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EEG TRANSFER ENTROPY TRACKS CHANGES IN INFORMATION TRANSFER ON THE ONSET OF VISION

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We investigate the pairwise mutual information and transfer entropy of ten-channel, free-running electroencephalographs measured from thirteen subjects under two behavioral conditions: eyes open resting and eyes closed resting. Mutual information measures nonlinear correlations; transfer entropy determines the directionality of information transfer. For all

channel pairs, mutual information is generally lower with eyes open compared to eyes closed indicating that EEG signals at different scalp sites become more dissimilar as the visual system is engaged. On the other hand, transfer entropy increases on average by almost two-fold when the eyes are opened. The largest one-way transfer entropies are to and from the Oz site consistent with the involvement of the occipital lobe in vision. The largest *net* transfer entropies are from F3 and F4 to almost all the other scalp sites.

Keywords: EEG, vision, mutual information, transfer entropy.

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1. Introduction

Human electroencephalographic (EEG) data have been used to assess information transfer between different scalp sites for a number of years by employing such measures as delayed mutual information[1,2], Granger causality[3], transfer entropy and a recent variant, symbolic transfer entropy[4]. Relative merits of all but the last are discussed in some detail by Cellucci *et al.*[5]. Staniek and Lehnertz[4] discuss the merits and advantages of symbolic transfer entropy. All of these techniques provide information not only on the magnitude of the interaction between brain regions, but more importantly, on the direction of information transfer. This ability to detect directionality provides useful information that can help elucidate underlying physiological processes.

In this contribution, we study the mutual information and the transfer entropy of multichannel free-running EEG's of normal human subjects under two behavioral conditions: eyes closed resting and eyes open resting. Both measures are calculated using a variant of the "adaptive binning" technique introduced by Cellucci *et al*[5]. The results show that there are dramatic differences both in the nature of the two measures under each of the behavioral conditions, as well as in the changes of their structure as the visual system is engaged.

2. Mutual Information, Transfer Entropy, and Adaptive Binning

Given a series of simultaneously measured values of two variables, $X = \{x_1, x_2, \ldots, x_N\}$ and $Y = \{y_1, y_2, \ldots, y_N\}$, there are a number of quantities that can be used to measure the extent to which the variables are correlated or to determine if there exists a causal relationship between them.

The *Mutual Information*, $I(X,Y)$, of X and Y, is the amount of information common to X and Y[6] and is estimated by

$$I(X,Y) = \sum_i p_{X,Y}(x_i, y_i) \log\left(\frac{p_{X,Y}(x_i, y_i)}{p_X(x_i) p_Y(y_i)} \right)$$

where $p_{X,Y}(x,y)$ is the joint probability distribution of X and Y, and $p_X(x)$ and $p_Y(y)$ are their respective marginal probabilities. $I(X,Y)$ is a measure of the amount of information about X given a measurement of Y and *vice versa*. More precisely, it is the average number of bits of Y that can be predicted by measuring X, where it can be shown that this is symmetrical $I(X,Y) = I(Y,X)$. It is a generalization of measures of cross-correlation such as Pearson's r. In general, it is a more useful measure to the extent that unlike r, it is sensitive to nonlinear correlations[7,8]

Correlations, linear or nonlinear, only indicate the extent to which two variables are similar. They say nothing about causal relationships. Neither can they indicate if two variables are similar not because they interact with each other, but because they are both driven by a third. These issues can be addressed by measures of causality or of information transfer. One such measure is Schreiber's transfer entropy[9] defined by,

$$T_{Y\to X} = \sum_k p(x_{k+1}, x_k, y_k)\log_2 \frac{p(x_{k+1} \mid x_k, y_k)}{p(x_{k+1} \mid x_k)}$$

where $p(x|y)$ are conditional probabilities. $T_{Y\text{->}X}$ is a measure of the influence of the sequence, Y, on the evolution of X. Unlike mutual information which is symmetric in X and Y, transfer entropy in general, is not:

$$T_{Y\to X} \neq T_{X\to Y}.$$

One is often interested in the net information transfer from Y to X, $T_{net} = T_{Y\text{->}X} - T_{X\text{->}Y}$. Hlavácková-Schindlera *et al.*[10] showed that transfer entropy is equivalent to the *conditional mutual information,* the mutual information of $\{x_1, x_2, \ldots, x_{N-1}\}$ and $\{x_2, x_3, \ldots, x_N\}$ given $\{y_1, y_2, \ldots, y_{N-1}\}$.

The distribution, $p_X(x_i)$ is estimated by subdividing the range, $x_{max} - x_{min}$, into n bins. Denoting by $O_x(i)$ the number of x data points in the ith bin, $p_X(x_i)$ is approximated by $O_x(i)/N$, where N is the total number of (x,y) data pairs. The distribution, $p_Y(y_i)$, is obtained similarly. The number of bins in the x and y- axes may, of course be different, but we take them here to be the same for the sake of simplicity. If $O_{xy}(i,j)$ is the number of (x,y) data points in the intersection of the ith bin on the x-axis and the jth bin on the y-axis, then $p_{X,Y}(x_i,y_j) = O_{xy}(i,j)/N$.

The choice of the number of bins into which the x- and y- axes are subdivided is crucial. If there are too many, one may end up, in the extreme, with occupation numbers of 0 or 1 which give no meaningful information. If there are too few, then it may not be possible to discern any structure in the distribution at all. Cellucci *et al.*[5] resolved this by an *adaptive partition* of the x-y plane. In this procedure, the x and y axes are partitioned such that all of the x bins and all of the y bins contain the same number of data points. This is accomplished by replacing elements of X and Y by their rank order so that, when

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there are no ties*, each of the data sets is mapped onto a permutation of the integers, 1, 2, …, *N.* Dividing the transformed data into *n* bins of equal size guarantees that all the bins have the same number of occupants. This partitions the *x-y* plane into n^2 cells, some of which may not be occupied. The number of bins per axis, *n,* is either estimated prior to the calculations of the distributions, or adjusted in the process of the calculation until the Cochran condition is satisfied – that is, that at least 80% of the occupied cells contain at least five points (see ref. 5).

3. Data

The data were obtained by Watanabe at Hahnemann University in 1999 and 2000 using Instep[11]. Free running, sixteen-channel records were obtained in eyes-open and eyes-closed conditions. However, because the Electrocap used in the measurements gave poor quality data in some channels, only ten channels are used here.

The Institutional Review Board of Hahnemann University reviewed all procedures involving human subjects. Informed consents were obtained from each participant. Multichannel signals were recorded from thirteen healthy adults. Monopolar recordings, referenced to linked earlobes, were obtained from F_z, C_z, P_z, O_z, F_3, F_4, C_3, C_4, P_3, and P_4. Vertical and horizontal eye movements were recorded, respectively, from electrode sites above and below the right eye and from near the outer canthi of each eye. Artifact-corrupted records were removed from the analyses. All EEG impedances were less than 5 KOhm. Signals were amplified with a gain of 18,000, and amplifier frequency cutoff settings of 0.03 Hz and 200 Hz were used. Signals were digitized at 1024 Hz using a twelve-bit digitizer. Multichannel records were obtained in two conditions: eyes closed, resting and eyes open, resting. Continuous artifact-free records were obtained from each subject in the two conditions. The resulting data files are at least twelve seconds long.

For later convenience, we label the scalp sites listed above by integer indices, 1, 2, …, 10, respectively. Thus, Fz will be referred to as channel 1, Oz as channel 4, etc. Using these integer indices, we label the channel pairs (i, j), $i = 1, 2, \ldots, 9$; $j = i + 1, i + 2, \ldots, 10$ with the consecutive integers 1, 2, …, 45. Thus, the channel pair Fz-Cz is channel pair 1, Fz-P4 is channel pair 9, Cz-Pz is channel pair 10, etc., until P3-P4 which is channel pair 45.

4. Analysis

If the (x,y) data are more or less uniformly distributed, it is possible to preselect an expected average *XY* cell occupancy and use this to estimate the number of bins into which each axis is to be subdivided that would satisfy the Cochran criterion (see ref. 5 for

*Ties can be resolved by assigning a higher rank to the entry that occurs earlier in the time series.

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details). This, however, is not generally possible for sparse, non-uniformly distributed data such as those we study here. This is illustrated by Fig. 1 which shows the fraction of cells that contain at least five points (*frac5*) as a function of the preselected expected average occupancy (*expect*). Here, we use data from the Fz and Cz scalp sites of one subject with eyes closed. Fig 1 shows that for this channel pair, one needs an expected average occupancy of at least 10 to satisfy the Cochran criterion.

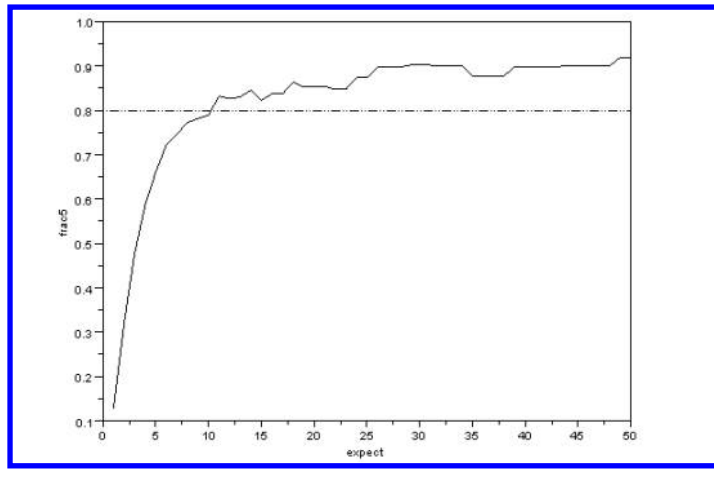

Fig. 1. The fraction of *XY* cells occupied by at least five points (*frac5*) *vs.* the preselected expected average occupancy (*expect*) for data from the Fz and Cz scalp sites of a subject with eyes closed. The dashed line represents the Cochran criterion.

In a multichannel EEG recording, the amplitude distribution of data from the different channels may be sufficiently different that a given value of *expect* satisfying the Cochran criterion for one channel pair would not be satisfactory for another. This is illustrated in Fig. 2 which shows the fraction of cells occupied by at least five points (*frac5*) for all channel pairs of a subject with eyes closed when *expect* = 10. Approximately half of the channel pairs satisfy the Cochran criterion, the other half do not. In view of this, we steer a more prudent course: start with an arbitrary value of *expect* = 5, say. After the joint distribution has been calculated, determine the fraction of cells occupied by at least five points. If the Cochran criterion is satisfied, keep the results of the calculation, otherwise increase the value of *expect* until the criterion is satisfied. We do this for the calculation of mutual information as well as transfer entropy. However, we require that at least 90% of all occupied cells contain at least 5 points – a more stringent criterion than Cochran's.

5. Results

Figure 3 shows the mutual information averaged over all subjects for all 45 channel pairs. On the whole, mutual information values for the eyes closed condition are greater than

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those for eyes open. This is prominently so in those channel pairs involving the frontal sites; Fz (channel pairs 1-9), F3 (channel pairs 31-35), and F4 (channel pairs 36-39).

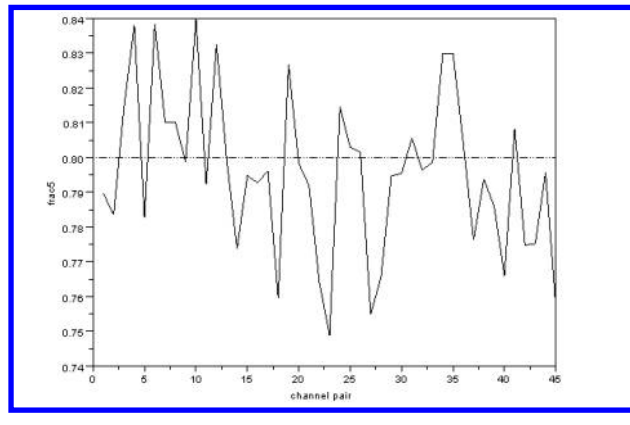

Fig. 2. The fraction of *XY* cells occupied by at least five points (*frac5*) for all channel pairs of a subject with eyes closed. The preselected expected average occupancy (*expect)* is 10. The dashed line represents the Cochran criterion.

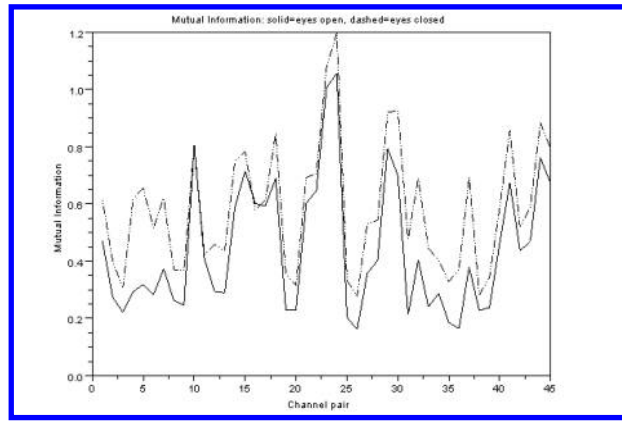

Fig.3. Mutual information for all channel pairs averaged over all subjects. Dashed line – eyes closed, solid line = eyes open.

Transfer entropy tells a more informative story. Fig.4 shows the one-way transfer entropies ($T_{x->Y}$ and $T_{Y->X}$) for both conditions. The left panel shows eyes closed, the right panel eyes open. The results shown are averages over all subjects. Using the indexing scheme for channel pairs described in Sec. 3, for a channel pair, (*j, k*), the solid lines connecting dots are transfer entropies from channel *j* to channel *k*. The dotted lines connecting open circles are transfer entropies going the other way around.

The transfer entropies for the eyes open condition are, on average, 1.8 times greater than those for the eyes closed. In the eyes open condition, transfer entropies from F3 and F4 to and from Oz (channel pairs 25 and 26) are among the highest – not

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surprising in view of the involvement of the occipital lobe in vision. Also prominent are F4 to C3, C4 and P4 (36, 37 and 39) and F3 to C3 (32).

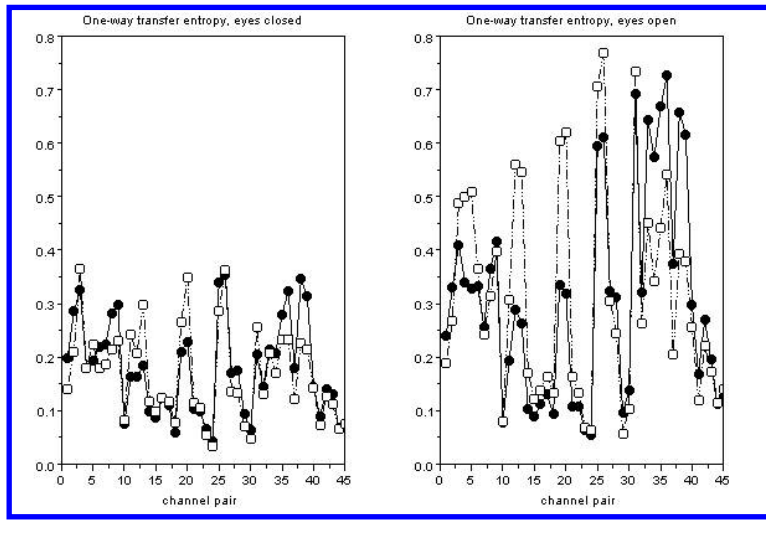

Fig. 4. One-way transfer entropies averaged over all subjects. Left panel: eyes closed, right panel: eyes open. For each channel pair (*j, k*) (see Sec. 3) the solid lines connecting dots are transfer entropies from channel *j* to channel *k*; dashed lines connecting open circles are from channel *k* to channel *j*.

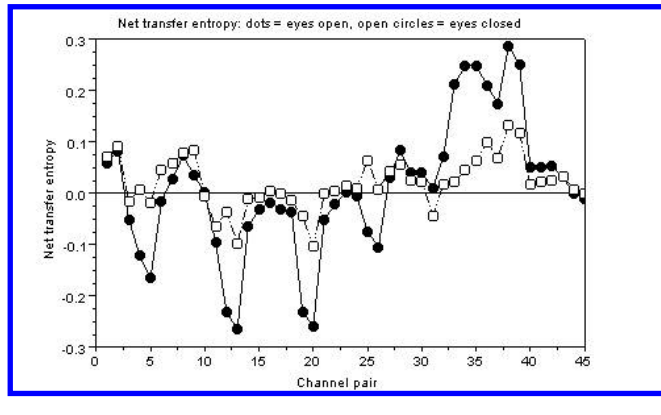

Fig. 5. Net transfer entropy between all channel pairs averaged over all subjects. Solid lines connecting dots: eyes open, dashed lines connecting open circles: eyes closed.

Figure 5 shows the *net* transfer entropy between all channel pairs averaged over all subjects. A positive value of the net entropy of the pair, (*j, k*), means that the net entropy transfer is from channel *j* to channel *k*. A negative value means that the transfer is the other way around.

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In almost all channel pairs, the magnitude of the net transfer entropy with eyes open is larger than that with eyes closed. There are even some instances when the direction of the net entropy transfer is reversed when the visual system is engaged.

The largest net transfer entropies with eyes open are from F3 and F4 to all the other channels. In Fig. 5, these are shown by the transfer entropy values of channel pairs 4, 5, 12, 13, 19, 20, 25 and 26 corresponding to the pairs F2-F3, F2-F4, C2-F3, C2-F4, Pz-F3, Pz-F4, Oz-F3 and Oz-F4 all of which have negative net transfer entropies; and channel pairs 33 – 39 corresponding to F3-C4, F3-P3, F3-P4, F4-C3, F4-C4, F4-P3, and F4-P4 all with positive values.

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6. Discussion

For almost all channel pairs (Fig. 3), the mutual information is smaller when the eyes are open, suggesting that when the visual system is engaged, the different scalp sites receive dissimilar information. As already noted, however, mutual information measures only correlations, not information transfer or causality. It is transfer entropy that can indicate the direction of information flow.

The one-way transfer entropies with eyes open are, on average, almost twice as large as those with eyes closed indicating, not surprisingly, that a lot of information is being transferred among various brain sites when the eyes are open. The largest one-way transfer entropies when the eyes are open are from the occipital site, Oz, to the frontal sites F3 and F4 and *vice versa*, confirming the well-known involvement of the occipital lobe in vision. Because both one-way entropy values are large, the *net* information transfer involving Oz is relatively small. The dominant net information transfers are those from F3 and F4 which seem to be sending large amounts of information to all the other sites. These results are consistent with the longstanding physiological understanding of visual processing. Information transfers from the occipital lobe to the frontal lobe, and following cognitive processing, information is distributed throughout the central nervous system.

Potential clinical applications of these analysis procedures warrant consideration. The treatment of traumatic brain injury is a particularly promising application. Brain injury, even mild traumatic brain injury, can disrupt functional connectivity and causal networks[12-15]. These results indicate that assessment of functional and causal networks can quantify post-injury abnormalities in patients who report ill-defined post-injury deficits ("Doc, I'm not the same.") when the patient's neuropsychological, imaging, and neurological examinations are unremarkable.

Biofeedback is a treatment process in which a physiological signal recorded from the patient is converted in real time to a signal (usually auditory or visual) that the patient can perceive. By a process that is not understood, the patient learns to alter the feedback signal resulting in a change in the physiological variable that controls the feedback. The best known and most systematically validated form of biofeedback is the operant control of blood pressure. In this application the feedback signal is controlled by blood pressure. In neurofeedback electroencephalographic signals control the feedback

signal. Neurofeedback has been used to treat several neuropsychiatric disorders including depression[16-17], post-traumatic stress disorder[18], traumatic brain injury[19-21] and chronic pain[22]. In these treatments the feedback signal to the patient is usually constructed from the spectral properties of the signal, for example alpha asymmetry. Using the analysis procedures developed here it would be possible to construct neurofeedback signals based on functional connectivity (mutual information) and/or causal network geometry (transfer entropy). This seems to be particularly relevant to the treatment of traumatic brain injury since, as outlined above, these injuries can, in some instances, result in a disruption of normal function and causal networks. A patient-specific protocol that addresses the network damage identified by connectivity/causality analysis may be more successful than a treatment based on spectral analysis.

It is possible to speculate about the physiological mechanism that may be the basis of successful neurotherapy. It is now recognized that neurogenesis (the formation of neurons) can occur in the adult mammal, including humans. Several procedures for stimulating adult neurogenesis have been identified. But neurogenesis alone is not enough. Newly formed neurons must be integrated into the networks that were damaged by the injury. We call this critical second step neurointegration. We speculate that neurointegration may be facilitated by neurofeedback treatment based on mutual information and on transfer entropy.

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