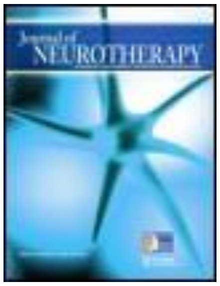

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Connectivity Assessment and Training: A Partial Directed Coherence Approach

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Connectivity Assessment and Training: A Partial Directed Coherence Approach

David Joffe, BA

ABSTRACT. *Background.* The multivariate autoregressive (MVAR) method to generate a linear model of multichannel signal processes has been employed in many fields but not applied to the assessment of quantitative electroencephalographic (QEEG) connectivity neurofeedback. A measure known as Partial Directed Coherence (PDC) derived in the MVAR framework can offer insensitivity to volume conduction and ability to provide information relating to the direction of information flow between electrode locations, as a function of frequency during QEEG assessment and neurofeedback.

Method. This article outlines a variety of reasons why PDC and other related metrics could play a more fundamental role in elucidating the causal relationships underlying EEG connectivity than can be provided though a multivariate analysis of coherence alone.

Results. Real-time PDC neurofeedback implementation issues are discussed, technical challenges are outlined, and research questions are proposed.

Conclusion. MVAR-based methods are an additional means of relating global to local EEG activity as well as helping to bridge QEEG assessment and neurofeedback protocol generation and treatment.

KEYWORDS. Coherence, connectivity, multivariate autoregressive model, MVAR, neurofeedback, partial directed coherence, QEEG

Connectivity has been defined as "the temporal correlation between spatially remote neurophysiological events" (Fingelkurts, Fingelkurts, & Kahkonen, 2005, p. 828). One of the most widely employed methods for correlating activity between pairs of electroencephalographic (EEG) electrodes is coherence, defined as "a correlational measure, varying between zero and one, of the variability in phase between two signals over time. This frequency-specific signal correlation suggests the extent to which two regions are cooperating on the same task" (Frederick, Timmermann, Russell, & Lubar, 2004). Brain connectivity can be characterized in terms of *functional* or *effective* connectivity. "Functional connectivity is defined as the temporal correlations among neurophysiological events in different neural systems, whereas effective connectivity is defined

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as the influence that one neural system exerts over another" (Mechelli, Penny, Price, Gitelman, & Frison, 2002). However, the distinction between these two terms is often blurred in practice, and therefore both terms are used interchangeably in this article.

Within the context of connectivity, neurofeedback (NFB) therapists have some general principles at their disposal to guide the conversion of quantitative EEG (QEEG) assessment information into NFB treatment protocols and treatment site selection. These strategies include normalization or "training to the Q," analysis of symptoms and their presumed neurophysiological mechanisms, use of psychometrics and/or cognitive task activation QEEG, and numerous other targeting approaches involving combinations of these.

Training at specific locations will often exert the greatest effect at those locations; however, other locations may also be affected to greater or lesser extents. For example, up and down regulation of 12 Hz activity summed between locations C3 and C4 has been reported to generate widespread changes in power and coherence across the cortex as a function of frequency (Delorme & Makeig, 2003). Egner, Zech, and Gruzelier (2004) also reported that training specific frequencies at specific locations on the scalp resulted in changes at other locations and frequencies. NFB clinicians are often distinguished by their ability to select a training site and frequency band that will raise or lower the amplitude of yet another frequency band at a seemingly unrelated electrode site.

Many coherence relationship pairings are in reality a function of one or more influencing sites or sources. These findings are not unexpected given the level of interconnectivity that characterizes the brain. One can reasonably argue that brain interconnectivity models support the idea that any QEEG metric computed at any particular scalp electrode location can also be affected to some extent by training at many other locations via a variety of metrics. The simultaneous or sequential effects of training one measure such as power, on another measure such as coherence, are complex and poorly understood. A shift in connectivity is not best accounted for in terms of one limited measure such as power, or coherence, but rather across all available measures. In other words, each of the QEEG measures in common use describes some limited aspect of a far more complex pattern of neural connectivity. Given these complexities, it may be productive at the outset to perform QEEG assessments and NFB using fundamental and inclusive connectivity analysis methods. Such fundamental measures may lead to a better understanding of the effects of training one particular measure on another, as they will both then be analyzed in common terms. In the search for a unified connectivity framework with an emphasis on integrating global (involving 19 or more sites) and local (typically involving 1 to 3 sites) aspects of connectivity, namely, causality and conduction, need to be addressed.

In a review of "Hudspeth's Method of Coherence Analysis," Lewis (2005) concluded that "in the conventional QEEG analysis of coherence values, the detection of a problematic paired-site value says little about its source location." In other words, any two particular scalp electrode locations, between which coherence is calculated, may themselves be influenced by one or more additional electrode sites, thus giving rise to a misleading estimate of coherence at one or more frequencies. One approach to addressing this problem might be to use partial coherence (Jenkins & Watts, 1969) to supplement current coherence metrics. Partial coherence "partials out" the contribution of any other locations, which may contribute to the shared activity measured between any two locations. The coherence remaining would then be the activity between the two locations that could not be accounted for by the influence of any other locations. However partial coherence alone still does not address the problem of causality because it cannot provide information relating to the *direction* of information flow. Brain networks have been described as *causal* in the sense that information flows or is actively transmitted from one location to another in an organized fashion (Sporns, 2003) rather than simultaneously from each location to every other. The flow of brain network information can be characterized in terms of EEG time series. Specifically, Weiner (1956) introduced the idea of causality in terms of predicting one time series from another.

NFB protocols do not currently incorporate causal information in an explicit fashion and the lack of causal information may make certain QEEG derived measures and training results hard to interpret. For example, if a "third" site is in fact driving the coherence or correlated relationship between two target sites, then clinicians may be chasing the effects rather than the causes of the problems they are attempting to remediate. Generally it is left up to the experienced practitioner to piece together the puzzle of global connectivity comprised of the interaction between all possible pairs of electrode sites. Although some NFB practitioners have been turning to functional neuropsychological testing and cognitive task-activated QEEG assessments to address this need (e.g., Thornton & Carmody, 2005), the manner in which a NFB clinician reduces interpretive complexity, and isolates key training variables in the neural function under investigation, often relates more to his or her own implicit causal reasoning than any formal paradigm or method of analysis.

Electrical transmission in the brain is dependent upon volume conduction and network connectivity. Volume conduction involves the passive transmission of electrical charge through the ionic medium of the brain, whereas network connectivity requires the active transmission, possible modification, and then retransmission of electrical signals over neuronal pathways. Volume conduction is virtually instantaneous and cannot account for the communication delays involved in network information transfer (Thatcher, Biver, & North, 2007). Although NFB training involves network connectivity, there is no evidence that cortical volume conduction can be changed, nor does it have any reported diagnostic value. However, volume conduction can act as a confounding variable in QEEG analysis by biasing various QEEG derived parameters, such as coherence (Barry, Clarke, McCarthy, & Selikowitz, 2005). Srinivasan, Winter, Ding, and Nunez (2007) reported that across all frequencies, EEG coherence can be elevated by volume conduction, including electrodes separated by less than 10 cm and more than 20 cm. They suggested the use of surface Laplacian techniques to reduce the effects of volume conduction on coherence.

Phase is intrinsically involved in the computation of coherence, and this lead or lag between any two measured EEG signals is readily available (Thatcher et al., 2007). Because volume conduction takes place almost instantaneously, any two signals that are out of phase, or that lead or lag each other, cannot be the result of volume conduction. Thus, volume conduction implies almost no phase difference. Ideally, rather than interpretation of coherence in the context of phase, it would be desirable for the algorithms involved in any unifying connectivity framework to suppress the effects of volume conduction. It is important not to confuse "zero lag links" or "high phase synchronization" or "nonlocal synchronization" with the instantaneous zero phase angle indicative of volume conduction. Zero lag cortical oscillations associated with coherent gamma activity (Knoblauch & Sommer, 2004) and alpha phase synchrony (Hebert, Lehmann, Tan, Travis, & Arenander, 2005) have been reported. Although the mechanisms postulated for this synchronization at a distance are complex, they involve not volume conduction but rather the simultaneous driving of two or more neural networks by one or more additional neural networks, or alternatively the emergent behavior of reciprocally connected networks (Amari, Nakahara, Wu, & Sakai, 2003).

To sum up, any practical integration of global multichannel QEEG assessment with local NFB in the context of connectivity would ideally involve some kind of unified signal processing framework that would allow the NFB practitioner to relate global and local information; be relatively insensitive to volume conduction; capture the causality (or predicted composition and direction of certain EEG measures), which is an intrinsic quality of brain networks; and scale naturally to any number, or scalp density, of recording electrodes. The QEEG analysis NeuroRep (Hudspeth, 1999) was designed to analyze "beyond the pairwise coherence comparisons and look at multivariate relationship patterns in the brain in order to determine the direction of the information-processing problem "flow" as well as the system of sites involved with a given problem" (Gismondi, 2007, p. 35). However, this article proposes a complementary multivariate approach, which although differing in certain key aspects also addresses the issue of directional EEG connectivity. This multivariate approach, although widely utilized in many other fields, has not yet apparently found widespread application in QEEG assessment relating to NFB.

THE MULTIVARIATE AUTOREGRESSIVE MODEL

If in the past, samples of an EEG channel A could somehow predict or estimate some portion of the current sample of an EEG channel B, then A could be influencing the changes of B over time, assuming there were no other channels influencing both A and B in a similar manner (Granger, 1969). By the definition of this influence, the use of past samples in time would not effectively model the portion of B caused by instantaneous volume conduction from A, for the simple reason that the current sample of channel A would not be included in the estimation process. Such a process or model would be largely insensitive to volume conduction. A significant portion of the current sample of the EEG measured at any location can indeed be predicted or estimated from a linear weighted combination of past samples measured at that same location (Rappelsberger & Petsche, 1975) or from past samples at another location. This is known mathematically as an autoregressive (AR) process. The AR process entails the summation of appropriately weighted samples of a signal's past activity to predict a significant portion of the same (or another) signal's current activity (Marple, 1980). The EEG is therefore considered to be an example of an AR process, or at least possess strong AR components. In the case of the EEG, between four and eight past samples are usually sufficient (Vaz, De Oliveira, & Principe, 1987) to generate a fairly accurate prediction of its current sample.

The efficiency of modeling the EEG using linear AR techniques does not imply that the brain itself operates according to primarily linear dynamic principles or that nonlinear techniques cannot be effective. However, although many nonlinear information flow analysis techniques have been applied to the EEG (see Natarajan, 2004), it has been suggested that the EEG can most parsimoniously be modeled as a linear process, except for certain types of epileptic seizures (Kaminski, 2005). Astolfi et al. (2005) noted that "linear measures . . . afford a rapid and straightforward characterization of functional connectivity" (p. 155).

The number of past samples required for an accurate estimate of the current EEG sample is referred to as the *order* of the process, and the weighting factors applied to the past samples are known as the *autoregressive coefficients*. Both the order and the value of the coefficients of the AR process may change as the raw EEG waveform and its spectral representation evolves over time as a function of changing state. The estimation of the optimal AR coefficients for any given order and particular EEG time series can be accomplished using many different algorithms, each with its own particular strengths and weaknesses involving tradeoffs relating to complexity, speed of computation, accuracy, sensitivity, and stability. In addition, the EEG spectrums generated from AR coefficients have an improved frequency resolution (Marple, 1987) when compared to the Fourier transform commonly used for QEEG analysis and NFB.

Because the brain is so densely interconnected, it is usually possible to predict a portion of the current activity measured at some scalp location A from past values measured at one or more additional scalp electrode locations B, C, D, and so on (Hesse, Moller, Arnold, & Schack, 2003). When taken as a whole then, a complete description of the linear causal relationships between all of the interacting locations can be provided if they are analyzed simultaneously by what is known as a multivariate autoregressive (MVAR) model (Kus, Kaminski, & Blinowska, 2004). Simulations have confirmed that if all of the signal source information is present in the set of locations measured, then the resulting MVAR process will correctly sort out the linear influences between all of the locations (Kaminski, 2005).

Honey, Kotter, Breakspear, and Sporns (2007) stated that "functional networks recovered from long windows of neural activity (minutes) largely overlap with the underlying structural network, and as a result, hubs in these long-run functional networks correspond to structural hubs." Consequently it is not unreasonable to hypothesize that for any block of EEG of sufficient duration, a set of AR coefficients can be computed characterizing the causal or directional relationship between every pair of measured scalp electrode locations. This would reflect to some extent the underlying anatomical structure-function relationships as well. Therefore, even though the EEG is nonstationary (i.e., constantly changing) the underlying pattern of connectivity will be reflected in the MVAR coefficients (Astolfi et al., 2007). However, the fundamental question pertaining to the relationship between cortical and scalp activity must still be addressed.

The EEG signal measured on the scalp is a distorted version of the signal present on the surface of the cortex (Freeman, Holmes, Burke, & Vanhatalo, 2003) because of the presence of intervening anatomical structures between the cortex and the scalp and certain electrical properties of the various structures that tend to "smear" out the electrical patterns as well as filter out higher frequency components. Information present at each scalp EEG electrode site is "a mixture of local, regional, and global sources" (Srinivasan, 2006). For these and other reasons, Pascual-Marqui (2007) stated, "This should be taken into account when interpreting the results of many publications with wire-diagrams based on significant connections between scalp electrode time series: these extracranial-based 'wires' do not necessarily correspond to 'wires' connecting the underlying cortices" (p. 6). However, the literature suggests that given a sufficiently high density of scalp electrodes, reasonably accurate estimates of cortical activity using MVAR methods (Astolfi, 2005) can be achieved.

Therefore, if the goal is to characterize electrocortical dynamics and generate neurologically plausible MVAR results, then the issue comes down to what spatial resolution (number and density of scalp electrodes), with or without EEG localization methods, is required to generate a reasonably accurate estimate of underlying electrocortical information flow within the frequency band range of interest based on scalp measurements. This will most likely require more than the standard 19 International 10–20 electrode montage currently used for both assessment and treatment in the neurofeedback context. The electrical activity measured on the scalp is a distorted representation of the underlying cortical activity, therefore the rationale underlying the application of MVAR methodology to 19-channel EEG scalp data is not an attempt to accurately characterize the underlying cortical electrodynamics but rather to help resolve ambiguities inherent in classical scalp based coherence measurements while indicating the directional flow of the distorted cortical dynamics present on the scalp.

RESEARCH

There is a small but growing MVAR/EEG literature. For example, EEG event related potentials were successfully subjected to MVAR analysis (Vasios, Matsopoulos, Nikita, & Uzunoglu, 2004). Schloegl (2006) characterized the goal of applying MVAR techniques to evoked potentials as being "to uncover the transient cooperation between different brain sites" (p. 159). A version of the MVAR-based directed transfer function, the short time directed transfer function, has been developed for analysis of rapidly changing EVP/ERP dynamics (Kaminski, Zygierewicz, Kus, & Crone, 2005). Schloegl, Trujillo-Barreto, Muler, and Gruber (2007) reported that the PDC detected an augmentation of induced EEG gamma-band responses to familiar objects. Another recent MVAR application to EEG analysis by this author involved the generation of MVAR matrices associated with 19-channel EEG collected during baseline and Ayahuasca drug induced states (Echenhofer, Wynia, & Joffe, 2007). Unique directional information flow patterns were reported, which discriminated baseline from Ayahuasca conditions.

METHODOLOGY

The MVAR coefficients characterizing the linear causal relationships between all of the measured scalp electrode locations can be assembled into one matrix (Kaminski, 2005) where the information at each matrix location corresponding to row I and column J represents the degree of influence of scalp location J on location I, according to the conventional notation. However, the MVAR EEG modeling process takes place in the time domain, whereas most QEEG assessment and NFB is performed in the frequency domain. Fortunately, the time domain influences between all locations can be transformed into the frequency domain by computing the Fourier transform of the MVAR coefficient matrix, and thus the influence of every location on every other can be calculated as a function of frequency as well (Kaminski, 2005). The frequency transformed MVAR coefficients can again be organized in the form of a matrix, in which the information at each matrix location corresponding to row I and column J now represents the influence of location J on location I as a function of frequency.

A normalized version of this frequency domain matrix can be defined. It is known as the partial directed coherence or PDC matrix (Kus et al., 2004). The magnitude of every element of each spectrum in the PDC matrix ranges from between 0 to 1, similar to coherence. However, the PDC differs from classical coherence in three important respects. First, the PDC between locations A and B is not necessarily symmetric. This means that the direction and amount of information flow between locations A and B at each frequency can be specified and that feedback, or bidirectional coupling influences, can be detected (Supp, Schloegl, Trujillo-Barreto, Muller, & Gruber, 2007). Second, because the PDC is a partial measure, it reflects the activity between two locations A and B at each frequency minus the influence of any other additional locations at that frequency. Third, the PDC can differentiate between direct and indirect causality (Astolfi et al., 2007). If location A influences location B at a particular frequency, and location B influences location C at the same frequency, then location A will not be characterized as directly influencing location C at that particular frequency, unless there truly exists a direct casual influence from A to C as well. Supp et al. (2007) described how "the multivariate PDC approach measures how several positions are 'effectively' connected (i.e. exclusively revealing direct connections by correcting for indirect influences) rather than merely describing pair-wise synchronicity" (p. 2). However this is not the end of the story as additional MVAR frequency domain measures (e.g., the directed transfer function; Kaminski & Blinowska, 1991) can be computed and used to characterize EEG information flow as well.

In summary, raw multichannel EEG can be modeled by an MVAR process, the coefficients of which are then converted into the frequency domain. PDC as a function of frequency can then be derived from the frequency domain representation of the MVAR process. Through both simulation and analysis of experimental data, Astolfi et al. (2007) characterized the performance of MVAR measures such as the PDC by establishing maximum error bounds for these metrics in multichannel EEG data blocks of varying lengths and signal-to-noise ratios. These results support the use of MVAR techniques for QEEG analysis.

Thus, the MVAR derived metric, PDC, can provide a unifying framework that meets the criteria just outlined, and in a manner that better reveals connectivity patterns while minimizing the contributions of volume conduction. In addition, zero lag nonlocal synchronization would still be modeled as well as the influence of additional electrode locations on the coherence computed between pairs of electrodes.

The author investigated PDC performance by processing numerous raw 19-channel EEG data files and noted a significant global reduction of the PDC at many frequencies between most pairs of electrodes, when compared to the standard coherence computed between those same pairs. In addition, the "shape" of the PDC frequency spectrum, as compared to the coherence frequency spectrum between any pair of scalp electrode sites often differed significantly as well. This strongly suggests that current NFB training methods derived from classical coherence assessments may not be based on the most accurate global dynamics picture available.

According to Thatcher et al. (2007), "connectivity is defined as the magnitude of coupling between different electrical energies recorded from different locations of the brain independent of volume conduction" (p. 6). Therefore, the PDC MVAR measure would appear to be ideally suited for connectivity analysis. The PDC has been discussed in the context of off-line assessment, but it may be possible to generate the PDC in real time.

Multivariate Feedback

Adaptive filters are widely utilized throughout the world of physiological signal processing and play explicit or implicit roles in all modern NFB implementations. Adaptive filters are designed to automatically minimize the difference between their predictions and some target signal(s). This is accomplished by feeding back the difference (or errors) between the prediction(s) and the actual target value(s) in such a manner as to improve the adaptive filter's predictions in the future. From an algorithmic perspective, this involves the use of one or more learning rules (Wang, Manry, & Schiano, 2000). Although different algorithms are designed to converge according to different schemes, given sufficient time a well-designed adaptive filter will converge to the best estimates possible, and in a stable manner. This resembles the process of NFB itself, which involves a continuous adaptation or error correction between the individual's internal state as represented by the neurofeedback signal and some desired target state.

PDC computations can be accomplished in real time using adaptive multivariate autoregression (Schloegl et al., 1997). Adaptive multivariate autoregression (AMVAR) filters also learn through the process of trial and error previously described. However, the process of learning in this context involves far more complex rules than the single channel case, as it takes place in a multichannel multivariate environment. Well-constructed AMVAR algorithms are also guaranteed to converge given sufficient time, assuming the raw EEG data are reasonably well behaved (i.e., not contaminated with artifact).

One of the most popular AMVAR filters that has been applied to both background EEG and evoked potentials is the Kalman filter (Tarvainen, 2004). Kalman filters played an indispensable role in the Apollo space program by helping astronauts navigate accurately to the moon in spite of the noisy nature of their observations (Cipra, 1993). Kalman and related filters work their magic by building accurate and constantly updated models of an incoming signal. In the case of Apollo, the signal consisted of measurements of the spacecraft's trajectory. In a similar manner, the Kalman class of adaptive filters builds a constantly updated model of the underlying multivariate multichannel autoregressive process which can be conceptualized as generating the EEG data *trajectory*. The inherent robustness of Kalman type filters in noisy real-time EEG settings (Dharwarkar, 2005) may be especially helpful in NFB applications where the acquired EEG is often contaminated by various kinds of artifact. The AMVAR filter generates a constantly updated (on a sample-by-sample basis) multivariate multichannel AR matrix, which can then be transformed into the PDC matrix using methods previously outlined in conjunction with the non-realtime MVAR case. However, great care must be taken when implementing AMVAR algorithms because of the nonstationary nature of the EEG. Nonstationarity, in this context, means that the time domain EEG, its frequency representation, and all the interchannel relationships in both of these domains tend to change often and abruptly without warning (Fingelkurts, 1998). Therefore AMVAR filters must be designed to balance the opposing necessities of rapidly tracking EEG transitions while maintaining sufficient inertia to provide stable and accurate NFB, and in a timely manner so as to satisfy the temporal constraints of classical conditioning and deconditioning (i.e., disentrainment) paradigms.

Only a relatively few enterprising neurotherapists perform full 19-channel hookups during NFB on a routine basis, although this practice is growing in popularity. Full-cap EEG hookups during NFB allow for both the rapid selection of different electrode locations required by various neurofeedback protocols as well as the acquisition of 19-channel EEG data for pre-post or simultaneous assessment purposes. Research software developed by the author in the mid-1990s supported the provision of NFB while 19-channel raw data were acquired in the background. This allowed for the offline characterization of global EEG effects associated with NFB training protocols targeted to specific locations. More recently Ibric, Dragomirescu, and Hudspeth (in press) also utilized full-cap montages to characterize real-time changes in connectivities during NFB. However, and to the best of the author's knowledge, EEG NFB involving all 19 channels simultaneously is currently implemented only during sLORETA (Pascual-Marqui, 2002) feedback, as provided on a number of commercial brain mapping and NFB systems, as full-cap data are required to generate either real-time or off-line LORETA based estimates of cortical activity (Congedo, Lubar, & Joffe, 2004).

In most cases, a minimum of 19 channels will be required to generate useful offline or real-time MVAR estimates. Using significantly fewer than 19 channels to generate AMVAR NFB for one or more target locations means that some real scalp "sources" may be ignored, potentially resulting in erroneous estimations of cause and effect (Eichler, 2005). Still, various electrode location influences can be largely sorted out and identified by MVAR or AMVAR based techniques if a sufficient number of channels are available (Eichler, 2006).

However, there may be situations where a 19-channel full-cap hookup is not required for the implementation of PDC-based NFB algorithms. For example, if a NFB protocol involves the measurement of the PDC between locations C3 and C4, and the contributing sources of information flow in the desired frequency band(s) are determined during the assessment phase to be largely restricted to only a few locations in addition to C3 and C4, it may be possible to implement a reasonably accurate AMVAR PDC algorithm using fewer than 19 channels. This example is predicated upon the assumption that the global EEG dynamics during the NFB phase will remain similar to those characterized during assessment. To verify the truth of this assumption it may be advisable to perform full-cap assessments periodically throughout the training phase, if less than a full-cap 19 location montage is utilized for PDC neurofeedback.

With the advent of newer 32 (and above) channel brain mapping and feedback systems, MVAR-based methods such as the PDC applied to scalp EEG will increase in accuracy relative to the underlying electrocortical dynamics. Still, 19-channel PDC applied in the context of NFB will present significant challenges to the programmer and/or systems designer because the computational overhead involved is significant. Implementing robust real-time PDC will require a level of signal-processing computation not previously encountered in the NFB setting. This will present difficult (but motivating to those so inclined) sets of trade-offs and compromises. The problem is "nontrivial," as the engineering expression goes; however, even on a modern PC running at a GHz clock speed, it is by no means intractable. The clinical results may very well justify efforts to develop suitable real-time PDC neurofeedback algorithms. Assuming real-time PDC implementation challenges can ultimately be overcome, it could be possible to train individuals using the PDC or any other MVAR-derived metric applied to any location or combination of locations, as is currently the practice with coherence, power, and asymmetry. In addition, Z-score-based PDC training, as well as other MVAR-derived metrics could also be implemented using MVAR Z-score values generated from the raw data supporting existing normative QEEG databases.

MVAR, AMVAR and Source Localization

All of the MVAR/AMVAR-based techniques, such as the PDC, can in theory be used to characterize cortical as well as scalp-based connectivity. Specifically, MVAR algorithms are applied to the EEG time series produced in each cortical region of interest by the localization methods. However, EEG localization techniques, as with all forms of EEG signal processing, involve performance trade-offs. MVAR models have been combined with EEG source localization methods in offline implementations, resulting in the generation of estimates of directional influence between cortical depth locations. Unfortunately, cross-talk between cortical regions is an unavoidable side effect of many of the EEG source localization methods currently in use. For example, prior to the application of MVAR, Hui and Leahy (2006) were required to employ a technique known as beamforming to eliminate spurious sources of communication between cortical regions, generated by their EEG localization methods.

AMVAR algorithms could also be integrated with real-time LORETA (Congedo et al., 2004) as well as other EEG inverse solutions such as subspace projection filtering combined with sLORETA (Congedo, 2006). This would impose additional levels of computational complexity and physical assumptions. With the addition of AMVAR techniques, the future of multichannel NFB could conceivably involve training specific connectivity patterns between cortical brain regions at depth, thus bringing the practice of NFB more closely into line with emerging neurophysiological models generated by other neuroimaging modalities such as fMRI, SPECT, or PET. However, this will most likely involve far denser scalp electrode arrays than the common 19-channel montage in current use. Once again, with the availability and cost of 32-channel QEEG mapping systems already within the grasp of the working neurotherapist, and such systems destined to become even more affordable as clinical applications mandate their use, the union of MVAR and localization techniques could eventually become an accepted standard of practice.

Clinical Research Questions

Following are a few of the many interesting connectivity related questions that might be fruitfully addressed using MVAR/AMVAR-based methods, and that possibly may lead to more optimal QEEG assessment and NFB training protocols:

1. If a QEEG metric is up or down trained at a particular location A, and A is influenced by locations B and C, or A influences B and C, will the metric measured at B and C also change proportionally to the influence?
2. If a QEEG metric is up or down trained at a particular location A but is influenced by locations B and C, will it take less time to achieve the training goal if locations B and C are trained directly or if A, B and C are trained simultaneously?
3. If a QEEG metric is up or down trained at a particular location A over some frequency band, and location B influences A over part of the band, and location C influences A over the rest of the band, will it be more efficient to train at B and C over different parts of the band simultaneously, than to train directly at A over the whole band?
4. AMVAR algorithms can be modified to compute the correlation between pairs of directional influences at the same or different frequencies or bands. Might there be a clinical utility in learning to use the

directed influence of a particular frequency or band from location A, to modify the directed influence(s) in the same or different band from location B? Can the brain adapt to and work with arbitrarily complex feedback algorithms?

5. Clinicians have reported that up and down training power followed by coherence training (or vice versa) is an effective way to treat various disorders. For example, one study (Walker, 2006) determined that power followed by coherence training was effective for reducing the frequency of seizures. To analyze the effect of training one modality, such as power, on the subsequent training of a modality such as coherence, might it be more productive to ask how the information flows underlying the observed power patterns relate to the information flows influencing the observed coherence patterns, or the reverse, thus reformulating the problem of sequencing or combining NFB protocols in terms of a least common denominator?
6. Given that "significant fluctuations in functional topology are observed across the sequence of networks recovered from consecutive shorter (seconds) time windows" (Honey et al., 2007, p. 10240), what are the optimal EEG data analysis lengths that should be employed to most effectively relate MVAR QEEG assessment to AMVAR-based NFB training?

SUMMARY

This article has shown that additional connectivity and information flow insights can be extracted during multichannel QEEG assessment using the technique of multivariate autoregressive analysis or MVAR to generate metrics such as the partial directed coherence or PDC. This technique can be implemented in real-time for NFB and provides a means of relating global EEG activity to local activity in both offline assessment and real-time training settings. MVAR could be integrated with other methods of analyzing global EEG connectivity, such as those employed by various EEG localization algorithms.

As practitioners and researchers attempt to categorize different connectivity assessment systems and begin to implement preliminary versions of these tools and work with clients, they will need to clarify how clinical decisions are made. This will include what connectivity links are to be trained, in what priority or sequence, and what connectivity measures are ignored. It can be argued that even now QEEG assessment reports often present a bewildering array of difficult-to-interpret connectivity abnormality information to the clinician. The proposed MVAR/AMVAR-based PDC approach can assist the NFB clinician to assimilate this information and fashion an effective treatment plan.

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