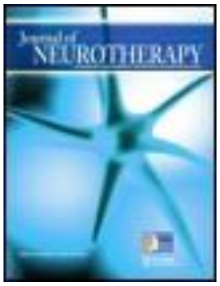

Journal of Neurotherapy: Investigations in Neuromodulation, Neurofeedback and Applied Neuroscience

Introduction to Advances in EEG Connectivity

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Published online: 12 Dec 2008.

To cite this article: Robert Coben PhD & William J. Hudspeth PhD (2008) Introduction to Advances in EEG Connectivity, Journal of Neurotherapy: Investigations in Neuromodulation, Neurofeedback and Applied Neuroscience, 12:2-3, 93-98, DOI: 10.1080/10874200802429843

To link to this article: http://dx.doi.org/10.1080/10874200802429843

Introduction to Advances in EEG Connectivity

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ABSTRACT. This special issue of the *Journal of Neurotherapy* has been devoted to Advances in EEG Connectivities. These purposes include providing education to our readers and collaboration among the scientists and authors. Multiple connectivity metrics have been defined with an emphasis on coherence and multivariate connectivity measures. The goals of connectivity measurements should include accuracy compared to known neurological networks and utility in assessment and application for intervention (e.g., EEG coherence training). It is hoped that the information contained in this special issue will form the basis for future advancements in EEG connectivity assessment and intervention.

KEYWORDS. Coherence, comodulation, connectivity, EEG, phase

This double issue and the companion issue of the *Journal of Neurotherapy* are devoted to Advances in Electroencephalography (EEG) Connectivity to educate our readers with collaboration among the scientists and authors. Competition between metrics or approaches is not considered important or necessary. The purposes of this endeavor included the following:

1. Presentation of the importance of such concepts in understanding neural and EEG activity.
2. Clarification of various metrics that relate to neural synchronization and provision of operational definitions of these.
3. Provide impetus for research utilizing such metrics.
4. Encourage and provide an appreciation of how neurofeedback approaches may be informed or enhanced through the use of these techniques.
5. Facilitate future research using such metrics that may compare and contrast their respective strengths and limitations.

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Journal of Neurotherapy, Vol. 12(2–3) 2008

doi: 10.1080/10874200802429843

In regard to EEG Connectivity, the functions of the brain are dependent on the synchronization of neuronal events and processes. Recent findings in translational neuroscience indicate that normal brain functioning depends on activity synchronization within distributed brain networks (He, Shulman, Snyder, & Corbetta, 2007). Furthermore, breakdown of such connectivity correlates with behavioral deficits in schizophrenia (Ford, Roach, Faustman, & Mathalon, 2008), attention (Roy, Steinmetz, Hsiao, Johnson, & Niebur, 2007), memory (Wolters & Raffone, 2008), and speech disorders (Prat, Keller, & Just, 2007). Of interest, enhanced synchronization of brain activity has been found following cognitive retraining (Miotto et al., 2006) and neurofeedback training with autistic children (Coben, 2007). Synchrony is assumed to occur when regions of the brain are performing similar operations within a reasonable period. This can be measured in several ways including functional magnetic resonance imaging (MRI), magnoencephalography, and with EEG technology. EEG connectivity approaches are ideal for such purposes given its excellent temporal resolution (Srinivasan, Winter, Ding, & Nunez, 2007). Other advantages include its frequency specificity (Wu et al., in press), the ability to measure multiple sources (Srinivasan et al., 2007), and the ability to eliminate correlated sources through advanced statistical techniques (Marzetti, Del Gratta, & Nolte, 2008).

In the current journal issue, Collura has done our field a great service by comparing, contrasting, and defining various metrics of connectivity. Mathematical definitions have been provided for coherence, cross spectral correlation, comodulation, phase delay, synchrony, and asymmetry. Both Hudspeth and Black, Hudspeth, Townsend and Bodenheimer-Davis have similarly provided such operational, mathematical definitions as it relates to coherence. This enables us all to "speak the same language" when discussing aspects of EEG connectivity. As an example, Thornton and Carmody have clarified that in their upcoming article in the companion issue of the *Journal of Neurotherapy* that Lexicor's metric labeled "coherence" is actually measuring spectral correlation. By far, the greatest emphasis was on the use of coherence metrics as the premiere means of measuring connectivity. A review of articles searchable through PubMed (a service of the National Library of Medicine including Medline) revealed 1,330 publications on EEG coherence, dating back to Walter (1968) around 40 years ago. There were only 100 articles found under the search term of *EEG phase delay* and 1 for *EEG comodulation*. There has been strong interest in EEG asymmetry, predating work on coherence (Strobos, 1960) and continued recent interest in this concept as it relates to psychiatric conditions (Putnam & McSweeney, 2008; Shankman et al., 2008).

Coherence was the focus of articles by Coben & Myers; Hudspeth; Joffe; Ibric et al., and Black et al. (to appear in the companion issue). By comparison, Thornton and Carmody have focused on spectral correlation and Kaiser on comodulation (in addition to coherence). Such metrics have been shown useful in these articles for such diverse clinical conditions as autism, traumatic brain injury, and childhood sexual abuse, in addition to the study of normally developing children and adults.

This issue represents a conceptual shift away from pairwise or bivariate coherence estimates toward more multivariate approaches to coherence assessment. Such an approach appears to be supported by recent EEG coherence research. Barry, Clarke, McCarthy, and Selikowitz (2005) showed the random and systematic interelectrode distance effects that distort pairwise coherence values. Adjustments for these errors are necessary for accurate data to be accumulated. Kus, Kaminski, and Blinowska (2004) were the first to demonstrate that multivariate assessments were more accurate than bivariate coherence estimations. This result was demonstrated mainly through the use multivariate autoregressive techniques as are discussed in Joffe's article in this issue. Using simulated data, Astolfi et al. (2007) demonstrated that such autoregressive techniques can be used to accurately estimate connectivity in high-density EEG recordings. Zeitler, Fries, and Gielen (2006) showed that coherence of multiunit neuronal activity was larger than for single-unit activity and that these estimates appear to be more accurate.

Thornton and Carmody, Joffe, and Hudspeth presented approaches that favor multivariate views of connectivity. Thornton's creation of his "flashlight technique" uses coherence (spectral correlation) values between a site and all other 18 sights and sums these values. This technique provides a multivariate estimate for site coherence related to all other sites. Joffe's article in this special issue demonstrates how multivariate autoregressive techniques such as partial directed coherence may be utilized to eliminate extraneous inputs so that information flow may be assessed more accurately. Hudspeth demonstrated the utility of multivariate coherence techniques more than 15 years ago (Hudspeth, 1994; Hudspeth & Pribram, 1992). This was performed elegantly through the use of a sophisticated principle components analysis algorithm that calculates coherences in a three-dimensional plane. His shared variance/focal connectivities measurements focus on average coherences between one site and other regions, emphasizing both inter- and intrahemispheric connectivities. All of these approaches emphasize multivariate approaches to connectivity assessment. By doing so, they reduce the redundancy in brain networks that adversely impacts pairwise coherence measurements. Multivariate measurements also seem to be more in line with actual functional anatomy, whereas pairwise estimates are subject to the influences of interelectrode distances.

Under the assumption that synchronization of brain regions forms the basis of neural activity (He et al., 2007), accurate assessment of connectivity should measure neurophysiological networks. Hudspeth, in the next issue, has shown that multivariate EEG connectivities are oriented toward known MRI white matter projections. This apparent face validity supports the principles that underline this approach. Additional support for this has come from a demonstration by Coben (2008).

Nunez and Srinivasan (2006) suggested that the effects of volume conduction on EEG coherence are important and independent of temporal frequency. Increases in coherence, as judged by pairwise measurements, are impacted by volume conduction for electrode sites within 10 cm of each other. As a result, coherences of moderately close electrodes have artificially elevated coherence that is not reflective of the reality of neurophysiological message transmission. This is true for referential or linked ears references. Nunez and Srinivasan (2006) suggested that laplacian montages may diminish these artifactual effects. However, this also comes with its own drawbacks impacted by spatial filtering and "edge effects" (Nunez et al., 1999; Nunez et al., 1997). The local laplacian technique has limitations including inaccurate estimates for longer interelectrode distances and for border electrodes (Cacioppo, Tassinary, & Bernston, 2007; He, 1999). Each EEG montage or reference carries its own strengths and limitations and provides a different view of the data. It should be kept in mind that all of these considerations apply only to pairwise coherence measurements. Multivariate estimates of connectivity have their value in their ability to reduce or eliminate the effects of redundancy or volume conduction.

Coben (2008) presented an initial demonstration of this fact and how multivariate estimates may correspond to neurophysiological and anatomical networks. Following the example in Nunez and Srinivasan (2006, p. 385), coherence between electrode site Fp2 and all others in the right hemisphere of a sample patient were compared. Different than the Nunez and Srinivasan (2006, p. 385) example, we used shared coherences or focal connectivities as defined in Hudspeth's article in the upcoming special issue. Intrahemispheric coherences were calculated only. To calculate shared coherences each electrode's pared coherence with all other intrahemispheric and midline electrodes are calculated. The shared coherence or focal connectivity value is the average of these 10 comparisons to a given electrode site. For example, the shared coherence at Fp2 is the average of coherences between

FIGURE 1. Shared coherence differences compared to Fp2 plotted compared to interelectrode distances. Distances above and below a difference of 10 correspond to neuronal pathways.

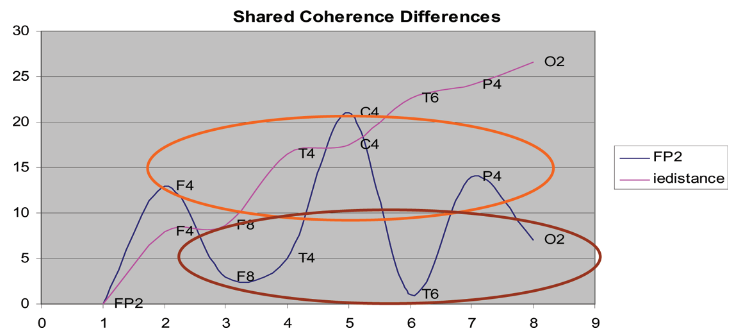

FIGURE 2. MRI-Diffusion Tensor Imaging images showing the superior lngitudingal, fasciculus, inferior longitudinal fasciculus and inferior fronto-occipital fasciculus. From Mori, S., Wakana, S., Nagae-Poetscher, L. M., & Van Zijl, P. C. M. (2005). *MRI atlas of human white matter*. Elsevier: Amsterdam, The Netherlands, by permission.

Fp2-F8, Fp2-F4, Fp2-Fz, Fp2-T4,Fp2-C4, Fp2-Cz, Fp2-T6, Fp2-P4, Fp2-Pz, Fp2-O2. Figure 1 shows the differences in shared coherences between Fp2 and all other intra-hemispheric sites along with a graph of inter-electrode distances. Two things are readily apparent in this demonstration. First, there is no longer any relationship between interelectrode distance and coherence as is the case when paired coherences are used. Second, when differences in shared coherences from Fp2 are graphed there appear to be two groups of distances that "hold together." The first group with distances from Fp2 of greater than 10 includes F4, C4, and P4. The second grouping with distances less than 10 include electrode sites F8, T4, T6, and O2.

Figure 2 is an image reprinted from Mori, Wakana, Nagae-Poetscher, and Van Zijl (2005). This figure shows known neuronal pathways as demonstrated by MRI-Diffusion Tensor Imaging. The inferior longitudinal fasciculus (brown) includes sites with coherence differences less than 10 compared to Fp2 including O2, T6, T4, F8. In comparison, the superior longitudinal fasciculus (yellow) includes sites P4,C4, F4, and possibly Fp2. This example demonstrates how the use of multivariate coherence techniques eliminates redundancy to the point where measurements may correspond to known neurophysiological networks. Clearly, further research is necessary to demonstrate this more comprehensively.

SUMMARY

This double issue and the upcoming companion issue of the *Journal of Neurotherapy* on EEG connectivity present operational/mathematical definitions for multiple concepts including coherence, cross spectral correlation, comodulation, phase delay, synchrony, and asymmetry. A significant emphasis has been placed on coherence as a measure of EEG connectivity. Multivariate measures of coherence have shown advancement over pairwise estimates in accuracy and utility. The goals of connectivity measurements should include accuracy compared to known neurological networks and utility in assessment and application for intervention (e.g., EEG coherence training). It is hoped that the information contained in these special issues will form the basis for future advancements in EEG connectivity assessment and intervention.

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