$) and control ($\overline{X} = 50.6$) subjects ($p = 0.564$). However, means for ACC subjects were lower than those for control subjects on 130 of the measures calculated for the 160-channel bands, suggesting a slightly lower overall coherence for the ACC group. Nevertheless, by sleep stage, there were no significant differences between the groups. By cortical regions, only 2 channel pairs differentiated the groups; mean coherence for F4-C4 during wakefulness and mean coherence for P3-O1 during REM sleep were both significantly lower for ACC subjects ($p < 0.05$).

## Discussion

The present finding that interhemispheric EEG coherence is low in ACC subjects relative to matched controls further validates the notion that the coherence function reflects interhemispheric activity across the corpus callosum. The finding that ACC subjects have an average coherence which is 13% less than that of controls parallels the pre- to postsurgery difference of 11.5% for 2 partial callosotomy patients reported earlier [6]. Thus, the magnitude of the coherence deficit produced by the absence of the corpus callosum is similar whether the absence appears in ACC or callosotomy.

The present results also parallel those of a previous study which showed that interhemispheric coherence of low-frequency (0–3 Hz) waves during sleep is reduced in acallosal infants relative to infants with an intact corpus callosum [5]. This parallel suggests that in ACC, there is an altered brain organization which is reliably indexed by low interhemispheric coherence and which is not modified by subsequent neuronal development in the brain.

There is also some indication in the present results that interhemispheric coherence differentiates the underlying anatomy of acallosal subjects. That interhemispheric coherence in the occipital channel pairs was least affected in any stage by ACC is consistent with the fact that the posterior commissure typically remains intact in ACC because of its independent development at the diencephalon-mesencephalon border [15]. This finding is also consistent with results from the callosotomy study in which it was observed that interhemispheric EEG coherence reflected the degree of anatomical section produced by surgery [6].

The present results have implications for the organization of brain processes in ACC. The finding that intrahemispheric coherence, in general, was not elevated during any sleep/waking stage in ACC supports the view [12] that there is no specialized intrahemispheric compensation for the missing corpus callosum among acallosal subjects. Rather, apart from a few exceptions, intrahemispheric processes in ACC appear to function at near normal levels. Further, the present results provide evidence that the posterior commissure is a likely alternative pathway for interhemispheric activity in posterior regions.

A post-hoc observation in the present data raises the possibility that compensatory activity might be reflected in the occipital coherence index. Specifically, 1 of the 80 interhemispheric channel bands registered a striking 10.6% elevation for the ACC group relative to the control group. This activity was recorded exclusively over the occipital region during the waking state for the delta band. Although it is very possible that this may be a spurious artifact of the large number of means calculated, the magnitude of the effect and its association with the occipital cortex raises the possibility that it may reflect some noncallosal compensatory activity. One might question why the posterior commissure, and not the anterior commissure, might compensate for the lack of a corpus callosum. The answer may be that because the primary visual cortex (area 17) is devoid of commissural connections [16], interhemispheric coherence is normally subserved by the posterior commissure. Clearly, further work is required to verify whether this observation is spurious or whether it might indeed reflect compensation via a normal interhemispheric brain pathway in ACC.

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