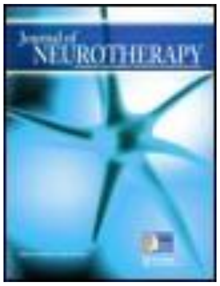

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Functional Connectivity and Aging: Comodulation and Coherence Differences

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Functional Connectivity and Aging: Comodulation and Coherence Differences

David A. Kaiser, PhD

ABSTRACT. *Introduction.* Misconceptions about coherence and comodulation has hindered their simultaneous use in assessing electroencephalography (EEG). Coherence refers to phase synchrony, whereas comodulation refers to magnitude synchrony. Child and adult EEG data were analyzed for age functions to demonstrate coherence and comodulation differences.

Method. Eyes closed resting EEG was analyzed for 101 children and adults between ages of 5 and 35 years (34 female, 67 male; M age = 17.5 years). Spectral analysis focused on site-centered connectivity of 10 frequency bands. Site-centered connectivity refers to averaged coherence or comodulation associated with a site, an estimate of its network traffic.

Results. Site-centered coherence and comodulation increased with age for frequencies below 30 Hz in most sites. Age-related changes in anterior connectivity occurred for adults but not for children. The strongest age function was found for alpha comodulation at electrode site T5. Differences in coherence and comodulation results are also reported.

Conclusion. Functional connectivity increases steadily with age. Anterior EEG connectivity increased during adulthood but not during childhood. This finding parallels previous research on anterior callosal myelination and suggests that EEG connectivity measures may in part reflect myelination patterns. A model that associates coherence and comodulation with feedforward and feedback activity of the brain is proposed. A Periodicity Table for creating new and potentially relevant psychophysiological coefficients was described.

KEYWORDS. Age, coherence, comodulation, EEG, entropy, maturation, periodicity table

Neurons can fire a hundred times a second or more but to process information autorhythmicity must be suppressed (Goldensohn & Purpura, 1963; Hopfield, 1999; Steriade & Llinás, 1988). Cortical minicolumns act as functional units and when autorhythmicity is suppressed in 2,000,000 units (6 cm^2), it can be detected by scalp electrodes (Calvin, 1995; Casanova & Tillquist, 2008; Cooper, Winter, Crow, & Walter, 1965; Mountcastle, 1957, 1978). Cortical networks consist of pools of minicolumns that synchronize or desynchronize to higher order information such as faces or words (Koelsch et al., 2002; Kowatari et al., 2004). We can detect cortical networks electroencephalographically by

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analyzing synchrony between near and distant brain sites (Gerloff et al., 2006; Mountcastle, 1997; Tiesinga & Sejnowski, 2004). Electroencephalography (EEG) patterns within and between cerebral hemispheres indicate that cortical networks increase in number, complexity, and functionality as the human brain matures (Eeg-Olofsson, 1980; Hudspeth & Pribram, 1992; Schack, Chen, Mescha, & Witte, 1999; Srinivasan, 1999; Stam, Hessels-van der Leij, Meulstee, & Vliegen, 2000; Thatcher, North, & Biver, 2007).

Scalp potentials reflect the number of inhibited neurons compared to uninhibited neurons at one location compared to another (Nunez, Wingeier, & Silberstein, 2001; Silberstein, 2004). Spectral magnitude is a summary of this rhythmic inhibition and power an estimate of its variability (Tenke & Kayser, 2005). Spectral analysis was invented to study heat diffusion (Fourier, 1822), but it was a century later when spectral analysis matured to include a coherence function, a measure of similarity between time series as a function of frequency (Hilbert, 1930; Wiener, 1930). Decades passed before a coherence function was applied to human EEG (Goldstein, 1970; Orr & Naitoh, 1976; Walter, 1968). Coherence may be estimated by comparing real and imaginary components of a waveform (Goodman, 1957), with a Hilbert transform (e.g., Boeijinga & Lopes da Silva, 1988) or inferred statistically (Arnhold, Grassberger, Lehnertz, & Elger, 1999; David, Cosmelli, & Friston, 2004; Lopes da Silva, Pijn, & Boeijinga, 1989; Stam & van Dijk, 2002). Magnitude synchrony was investigated early on (Barcaro, Denoth, Murri, Navona, & Stefanini, 1986; Larsen, 1969), but coherence and spectral correlation were defined similarly, limiting research. In the past, coherence was described as an estimate of the correlation coefficient between the Fourier components of two time-series at a given frequency (Mellors, Vernon, & Thomson, 1998; paraphrasing Priestley, 1981), but this is in error as magnitude synchrony is not phase synchrony.

Few have investigated magnitude synchrony as thoroughly as Sterman and Kaiser (1999, 2001; also Kaiser, 2006a, 2006b), who drew renewed attention to this form of synchrony and called it comodulation (see Figure 1). Comodulation analysis was used by this team to evaluate spatial resolution of EEG topography. According to the low spatial resolution hypothesis, electrical potentials at the scalp should be similar regardless of sensor location (Nunez, 1981). Although spatial resolution is always a concern with EEG, comodulation identified anticipated functional groupings at 10–20 electrode positions, proving that some topographic resolution at the scalp exists, even with a referential montage (Kaiser, 1994).

Complementary properties typically exclude each other but at the same time complement each other mutually to give a complete view of the phenomenon under study (Atmanspacher, Romer, & Walach, 2002; Bohr, 1948). Coherence and comodulation are complementary spectral properties. Coherence is a normalized measure of similarity between two signals in terms of phase difference. Comodulation is a normalized measure of similarity between two signals in terms of magnitude difference. Together they specify linear and symmetrical unispectral dependence between two (pseudostationary) signals based on temporal variation. Coherence is estimated by cross-spectra to autospectra averaged over time (Goodman, 1957). Comodulation is estimated by mean cross-product of normalized spectral magnitude over time, a Pearson (1896) product moment correlation of spectral magnitudes. In addition, phase difference (or lag) and magnitude difference (or asymmetry) complement these measures, specifying linear and symmetrical unispectral dependence between signals ignoring temporal variation. All of these measures

FIGURE 1. The relationship between coherence and comodulation.

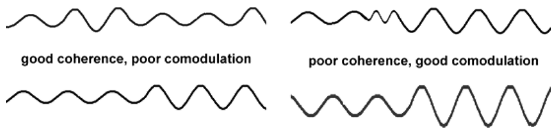
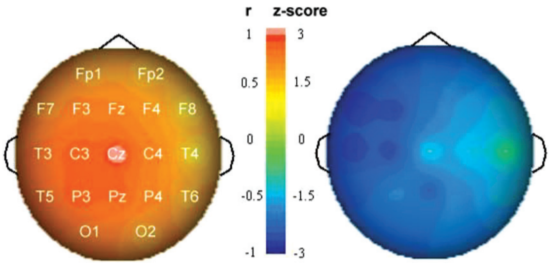


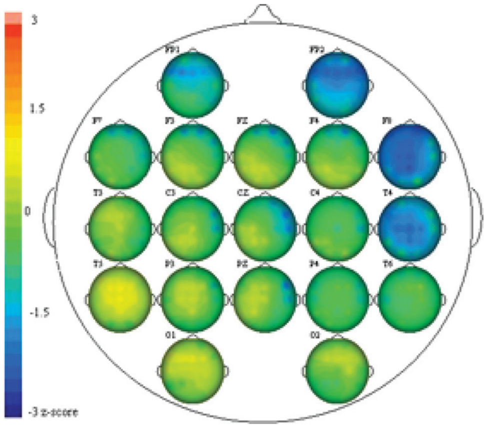
FIGURE 2. The 10–20 international electrode positions.



produce 19 auto-pairings and 171 pairings for 10–20 international electrode positions; see Figures 2 and 3. (Which increases to 73 autos and 2,628 pairings for the 10–10 electrode position.) Combined, these four measures provide thorough assessment of functional connectivity (see Figure 4).

Neurotherapists attempt to restore impaired collaborations within and between brain areas by momentarily adjusting EEG toward a preconceived ideal based on a client's age or maturational state. Mental fitness is conceived as a healthy blend of EEG rhythms and synchronies; unfortunately, the extent of our understanding of an ideal (adaptive) physiology is limited in part by the number and sophistication of parameters used to characterize brain wave activity. Currently, most neurotherapists rely on a handful of indices that may be summarized as consistency or difference of magnitude or phase for one or more sites at one or more frequencies (see Table 1).

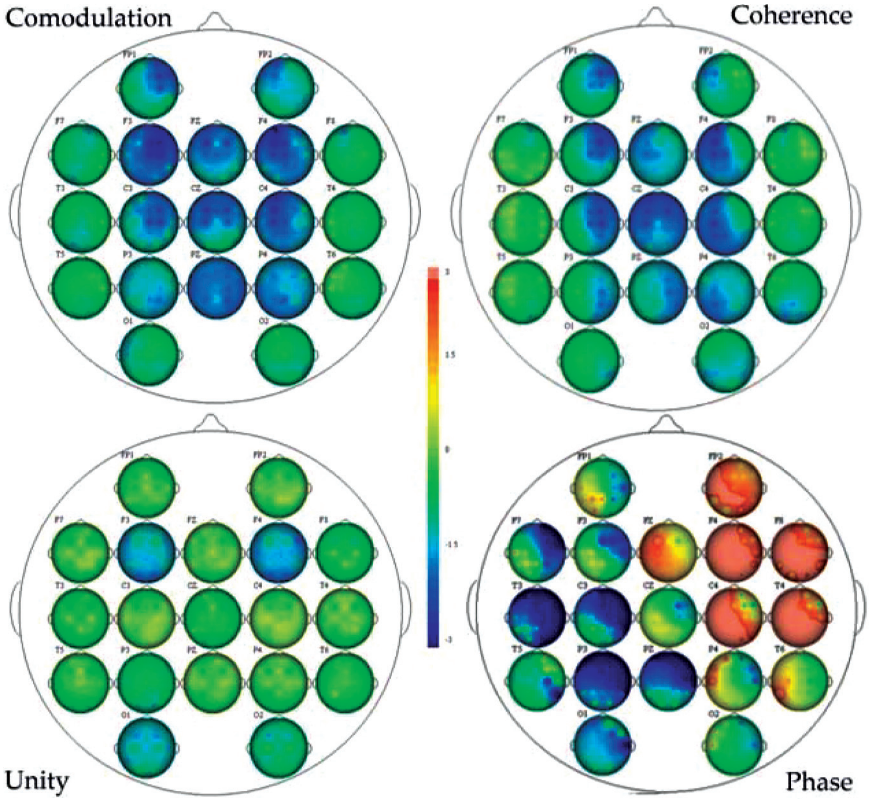
FIGURE 3. The 10–20 international electrode positions with 19 auto-pairings and 171 pairings.



Measurement of any relationship between two or more EEG periodicities involves a number of computational freedoms including formulation, montage selection, and statistical normalization (see Figure 5). Nunez et al. (1997) concluded that "studies of coherence and brain state should include several different kinds of estimates to take full advantage of information in recorded signals" (p. 470). Toward this end a "Periodicity Table" is proposed, a framework that organizes forms of EEG synchrony into groups based on number of signals, number of coupled frequencies, and whether we examine differences across time or ignore time altogether. Coherence and comodulation are positioned in adjacent cells in this framework. As shown in Table 1, spectral magnitude and its square (spectral power) share the same cell. In fact any central tendency of EEG could share this cell including median frequency, modal frequency, or 95% spectral edge (Drake, Pakalnis, & Newell, 1996).

By analyzing EEG synchronization between electrode sites, we evaluate the likelihood that cortical networks are functional enough to manage age-appropriate challenges, especially self-regulation. Does a specific challenge such as reading or rest have anticipated psychophysiology? To what extent is the dominant frequency present? Is there age-appropriate hyperpolarization? Are sufficient fast frequencies present or do slow rhythms dominate? Are faster frequencies synchronized with slower ones or acting independently? We decompose EEG into an orderly arrangement of clinical clues, and the Periodicity Table is an extension of this principle. Keep in mind, however, that when we transform four-dimensional (or e-dimensional) electrochemistry into coefficients we presuppose an afluidity associated with these signals. We are asserting that anyone's EEG can be locked into a limited range of responses, which may reasonably approximate abnormal psychophysiology (Hughes & John, 1999) but is hardly the dynamic of a healthy brain.

FIGURE 4. The 10–20 international electrode positions for the measures of comodulation, coherence, unity, and phase.



The goal of this article is to differentiate phase synchrony from magnitude synchrony (coherence, comodulation) and to determine how both forms of synchrony might vary as a function of age and topography. Given the large number of possible cortical networks detectable at a 10–20 electrode position using single-Hz frequency divisions, conventional bands were analyzed and site pairings were reduced to site-centered averages to reduce Type I and II error.

METHOD

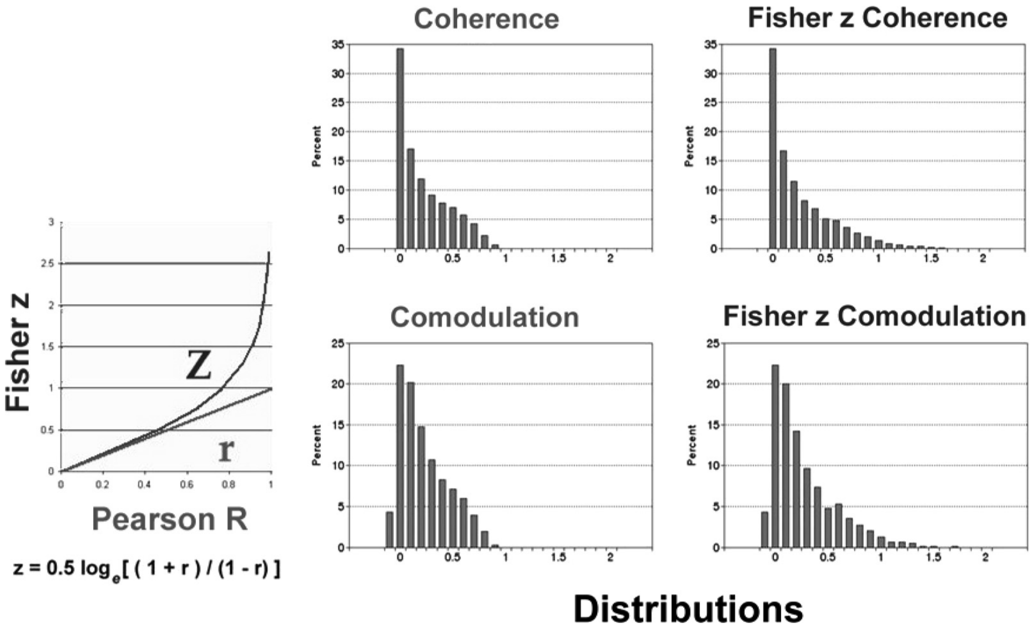
Participants

EEG was acquired from 101 healthy participants (96 right-handed, 5 mixed dominance or left-handed), of which 43 were children between the ages of 5 and 16 ($M = 10.5$ years, 19 female, 24 male), and 58 were adults, of ages 18 to 35 ($M = 22.7$ years, 15 female, 43 male; group $M = 17.5$ years). Participants underwent eyes closed and open baseline and task conditions. Handedness was determined by a modified Edinburgh Handedness Inventory (Oldfield, 1971) and/or confirmed by writing samples from each hand. Participants reported no history of a neurological disorder, no use of a controlled substance 24 hr prior to the study, and no recent experiences that could be expected to alter psychophysiology (e.g., disturbed sleeping habits, atypical stress). Participants were recruited from University of California at Los Angeles; California State University, Northridge; Rochester Institute of Technology; and clinician offices. Informed consent was obtained from each adult prior to his or her participation, using a form approved by a Veterans'

TABLE 1. A Periodicity Table of spectral measures popular within neurotherapists.

			ELECTRODE SITES					
			1		**2**		**Many**	
			State	Stability	State	Stability	State	Stability
FREQUENCY TYPE	**1**	Magn.	Power, Magnitude		Asymmetry	Comodulation		
		Phase			Phase lag	Coherence		
	2	Magn.	Band ratio					
		Phase						
	Many	Magn.	Relative Power		Spectral Correlation Coefficient			
		Phase						

FIGURE 5. The distributions of coherence and Fisher *z* coherence and comodulation and Fisher *Z* comodulation.



Administration Human Study Committee or RIT Institutional Review Board. Informed consent was obtained from a parent or guardian for each child.

Materials

EEG was recorded with either a Neurosearch-24 (Lexicor Medical Technologies, Inc., Augusta GA) or NeuroNavigator (J&J Engineering, Inc., Poulsbo, WA) using 12-bit or 16-bit A/D, respectively. Signals were digitized at 512 or 1024 samples per second, down-sampled and displayed 128 times per second. High pass filters were set at 1.5 Hz for both units and 38 Hz or 45 Hz for Neurosearch or NeuroNavigator units, with rolloffs of 12 and 48 Db per octave, respectively. Common mode rejection ratio was 90 dB at 60 Hz, with notch filtering at 60 Hz. Topographic EEG was recorded from scalp referenced to linked ears using sized elastic lycra caps (Electro-Cap International, Inc., Eaton, OH) of 20 electrode ports arranged by the International 10–20 electrode placement system (Jasper, 1958).

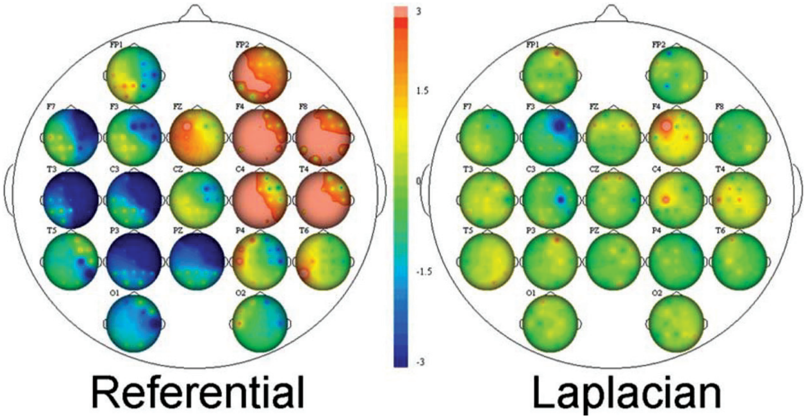
Procedure

EEG was acquired at Sepulveda Veterans Administration Medical Center Neuropsychology Laboratory or RIT Psychology Lab or clinician office. Participants were tested individually, often in a dimly lit electrically shielded and sound-attenuated room. Electrode impedances were kept below 10 K Ohms. Eyes closed baseline conditions of 2 min or longer were recorded twice, generally spaced apart by 30 to 60 min. Data were remontaged using a Laplacian spherical harmonic expansion (Lagerlund, Sharbrough, Busacker, & Cicora, 1995; Pascual-Marqui, Gonzalez-Andino, Valdes-Sosa, & Biscay-Lirio, 1988; Shaw & Koles, 1989; see Figure 6), although only the referential montage data were analyzed for this study.

Data Analysis

EEG records were inspected for artifacts, and contaminated segments were eliminated prior to spectral analysis. If artifact was present in any channel, spectral coefficients from all 19 recording channels were ignored for its duration. As little as a 100-ms segment could be eliminated in this fashion. Only eyes closed baseline recordings were analyzed, and values represented averages of replicated recordings from each participant. Digitized signals underwent cosine tapering using a Blackman-Harris 4-term function with 75% data window overlap, which produces equal representation of all signals in both time and

FIGURE 6. Differences between Referencial and Laplacian montages.



frequency domains (Kaiser & Sterman, 2001). Spectral analysis was performed on 10 bands: 2–4 Hz delta, 4–8 Hz theta, 8–12 Hz alpha, 12–15 Hz sensorimotor range, 15–18 Hz beta 1, 18–24 Hz beta 2, 24–30 Hz beta 3, 30–36 Hz gamma 1, and 36–45 Hz gamma 2. As low pass filters on one of the units precluded accurate fast frequencies (38 Hz low pass), no conclusions were drawn from gamma 2 analysis. Comodulation and coherence of 171 unique site pairs were reduced to 19 site-centered means. All site connectivity values were furthered averaged to provide global connectivity indices of specific frequencies. Fisher *z* transformation of coherence and comodulation values normalized distributions (Fisher, 1921) and a Bonferroni (1936) correction minimized Type I error.

RESULTS

The analyses were restricted to site-centered and global formulations of comodulation and coherence. As can be seen in Tables 2 and 3, both coherence and comodulation increased significantly with age in all but fast frequencies. However, topographically, comodulation increased at all sites, but coherence increases were largely restricted to posterior sites. The strongest age function was observed for site T5 in terms of alpha comodulation ($r = .75$, $p < .0001$; see Figure 7). Anterior coherence and comodulation increased with age for adults ($p < .0001$), but not for children (see Tables 4 and 5). Global coherence and comodulation increased with age in most frequencies (see Table 6).

DISCUSSION

Both coherence and comodulation reflect brain maturity, as evidenced by significant age correlations. Inhibition of neural autorhythmicity increased consistently with age (between ages 5 and 35), but the limits of the age-based increases throughout the lifespan could not be determined. It is possible that coupling rates asymptote or even accelerate during later years. With this information, it might be possible to detect certain neurodegenerative diseases prior to

TABLE 2. Correlation between age and site coherence.

Coherence	Delta	Theta	Alpha	SMR	Beta1	Beta2	Beta3	Gamma1
FP1	.297	.205	.233	.357	**.383**	**.409**	.295	.128
FP2	.307	.203	.218	.347	.377	**.399**	.300	.148
F7	.292	.294	.209	.362	.377	**.417**	.278	.060
F3	.244	.203	.174	.273	.310	.341	.249	.088
FZ	.292	.246	.168	.271	.304	.330	.246	.101
F4	.177	.170	.145	.270	.320	.352	.289	.116
F8	.147	.168	.160	.286	.358	**.411**	.280	.102
T3	**.607**	**.544**	.312	**.481**	**.400**	**.420**	.280	.132
C3	**.553**	**.400**	.266	.315	.372	**.416**	.294	.159
CZ	**.522**	.359	.175	.278	.330	.345	.214	.128
C4	**.518**	.363	.205	.286	.320	**.401**	.289	.159
T4	**.476**	**.427**	.174	.344	.272	**.340**	.251	.167
T5	**.581**	**.538**	**.527**	**.534**	**.449**	**.454**	.279	.178
P3	**.615**	**.506**	**.458**	**.509**	**.467**	**.509**	.334	.223
PZ	**.641**	**.497**	**.405**	**.476**	**.429**	**.477**	.335	.229
P4	**.590**	**.466**	**.495**	**.483**	**.400**	**.474**	.307	.203
T6	**.491**	**.425**	**.526**	**.509**	.315	**.398**	.236	.138
O1	**.585**	**.613**	**.572**	**.602**	**.558**	**.578**	**.388**	.281
O2	**.568**	**.590**	**.604**	**.596**	**.528**	**.552**	.342	.248

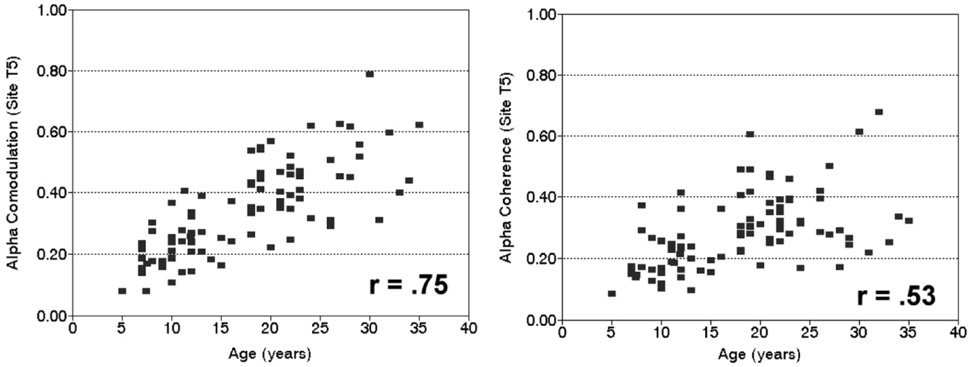
Note. Significant correlations are in bold. $t(99) > 4.055$, $p < .0001$. SMR = sensorimotor range.

TABLE 3. Correlation between age and site comodulation.

Comodulation	Delta	Theta	Alpha	SMR	Beta1	Beta2	Beta3	Gamma1
FP1	**.467**	.305	**.396**	**.432**	**.506**	**.484**	.330	.123
FP2	**.453**	.316	.376	**.426**	**.513**	**.488**	.373	.131
F7	**.439**	.385	**.427**	**.460**	**.518**	**.508**	.315	.047
F3	.371	.312	**.384**	**.394**	**.470**	**.475**	.310	.071
FZ	**.400**	.349	**.382**	**.386**	**.475**	**.474**	.325	.103
F4	.300	.294	.351	**.38**	**.485**	**.478**	.336	.108
F8	.267	.308	.370	.376	**.505**	**.514**	.316	.094
T3	**.653**	**.632**	**.588**	**.533**	**.519**	**.468**	.243	.038
C3	**.623**	**.509**	**.464**	**.475**	**.534**	**.555**	.353	.129
CZ	**.616**	**.469**	**.393**	**.423**	**.481**	**.482**	.281	.114
C4	**.607**	**.485**	**.442**	**.442**	**.489**	**.539**	.343	.136
T4	**.558**	**.555**	**.449**	**.436**	.366	.412	.294	.135
T5	**.638**	**.685**	**.749**	**.627**	**.582**	**.616**	.331	.135
P3	**.669**	**.633**	**.650**	**.619**	**.604**	**.655**	**.395**	.188
PZ	**.665**	**.584**	**.577**	**.555**	**.548**	**.592**	.368	.182
P4	**.660**	**.601**	**.651**	**.573**	**.519**	**.58**	.351	.153
T6	**.575**	**.607**	**.665**	**.577**	**.418**	**.478**	.257	.072
O1	**.620**	**.701**	**.727**	**.628**	**.595**	**.638**	**.411**	.246
O2	**.619**	**.683**	**.710**	**.605**	**.584**	**.586**	.356	.206

Note. Significant correlations are in bold. $t(99) > 4.055$, $p < .0001$. SMR = sensorimotor range.

FIGURE 7. The alpha comodulation at T5 for adults and children.



significant presentation of symptoms by simply evaluating EEG-connectivity quotients for one's age (Rossini, Rossi, Babiloni, & Polich, 2007).

No significant age–connectivity relationship was found for anterior sites during childhood, but significant relationships emerged during adulthood, a finding that parallels callosal myelination between frontal lobes. The genu and midbody of the corpus callosal begins its myelination in earnest after puberty and continues throughout the life span, especially in terms of large diameter myelin density (Aboitiz et al., 1992). Also, the left posterior temporal cortex appears to have the most protracted course of maturation compared to all other cortical regions (Sowell et al., 2003), and confirmed by alpha comodulation at site T5, the strongest relationship between functional connectivity measures and age.

Millisecond delays have little impact on comodulation, but they devastate coherence

TABLE 4. Correlation of age and site coherence within childhood and adulthood (43 children, 58 adults).

Coherence	Delta	Theta	Alpha	SMR	Beta1	Beta2	Beta3	Gamma1
Child								
FP1	.140	.317	.414	**.627**	.543	.318	.016	.107
FP2	.055	.252	.371	**.578**	.477	.316	.047	.110
F7	.106	.273	.405	**.620**	**.586**	.388	.007	.142
F3	.279	.378	.408	**.578**	.501	.378	.012	.114
FZ	.318	.377	.380	**.566**	.456	.286	.047	.158
F4	.231	.328	.342	.543	.448	.290	.039	.158
F8	.168	.049	.274	.430	.401	.160	.119	.183
T3	.263	.372	.279	.362	.428	.265	.061	.031
C3	.271	.339	.270	.366	.364	.191	.080	.177
CZ	.285	.252	.215	.378	.321	.141	.128	.220
C4	.205	.228	.155	.304	.261	.060	.159	.233
T4	.020	.086	.046	.088	.139	.019	.032	.082
T5	.238	.278	.294	.106	.209	.079	.148	.221
P3	.250	.309	.231	.232	.208	.133	.103	.213
PZ	.256	.255	.132	.216	.131	.094	.113	.217
P4	.193	.177	.175	.101	.058	.002	.127	.245
T6	.137	.047	.244	.022	.003	.101	.170	.280
O1	.305	.294	.279	.216	.182	.028	.139	.220
O2	.329	.263	.266	.213	.138	.025	.144	.205
Adult								
FP1	.315	**.557**	**.596**	**.518**	**.592**	**.561**	.449	.296
FP2	.302	**.545**	**.583**	**.515**	**.574**	**.536**	.436	.245
F7	.465	**.572**	**.571**	**.573**	**.576**	**.544**	.459	.237
F3	**.503**	**.560**	**.576**	**.528**	**.557**	**.544**	.441	.238
FZ	**.513**	**.573**	**.578**	**.558**	**.597**	**.595**	**.516**	.295
F4	.471	**.553**	**.593**	**.543**	**.591**	**.576**	.478	.260
F8	.387	.478	**.548**	**.507**	**.554**	**.540**	.408	.199
T3	.035	.163	.116	.096	.230	.140	.053	.020
C3	.359	.465	.404	.392	.494	.472	.285	.140
CZ	.458	**.530**	.445	.450	**.546**	**.521**	.346	.179
C4	.391	.482	.335	.396	**.503**	**.507**	.298	.168
T4	.106	.222	.008	.141	.304	.252	.151	.206
T5	.214	.155	.002	.237	.130	.202	.176	.115
P3	.029	.154	.056	.090	.121	.078	.003	.011
PZ	.215	.333	.195	.143	.334	.298	.132	.059
P4	.059	.198	.095	.022	.205	.195	.082	.065
T6	.276	.229	.089	.169	.208	.063	.044	.055
O1	.385	.216	.007	.219	.120	.088	.034	.035
O2	.321	.178	.025	.145	.102	.027	.033	.045

Note. Significant correlations are in bold. $p < .0001$. SMR = sensorimotor range.

(Govindan, Raethjen, Arning, Kopper, & Deuschl, 2006). Comodulation requires that similar numbers of neurons be inhibited or uninhibited within modest time constraints, whereas coherence requires stringent timing, highly synchronized disinhibition of neural groups for bursts to occur at exactly specified moments in time (lagged or simultaneous) across the cortices (Contreras, Destexhe, Sejnowski, & Steriade, 1996). The exquisite time-locking may be a product of the reticular thalamic nucleus (RTN). The relatively compact sheathing of RTN acts as a functional bottleneck, inhibiting adjacent thalamic neural groups uniformly, and this uniform synchronization propagates

TABLE 5. Correlation of age and site comodulation within childhood and adulthood (43 children, 58 adults).

Comodulation	Delta	Theta	Alpha	SMR	Beta1	Beta2	Beta3	Gamma1
Child								
FP1	.131	.309	.538	.532	.484	.248	.120	.208
FP2	.012	.295	.497	.464	.467	.277	.068	.208
F7	.145	.278	.540	.529	.459	.267	.091	.261
F3	.341	.381	.522	.500	.446	.357	.069	.189
FZ	.357	.398	.506	.473	.438	.288	.076	.218
F4	.213	.301	.449	.392	.384	.221	.112	.248
F8	.121	.027	.350	.260	.318	.092	.178	.279
T3	.236	.368	.451	.325	.423	.255	.040	.153
C3	.279	.371	.348	.361	.346	.251	.095	.242
CZ	.277	.275	.350	.360	.312	.180	.134	.272
C4	.207	.245	.246	.290	.266	.085	.189	.294
T4	.009	.135	.193	.121	.135	.010	.067	.160
T5	.221	.291	.446	.111	.183	.204	.188	.311
P3	.201	.318	.352	.251	.243	.280	.095	.243
PZ	.220	.275	.264	.244	.211	.169	.091	.257
P4	.193	.210	.272	.180	.147	.042	.135	.292
T6	.140	.102	.279	.269	.037	.016	.170	.318
O1	.275	.284	.427	.316	.227	.139	.167	.270
O2	.316	.288	.348	.267	.132	.066	.176	.242
Adult								
FP1	.229	**.555**	**.623**	.460	**.636**	**.581**	.360	.153
FP2	.173	**.530**	**.603**	.465	**.616**	**.580**	.339	.082
F7	.413	**.609**	**.624**	**.547**	**.656**	**.600**	.374	.104
F3	**.504**	**.604**	**.633**	**.517**	**.619**	**.603**	.391	.156
FZ	**.515**	**.613**	**.628**	**.530**	**.677**	**.655**	.480	.211
F4	.482	**.619**	**.620**	**.533**	**.676**	**.638**	.442	.180
F8	.305	**.537**	**.592**	.473	**.605**	**.607**	.333	.107
T3	.124	.376	.320	.080	.307	.198	.009	.054
C3	.385	**.530**	.446	.413	**.575**	**.526**	.274	.075
CZ	**.493**	**.578**	.468	.460	**.622**	**.593**	.337	.123
C4	.406	**.556**	.406	.409	**.611**	**.575**	.286	.112
T4	.084	.362	.179	.133	.362	.297	.193	.208
T5	.039	.188	.343	.026	.225	.113	.045	.105
P3	.204	.404	.305	.098	.381	.306	.113	.018
PZ	.273	.468	.330	.160	.453	.379	.162	.023
P4	.161	.372	.283	.050	.350	.288	.105	.022
T6	.129	.087	.199	.087	.107	.068	.013	.006
O1	.254	.060	.234	.078	.113	.104	.061	.034
O2	.168	.115	.253	.055	.113	.082	.039	.040

Note. Significant correlations are in bold. $p < .0001$. SMR = sensorimotor range.

TABLE 6. Correlation of global coherence and comodulation with age.

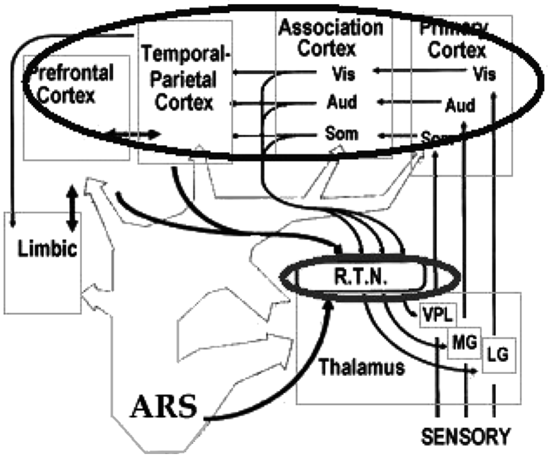
	Delta	Theta	Alpha	SMR	Beta1	Beta2	Beta3	Gamma1
Coherence	**.574**	**.450**	**.413**	**.519**	**.460**	**.504**	**.333**	.173
Comodulation	**.655**	**.565**	**.614**	**.601**	**.606**	**.617**	**.372**	.135

Note. Significant correlations are in bold. $p < .001$. SMR = sensorimotor range.

outward and time-locks large expanses of cortex (Huguenard & McCormick, 2007; Steriade, Gloor, Llinas, Lopes da Silva, & Mesulam, 1990). This could explain high scalp-measured coherences (minus volume conduction contributions) and may suggest that phase relationships between neurons inform us about RTN involvement in EEG rhythms. In other words, phase difference between sites may reflect differences in sensory gating (i.e., general involvement of the feedforward system of the brain) possibly in the thalamocortical loop. Given this possibility, magnitude relationships might reflect an orthogonal process, the feedback system of the brain. The corticothalamic system modulates sensory processing and is less time sensitive (Steriade, 2006), as is comodulation. This model is speculative, based on RTN physiology and its position in sensory processing (see Figure 8), but it may help in interpreting differences between comodulation and coherence in terms of information processing. If true, phase-based training would preferentially engage the thalamocortical loops and magnitude-based training the corticothalamic loops.

There are numerous ways that two active brain sites may be synchronized in the frequency domain. Some of these ways will be relevant to mental activity and/or self-regulation, whereas others may not be. Table 7 is an example Periodicity Table completed with novel measures as well as measures from physics and information sciences (Chandran, 1994; Judah & Wright, 1990). Note how general properties (number of frequencies, sites, stability) are represented by dynamic or static versions (e.g., comodulation, magnitude asymmetry) and each version is instantiated mathematically (e.g., Hilbert transform, Pearson product moment). Stability and state refer to two complementary forms of variation (temporal, nontemporal), and both concepts cross disciplinary boundaries well. Finally, concepts may be instantiated with any number of mathematical formulations and are not tied to any one set of operations, thus the idea that a concept possesses or is attached to a single mathematical formulation is incorrect (Nunez et al., 1997), and a linguistic definition is more accurate than a mathematical formulation.

FIGURE 8. The corticothalamic feedback system of the brain as related to comodulation and coherence.



By contrasting cells within the Periodicity Table, impairments missed by two measures in isolation may be revealed by their composite. Disparate measures (e.g., phase consistency vs. magnitude asymmetry) can be compared readily in the statistical realm, as Figure 4 attests. Three examples of cross-table comparisons are depicted in Figure 9. A z-score contrast of magnitude consistency to phase consistency known as *corticality* may have physiological utility (Lambos, 2008) as well as activity (magnitude) compared to connectivity (comodulation), a measure known as *focality*. When site activity does not correlate well with site connectivity, a brain area is hyperfocal, its pattern of activity out of synch with its connections (Kaiser, 2007b). Finally, a comparison of relative to absolute power, called *cordance*, appears in the study of depression (Leuchter et al., 1994). Furthermore it should also be noted that the table was formulated with sinusoidal signals in mind, as sinusoids are created by independent generators like those within the brain, but it could just as readily incorporate a wide range of signal morphologies (square waves, triangular).

In sum, the human brain is the most organized phenomena in nature, a synchronous

TABLE 7. A Periodicity table with examples in each cell.

			ELECTRODE SITES					
			1		2		Many	
			Local		Network		System	
			State	Stability	State	Stability	State	Stability
FREQUENCY SPECTRUM	0		**Amplitude**	**Autocorrelation**	**Reversals**	**Reversal variability**	**Peak amplitude**	**Peak autocorrelation**
	1	Magn.	**Magnitude**	**Automodulation**	**Unity**	**Comodulation**	**Rogue site**	**Site comodulation**
		Phase	**Autophase**	**Autoherence**	**Phase lag**	**Coherence**	**Rogue phase**	**Site coherence**
	2	Magn.	**Biamplitude**	**Bimodulation**	**Cross-biamplitude**	**Cross-bimodulation**	**Site Biamplitude**	**Site bimodulation**
		Phase	**Biphase**	**Bicoherence**	**Cross-biphase**	**Cross-bicoherence**	**Site biphase**	**Site bicoherence**
	Multi-	Magn.	**Spectral Entropy**	**Trimodulation**	**Joint entropy**	**Entropy modulation**	**Rogue frequency**	**Global comodulation**
		Phase	**Phase entropy**	**Triherence**	**Joint phase entropy**	**Phase entropy modulation**	**Rogue frequency by phase**	**Global coherence**

Note. Local activity (column 1): Amplitude is voltage per unit time. Magnitude is a linear summation of burst incidence, duration, and intensity or amplitude. Autophase is "phase slippage" or mean phase difference of a given frequency from one epoch to the next. One formulation is Arctan $[(\Sigma \cos_t \sin_{t+1} - \Sigma \cos_{t+1} \sin_t)^2/(\Sigma \cos_t \sin_{t+1} + \Sigma \cos_{t+1} \sin_t)^2]$ where t is current sample. Biamplitude is a ratio of spectral activity of one frequency to another, such as theta/beta power ratios (Lubar, Swartwood, Swartwood, & O'Donnell, 1995; Monastra et al., 2005). Biphase (or phase bicoherence) is mean phase difference between frequencies and it is monitored during anesthesia and neonatally (Shils, Litt, Skolnick, & Stecker, 1996; Witte et al., 2004). Spectral entropy is number of possible arrangements inherent in a signal, logarithmically-compressed (Shannon, 1948). Nunes (2004) likened spectral entropy to freedom: "conscious cortex is free to move among a huge number of available microstates" as long as the same macrostate is produced. Disorderly (high freedom) EEG is associated with mental effort and wakefulness while orderly EEG occur with sleep, isoelectricity, and non-responsiveness. Spectral entropy is monitored during anesthesia (Lipping, Ferenets, Mortier, & Struys, 2007): As entropy decreases, fewer magnitude combinations are available and level of consciousness decreases. Increasing cortical microstate arrangeability has neurotherapeutic implication (e.g., Martin, 2006). Phase entropy is phase freedom or independence (Breakspear, 2002).
Stability of activity (column 2): Autocorrelation is the auto-correlogram peak for a signal for all possible time lags. One formulation is $\Sigma\ (z_{t*}\ z_{t+1})/n$ where z refers to z-score of voltages and t to current sample and n total number of samples. Automodulation is magnitude consistency of a given frequency across time. One formulation is $\Sigma\ (z_{t*}\ z_{t+1})/n$ where z refers to z-score of magnitudes and t the current sample and n total number of samples. Autoherence is phase consistency of a given frequency across time. Bimodulation is magnitude consistency between frequencies (see Figure 10). One formulation is time-displaced bimodulation is $\Sigma\ (z_{a*}\ z^{b+t})/n$ where z refers to z-score of magnitude of two frequencies a and b, t equals time moments removed from signal a, and n number of samples. Trimodulation is magnitude consistency among three frequencies, i.e., mean normalized round-robin cross-product. Triherence (or tricoherence) is phase consistency among frequencies (Chandran, 1994).
Network state or connectivity (column 3): Reversals refer to temporal density of voltage polarity reversals in a signal. Unity is magnitude asymmetry subtracted from one with valence ignored, $1-|A-B|/(A+B)$. Sites attain unity $(+1)$ when no

TABLE 7 (continued)

difference in mean magnitude exists and there is disunity as differences increase. Unity may be especially useful in homologue assessment (Kaiser, 2007a; Figure 4). A more common magnitude asymmetry index is difference between sites compared to its sum, $(A-B)/(A+B)$ (Strobos, 1960). Phase lag (phase asymmetry) is mean phase difference between sites. Cross-biamplitude compares spectral activity at a given frequency to activity in another frequency at another site (Schack et al., 2001). Frontal theta activity may be compared to simultaneous posterior alpha activity, or at different times (lags). Cross-biphase is mean phase difference between sites for different frequencies. Joint entropy is a measure of mutual information of two signals in terms of spectral magnitude or power, which is valuable to artifact detection (Jung et al., 2000; Makeig, Jung, Ghahremani, Bell, & Sejnowski, 1996). Autocorrelation of joint entropy (entropy modulation) over time provides a stability index. The spectral correlation coefficient (SCC) of Lexicor Medical Technology, Inc. estimates similarity of spectral constituents between signals by correlating sub-range spectral values, a rough estimate of joint entropy. In physics SCC refers to magnitude consistency (Eberly & Kujawski, 1968; Won, Kimb, & Mina, 2004). Joint phase entropy is a measure of mutual phase information (Barnett & Phoenix, 1991). Autocorrelation of joint phase entropy over time provides a stability index (phase entropy modulation).

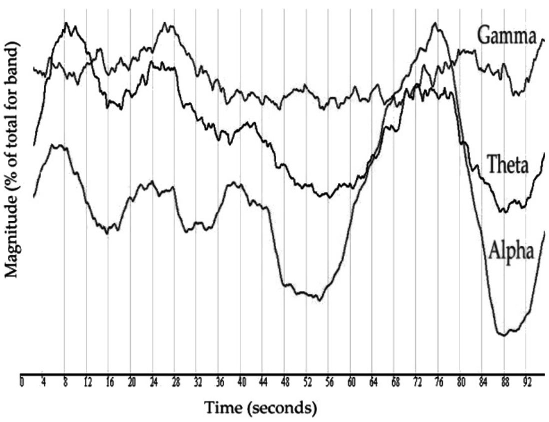
Network stability (column 4): Reversal variability is standard deviation of reversal density per epoch. Comodulation is magnitude consistency between sites at a given frequency. One formulation is $\Sigma\,(z_{a*}\, z_b)/n$ where z is normalized magnitude for signals a and b and n is number of evenly spaced samples. Coherence is phase consistency between sites at a given frequency. Cross-bimodulation is magnitude consistency of a given frequency at one site compared to another frequency at another site (see Figure 10). Cross-bicoherence is phase consistency of a given frequency at one site compared to another frequency at another site (Saltzberg, Burton, Birch, Fletcher, & Michaels, 1986).

System state (column 5): Peak amplitude is site of highest voltage. Rogue site estimates a topographic pattern of magnitude independence. Whichever site is least like all others in auto-normalized magnitude is termed rogue and percent of time spent rogue is computed (Kaiser, 2004). Rogue phase (or rogue site by phase) estimates a topographic pattern of phase independence. Each site is compared to all others on Autophase (or homologue phase, or mean cross-phase) and percent time spent rogue is determined. Site biamplitude is mean ratio of spectral activity at a given frequency compared to mean spectral activity for all other sites at another frequency. Site biphase is mean phase difference for a given frequency at a site compared to all other sites for another frequency. Rogue frequency estimates independence across topography and spectrum, using maximum percent time spent rogue for auto-normalized magnitudes at any frequency. Rogue frequency-phase estimates independence across topography and spectrum using autophase (or homologue) phase.

System stability (column 6): Peak autocorrelation is site of highest autocorrelation for any time lag. Site comodulation is mean comodulation of all electrode partners (19 pairings minus 1 auto-comparison), an estimate of network traffic or common activity at each site. Site coherence is mean coherence of all electrode partners, a phase-based estimate of network traffic. Site bimodulation is spectral activity at a given frequency correlated with mean spectral activity for all other sites at another frequency. Site bicoherence is bicoherence of a given frequency at one site compared to mean spectral activity of remaining sites (i.e., mean cospectrum, quaspectrum).

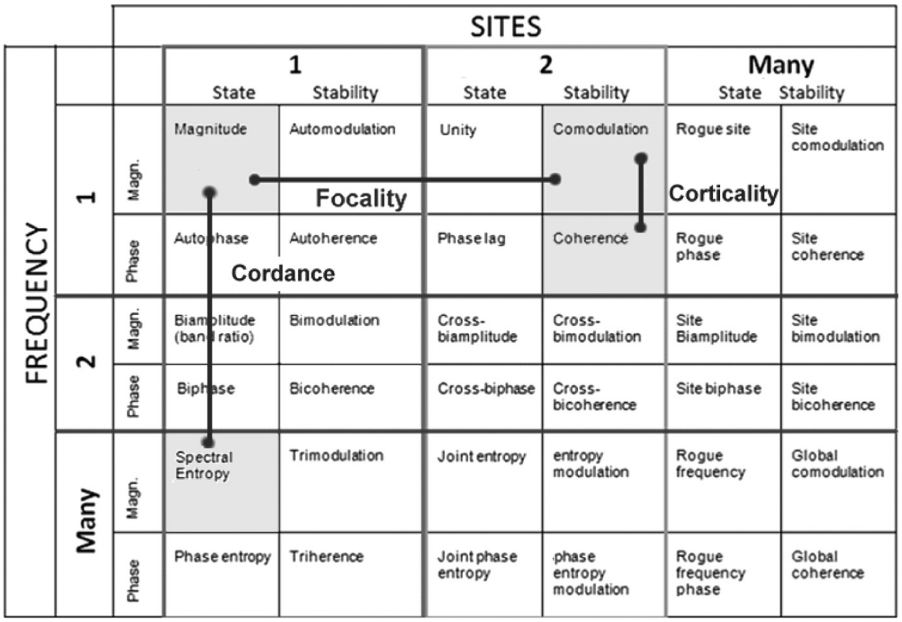
Global comodulation is a single number to summarize comodulation of 171 site-pairings for a frequency range, an estimate of total network activity. Global coherence is a phase-based estimate of total network activity, a summary of all site-pair coherences.

FIGURE 9. The cross-table comparisons of magnitude and time for gamma, theta, and alpha.



blend of infinite energy and freedom. Understanding the spatiotemporal mystery requires that investigations become more organized. Toward this end, a Periodicity Table was proposed as a means to categorize synchrony manifestations and as a tool for generating new and potentially relevant psychophysiological indices. Introduction of the Periodicity Table, with its variety of novel and unfamiliar spectral properties, may initially generate more questions than it answers, but in the end a framework provides a diligence currently lacking in brain function analysis, a comprehensive approach for evaluating EEG periodicities.

FIGURE 10. Moderate bimodulation of theta and alpha is observed in this short record. Theta and alpha magnitudes correlate reasonably well but neither correlates well with gamma magnitude across time.



			SITES					
			1		2		Many	
			State	Stability	State	Stability	State	Stability
FREQUENCY	1	Magn.	Magnitude	Automodulation	Unity	Comodulation	Rogue site	Site comodulation
		Phase	Autophase	Autoherence	Phase lag	Coherence	Rogue phase	Site coherence
	2	Magn.	Biamplitude (band ratio)	Bimodulation	Cross-biamplitude	Cross-bimodulation	Site Biamplitude	Site bimodulation
		Phase	Biphase	Bicoherence	Cross-biphase	Cross-bicoherence	Site biphase	Site bicoherence
	Many	Magn.	Spectral Entropy	Trimodulation	Joint entropy	entropy modulation	Rogue frequency	Global comodulation
		Phase	Phase entropy	Triherence	Joint phase entropy	phase entropy modulation	Rogue frequency phase	Global coherence

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