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Cyclic Cortical Reorganization during Early Childhood

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EEG coherence was computed from 8 left and 8 right intrahemispheric electrode pairs from 253 children ranging in mean age from 6 months to 7 years. The first derivative of mean coherence was computed in order to study growth spurts or rapid changes in mean coherence over the early childhood period. Growth spurts in EEG coherence were approximately 6 months to 1 year in duration and involved a cyclical process composed of a sequential lengthening of intracortical connections in the left hemisphere and a sequential contraction of intracortical connections in the right hemisphere. Each growth spurt cycle had a period of approximately 2 to 4 years and involved both a rostral–caudal expansion and contraction as well as a lateral-to-medial rotation. Data support the view that the functions of the left and right hemisphere are established early in human development through complementary developmental sequences and that these sequences appear to recapitulate differences in adult hemispheric function.

Previous research has demonstrated growth spurts in frontal lobe intracortical connections during the postnatal period from 6 months to adulthood (Thatcher, Walker, & Giudice, 1987; Thatcher, 1991, 1992a). The postnatal growth spurts, defined as increases in either the number or the strength of cortical synaptic connections, were approximately 6 months to 1 year in duration and involved a cyclical process composed of a sequential lengthening of intracortical connections in the left hemisphere and a sequential contraction of intracortical connections in the right hemisphere (Thatcher, 1992a). Each growth spurt cycle had a period of approximately 4 years and involved both a rostral–caudal expansion and contraction as well as a lateral-to-medial rotation. It was hypothesized (Thatcher, 1992a,b) that each growth spurt cycle involved a propagated wave of nerve growth factor such that the leading edge of the wave resulted in the local production of a surplus of synaptic connections while the trailing edge was followed by a pruning of excess connections.

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The anatomical pattern of the traveling wave of intracortical growth spurts suggested a convergence process that narrows the disparity between structure and function by iteratively sculpting and reshaping the brain's microanatomy to meet the needs of diverse and unpredictable environments (Thatcher, 1992a). The anatomical pattern of postnatal growth spurts also suggested a complementary recapitulation of the differences in hemispheric function observed in the adult. For example, the developmental sequence of the left hemisphere from short distance to long distance frontal connections was likened to a developmental process that sequentially integrates differentiated subsystems. Consequently, the left hemisphere developmental sequence was characterized as "integration of differentiation." In contrast, the development of the right hemisphere, from long distance to short distance connections, was likened to a process of sequential differentiation of a previously integrated system. Accordingly, the complementary right hemisphere developmental sequence was characterized as "differentiation of integration" (Thatcher, 1992a).

PURPOSE OF THE PRESENT STUDY

The purpose of the present study was to provide a detailed evaluation of the iterative growth spurt processes reported previously (Thatcher, 1992a) by focusing on the early childhood period from 6 months to 7 years. This is a period when the largest number of growth spurts are observed and it is a period that contains the first complete developmental cycle. This study will examine the factor structure of EEG coherence presented by Thatcher (1991) through a detailed analysis of the events comprising the period from 6 months to 7 years in order to investigate the following issues: (1) What are the rates of growth along the rostral–caudal and lateral–medial anatomical dimensions? (2) Are there special ages or growth periods involving unique frontal lobe development? and (3) What is the significance of the presence of nonlinear dynamical equilibrium processes such as competition, cooperation, and nonlinear oscillations between developing intracortical systems?

Cortico–Cortical Connections and EEG Coherence

The present study used measures of EEG coherence to estimate changes in the maturation of cortico–cortical connections. Accordingly, a brief introduction to the mathematical and neurophysiological foundations of EEG coherence is necessary to provide a basis by which the conclusions of this study can be understood. Coherence is mathematically analogous to a cross-correlation in the frequency domain. It is a measure of the degree of "phase synchrony" or "shared activity" between spatially separated generators (Otnes & Enochson, 1972; Bendat & Peirsol, 1980; Glaser & Ruchkin, 1976). The application of coherence measures to the human scalp EEG have shown that EEG coherence reflects the coupling

between neocortical neurons (Lopez da Silva, Pijn, & Boeijinga, 1989, 1991; Nunez, 1981, 1989; Tucker, Roth, & Blair, 1986; Thatcher, McAlaster, Lester, Horst, & Cantor, 1983). Recently, a "two-compartmental" model of EEG coherence was developed (Thatcher, Krause, & Hrybyk, 1986; Pascual-Marqui, Valdes-Sosa, & Alvarez-Amador, 1988) based upon Braitenberg's (1978) two-compartment analysis of cortical axonal fiber systems in which compartment "A" is composed of the basal dendrites that receive input primarily from the axon collaterals from neighboring or "short distance" pyramidal cells, while compartment "B" is composed of the apical dendrites of cortical pyramidal cells that receive input primarily from "long distance" intracortical connections. The short distance A system primarily involves local interactions on the order of millimeters to a few centimeters, while the long distance B system involves long-range interactions on the order of several centimeters, which represent the majority of white matter fibers. These two systems exhibit two different network properties. System B, due to reciprocal connections and invariant apical dendrite terminations, is involved in long distance feedback or loop systems. In contrast, system A, due to the variable depths of the basal dendrites, is not involved in reciprocal loop processes but rather in a diffusion type of transmission process (Thatcher et al., 1986; Pascual-Marqui et al., 1988; Braitenberg, 1978).

The following mathematical equation was developed to describe the magnitude and slope of decline of human EEG coherence with interelectrode distance (Thatcher et al., 1986; Pascual-Marqui et al., 1988):

$$\text{Coherence} = A_i\, e^{-kd} + B_i\, e^{kd} \sin kd, \tag{1}$$

where A_i, B_i, and k are functions of frequency and d is scalp interelectrode distance in centimeters. The first term on the right side of Eq. (1) corresponds to the operation of the A system while the second term corresponds to the operation of the B system.

While the moment-to-moment changes in EEG coherence with interelectrode distance can be understood by Eq. (1), changes in the development of coherence over long spans of time (i.e., months and years) require additional consideration. One consideration is that developmental changes in EEG coherence in a large group of subjects reflect changes in the mean coupling constants between connected neuronal networks. For example, if we assume that volume conduction has been controlled, then we can postulate a relationship between EEG coherence and two primary factors: (1) the number of cortico–cortical connections between neural assembles and (2) the synaptic strength of connections between neural assemblies (the terms cortico–cortical connections and intracortical connections are considered synonymous). This relationship is described as

$$\text{Coherence} = (C_{ij} \times S_{ij}), \quad (2)$$

where C_{ij} is a connection matrix of the number or density of connections between neural systems i and j and S_{ij} is the synaptic strength of those connections. Equation (2) provides a logical means by which developmental changes in EEG coherence can be interpreted in terms of changes in the number and strength of connections between assemblies of neurons (Thatcher et al., 1986, 1987; Pascual-Marqui et al., 1988). For example, increased coherence is due to an increase in the number and/or strength of connections and, conversely, decreased coherence is due to a decreased number and/or reduced strength of connections. The neurophysiological mechanisms responsible for the changes in the numbers or strengths of connections may include axonal sprouting, synaptogenesis, mylenation, expansion of existing synaptic terminals, pruning of synaptic connections, presynaptic changes in the amount of neurotransmitter, and changes in the postsynaptic response to a given neurotransmitter (see discussions by Purves, 1988; and Huttenlocher, 1984). Currently, measures of EEG coherence cannot discern between these various possibilities.

METHODS

Subjects. A total of 436 normal children ranging in age from 2 months to 16.564 years of age were included in the Thatcher (1991) analysis. This age range of children was selected because it contained an adequately large sample size at each age period (*N*s ranged from 15 to 53 per age group); it covered the developmental period from near bith to early adulthood and the data set during this period was especially stable and robust (i.e., relatively equal variances and constant coefficients of variation across age). A variety of measures were obtained from each child, including a neurological and developmental history, full-scale I.Q., measures of school achievement, measures of motor development, measures of skull size, and measures of handedness. Details of the methods of recruitment as well as psychometric, handedness, and neuropsychological examinations are provided elsewhere (Thatcher, Lester, McAlaster, & Horst, 1982, Thatcher et al., 1983; Thatcher & Lester, 1985). The children were classified as normal based upon the following criteria: (1) an uneventful prenatal, perinatal, and postnatal period; (2) no disorders of consciousness; (3) no head injury with cerebral symptoms; (4) no history of central nervous diseases; (5) no convulsions of an emotional, febrile, or other nature; (6) no obvious mental diseases; and (7) no abnormal deviation with regard to mental and physical development (Thatcher et al., 1987; Thatcher, 1991). The demographics of the data were 242 males and 194 females and handedness of children over the age of 2 (i.e., when handedness could be measured using the Edinberg Scale, Thatcher et al., 1982) was approximately 88% right-handed, 9% left-handed, and 3% ambidextrous.

The present study is limited to the mean age range from 0.513 to 7.013 years, which represents a total of 253 children considered normal based upon the above criteria. Of the subset of 253 children between the ages of 0.513 and 7.013 years, approximately 72% of the children were caucasian and 28% were black. Fifty-eight percent were males, 42% females, and for children older than 2 years 88% were right-handed and 11% were left-handed (we considered measures of handedness as unreliable before the age of 2).

Electroencephalographic acquisition and analysis. Grass silver disk electrodes were applied to the 19 scalp sites of the International 10/20 system. A transorbital eye channel (electrooculogram or EOG) was used to measure eye movements, and all scalp recordings were

referenced to linked ear lobes. Impedance measures for all channels were generally less than 5000 ohms. Amplifier bandwidths were nominally 0.5 to 30 Hz, the outputs being 3 db down at these frequencies. The EEG activity was digitized on-line by a PDP 11/03 data acquisition system. An on-line artifact rejection routine was used which excluded segments of EEG if the voltage in any channel exceeded a preset limit determined at the beginning of each session to be typical of the subject's resting EEG and EOG.

One minute of artifact-free EEG was obtained at a digitization rate of 100 Hz. The EEG segments were analyzed off-line by a PDP 11/70 computer and plotted by a Versatec printer/plotter. Each subject's EEG was then visually examined and edited to eliminate any artifacts that may have passed through the on-line artifact rejection process.

EEG coherence was computed for all pairwise combinations of the following 16 channels (O1,O2,P3,P4,T5,T6,T3,T4,C3,C4,F7,F8,F3,F4,F1,F2). According to the International 10/20 system, distances between electrodes vary as a function of anterior–posterior and medial–lateral skull size. The values given in the text were estimated based upon mean skull size for mean ages 1 to 7 years and were rounded to the nearest centimeter (e.g., 6 cm for adjacent electrode pairs). The mathematical and digital signal processing procedures used to compute the EEG power spectrum and EEG coherence are described elsewhere (Thatcher et al., 1983, 1986, 1987).

Statistical analyses. In previous studies (Thatcher et al., 1987), 2- to 4-year oscillations in the lifespan development of EEG coherence and phase were commonly evident using 1-year means. In order to increase the frequency resolution of the rhythms of coherence, sliding averages were computed using 1-year epochs and .25-year increments from a mean age of .513 years to a mean age of 15.98 years (Thatcher, 1991). Statistical independence of subjects was attained at 1-year intervals with a 25% increase in new subjects with each .25-year increment (i.e., unique subjects within a mean was 25% for means separated by one step, 50% for means separated by two steps, 75% for means separated by three steps, and 100% independence of subjects for means separated by four steps). This procedure provided a total of 64 means and a .5-year frequency resolution. The statistical stability of the sliding averages was established by evaluations of the variance of the samples. There were no variance outliers (e.g., extreme Cook scores, Wilkinson, 1987) and there was no statistically significant heterogeneity of variance across age. The interpretation of EEG coherence is facilitated by analyses that correspond to known cortico–cortical connection systems. Since approximately 95% of the cortical white matter involves axons connecting intrahemispheric cortico–cortical regions (Nunez, 1981), the present study will focus primarily on analyses of intrahemispheric cortico–cortical electrode derivations. Homologous interhemispheric (e.g., F3/F4) analyses were also conducted; however, these analyses were essentially redundant to the intrahemispheric analyses (i.e., correlations with intrahemispheric electrodes of $>.80$) and did not yield unique factors or significant effects by themselves. The nonhomogeneous interhemispheric electrode combinations (e.g., F3/P4) were not analyzed since they represented a very small fraction of the known cortico–cortical fiber systems (Szentagothai, 1978; Braitenberg, 1978).

Factor analyses. As described in Thatcher (1991) principal components analysis and different factor analysis rotations (i.e., varimax and quadramax, Wilkinson, 1987) were conducted separately for each of the four EEG frequency bands. The rows of the analyses were the 64 time points and the columns of the analyses were the mean EEG coherence values from the 112 intrahemispheric scalp locations (i.e., each electrode with respect to all other intrahemispheric electrodes, $7 \times 8 = 56$ per hemisphere). To simplify the analysis and to increase reliability only eigenvalues greater than 1% of the variance were evaluated. The factor analyses revealed that from 9 to 11 factors accounted for at least 90% of the variance within each frequency band (i.e., delta, theta, alpha, and beta). Furthermore, the factors for the different frequency bands were consistently periodic and showed consistent anatomical patterns (Thatcher, 1991).

For example, the factor analysis revealed that the factors for the different frequency bands were periodic and showed similar anatomical patterns independent of frequency and consistently exhibited differential factor loadings between the left and right hemispheres (Thatcher, 1991).

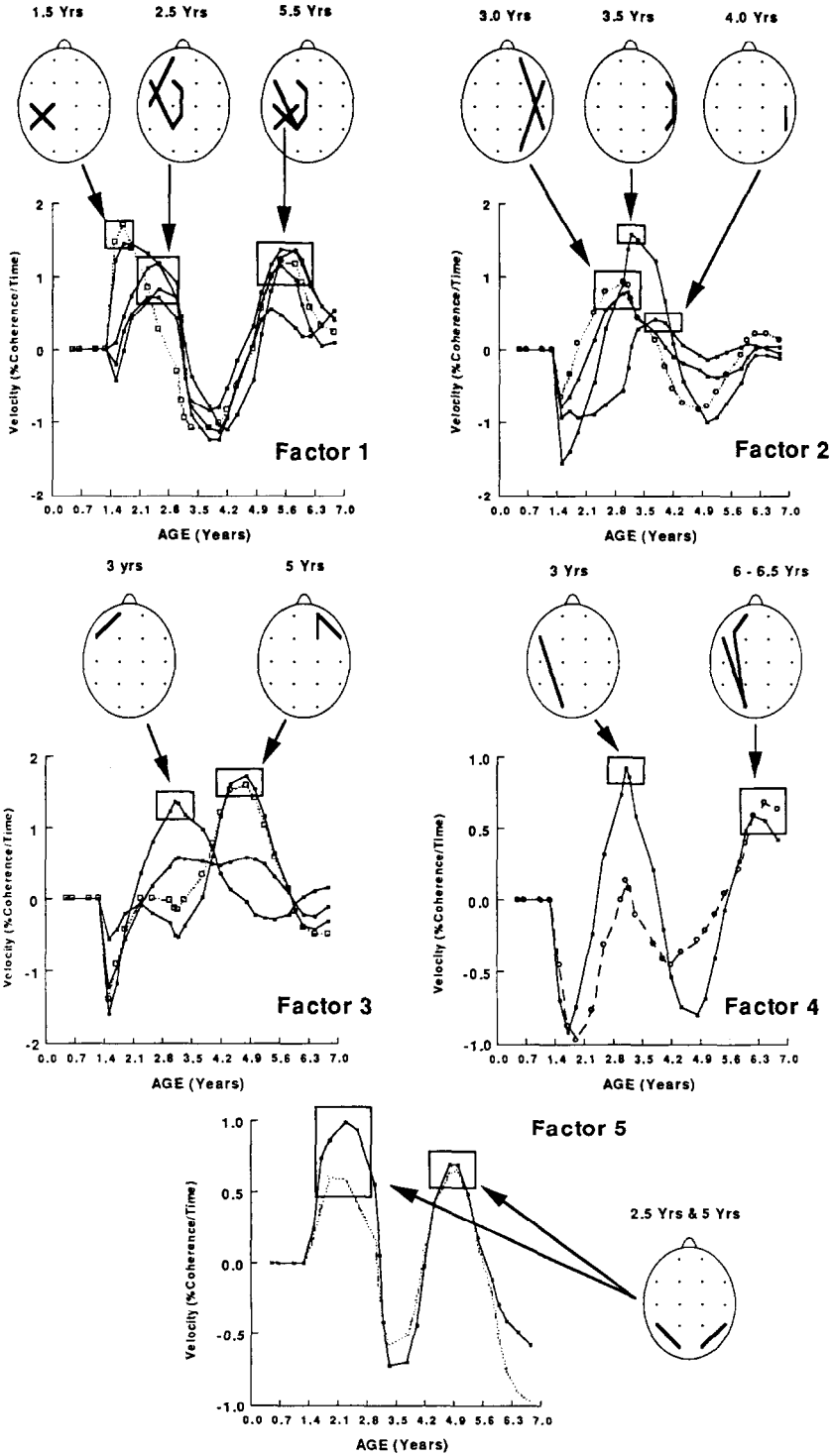
Computation of the first derivative. A four-point least squares procedure was used to compute the first derivative (i.e., velocity) or instantaneous rate of change in EEG coherence means from the 436 children in each developmental time series (Savitzky & Golay, 1964). The procedure involved the convolution of a quadratic function to compute the first and second derivatives (i.e., velocity and acceleration in percentage mean coherence/time as the limit approached zero). The first four points (mean ages of .513 to 1.292 years) were used to estimate the derivatives, and these points were set to zero. Therefore, no estimates of growth spurts prior to 1.495 years of age were made.

Definition of growth spurts. Growth spurts were defined by peaks of velocity or those postnatal ages where there was a maximum increase in mean coherence as measured by the first derivative. The point of maximum increase in EEG coherence (i.e., peak velocity) was considered to reflect an increase in the number and/or strength of connections between two or more intracortical systems as per Eq. (2). The criteria for defining a peak in velocity as a growth spurt were: (1) Only "in-phase" EEG coherence trajectories that loaded >.80 on a factor were evaluated. The criteria of in-phase developmental trajectories were generally satisfied by a significant loading on a given factor (Thatcher, 1992a). That is, each factor represents the commonality between developmental trajectories of EEG coherence and, therefore, by definition a factor reflects in-phase activity. In-phase trajectories were considered important since they reflect shared activity between specific intracortical connection systems and not localized or spurious changes. (2) The velocity peaks must be positive. The latter was based upon Eq. (2) and the fact that postnatal synaptogenesis often involves the production of a surplus of synapses followed by a pruning of synapses (Purves, 1988). Presumably, the positive first-derivative peaks correspond to the overproduction phase, while the negative peaks correspond to the pruning phase. The velocity or first derivative was selected rather than the second derivative or peaks in mean coherence because velocity reflects the point in time when growth or change in coherence is at a maximum.

RESULTS

Factor Analyses of Intrahemispheric Coherence Maturation

The head diagrams in Fig. 1 are from Thatcher (1991) and show the interelectrode combinations which loaded .80 or greater in the factor analysis of the theta frequency band. Replicated and stable factor structures were observed in the delta, theta, alpha, and beta frequency bands (Thatcher, 1991) and the critical features of this study such as cyclic recurrence of growth spurts and the spatial dimensions were present in all frequency bands. Therefore, because of space limitations only the analyses of the theta frequency band are shown in Fig. 1. The graphs below each set of head diagrams are the velocity curves computed from the mean EEG coherence. The ages at which growth spurts occurred are marked by arrows pointing to the various peaks in velocity. Although most of the first-derivative peaks were single points, several peaks were broad, involving more than one point. Therefore, for clarity only approximate ages of first-derivative peaks are represented in the text and figures. Since Julian ages were used (Thatcher et al., 1987) the designation of the age of a first-derivative peak was the 6-month period it was nearest


1.5 Yrs
2.5 Yrs
5.5 Yrs
Velocity (%Coherence/Time)
Factor 1
AGE (Years)
3.0 Yrs
3.5 Yrs
4.0 Yrs
Velocity (%Coherence/Time)
Factor 2
AGE (Years)
3 yrs
5 Yrs
Velocity (%Coherence/Time)
Factor 3
AGE (Years)
3 Yrs
6 - 6.5 Yrs
Velocity (%Coherence/Time)
Factor 4
AGE (Years)
Factor 5
2.5 Yrs & 5 Yrs
Velocity (%Coherence/Time)
AGE (Years)

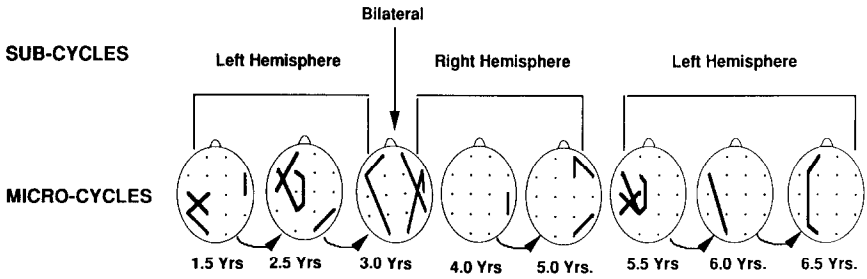


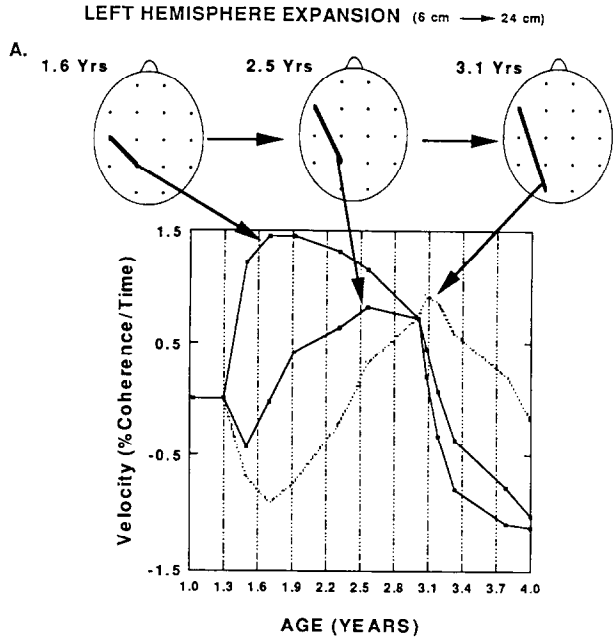
FIG. 2. Summary of the sequence and anatomical distribution of the growth spurts shown in Fig. 1. Lines connecting two electrode locations correspond to the electrode locations in Fig. 1 for the various developmental trajectories that loaded (>.80) on the first five factors from Thatcher (1991). Microcycles were defined by a developmental sequence involving a predominant rostral–caudal lengthening of interelectrode distances and a predominant lateral–medial rotation that cycles from the left hemisphere to bilateral to right hemisphere in approximately 4 years.

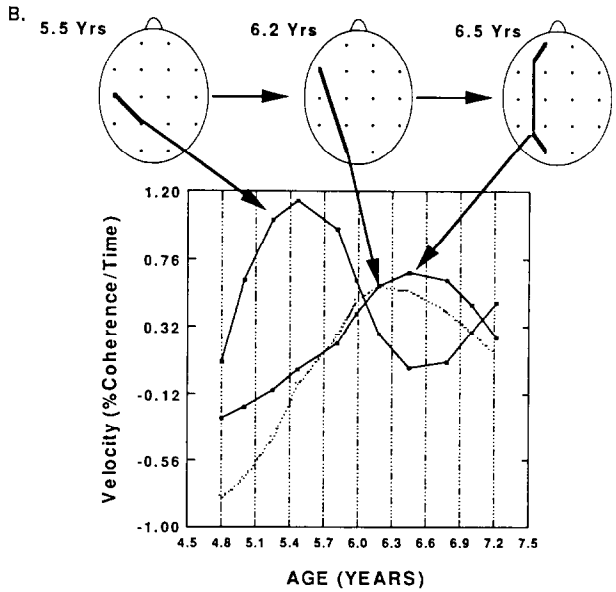
to. As shown in Fig. 1, left temporal–frontal and left parietal–frontal developmental trajectories loaded on factor 1, right temporal–frontal developmental trajectories loaded on factor 2, bilateral local frontal trajectories loaded on factor 3, left occipital frontal trajectories loaded on factor 4, and bilateral posterior cortical trajectories loaded on factor 5. Periodic in-phase activity was present at different ages for each of the five factors. The fact that multiple electrode combinations were often involved indicated that the "growth spurts" or in-phase activity reflected the involvement of relatively large numbers of neuronal systems over relatively short periods of time (e.g., 6 months to 1 year).

Cyclic Microcycles of Development

Figure 2 is a summary of the ages and periods of in-phase activity for the five factor groupings shown in Fig. 1. An iterative and sequential anatomical pattern of growth spurts was evident. For example, at age 1.5 years growth spurts were relatively localized (e.g., 6-cm interelectrode distances) and confined to the parietal and central to lateral–temporal regions. At age 2.5 years there was a lengthening along the rostral–caudal dimension (e.g., 12-cm interelectrode distances) with a lateral-to-medial rotation of parietal–frontal relations to include left parietal to left dorsal

FIG. 1. The velocity curves or the first derivatives (mean percentage coherence/time) of the developmental trajectories of mean EEG coherence from the subgroupings of electrode pairs that had the highest factor loadings (e.g., >.80) (Thatcher, 1991). Growth spurts were defined by a positive peak in the first derivative (i.e., a postnatal time of maximum growth) in multiple interelectrode combinations. Since each of the trajectories loaded heavily on a factor (i.e., >.80) this was considered sufficient evidence that a trajectory represented in-phase or anatomical synchrony of growth. See Fig. 2 to determine more precisely which intracortical connections exhibited growth spurts at the different postnatal ages.


LEFT HEMISPHERE EXPANSION (6 cm → 24 cm)
A.
1.6 Yrs
2.5 Yrs
3.1 Yrs
Velocity (%Coherence/Time)
1.5
0.5
-0.5
-1.5
1.0 1.3 1.6 1.9 2.2 2.5 2.8 3.1 3.4 3.7 4.0
AGE (YEARS)


B.
5.5 Yrs
6.2 Yrs
6.5 Yrs
Velocity (%Coherence/Time)
1.20
0.76
0.32
-0.12
-0.56
-1.00
4.5 4.8 5.1 5.4 5.7 6.0 6.3 6.6 6.9 7.2 7.5
AGE (YEARS)

medial–frontal regions (i.e., P3–F3 and T3–F1). At age 3 years there was a further lengthening of intracortical relations along the rostral–caudal dimension (e.g., 18- to 24-cm interelectrode distances) with continued involvement of dorsal medial–frontal to posterior cortex. This sequence of lengthening along the rostral–caudal dimension and rotation along the lateral-to-medial dimension between 1.5 and 3 years was repeated again between ages 5.5 and 6.5 years and is referred to as a "microcycle" of cortical development. The labeling of a predominant pattern as a microcycle or a subcycle is used to emphasize the presence of a sequential pattern. The important point, whether a sequence is labeled as a microcycle or a subcycle, is that the predominant sequence of left hemisphere–bilateral–right hemisphere represented a cyclic anatomical pattern.

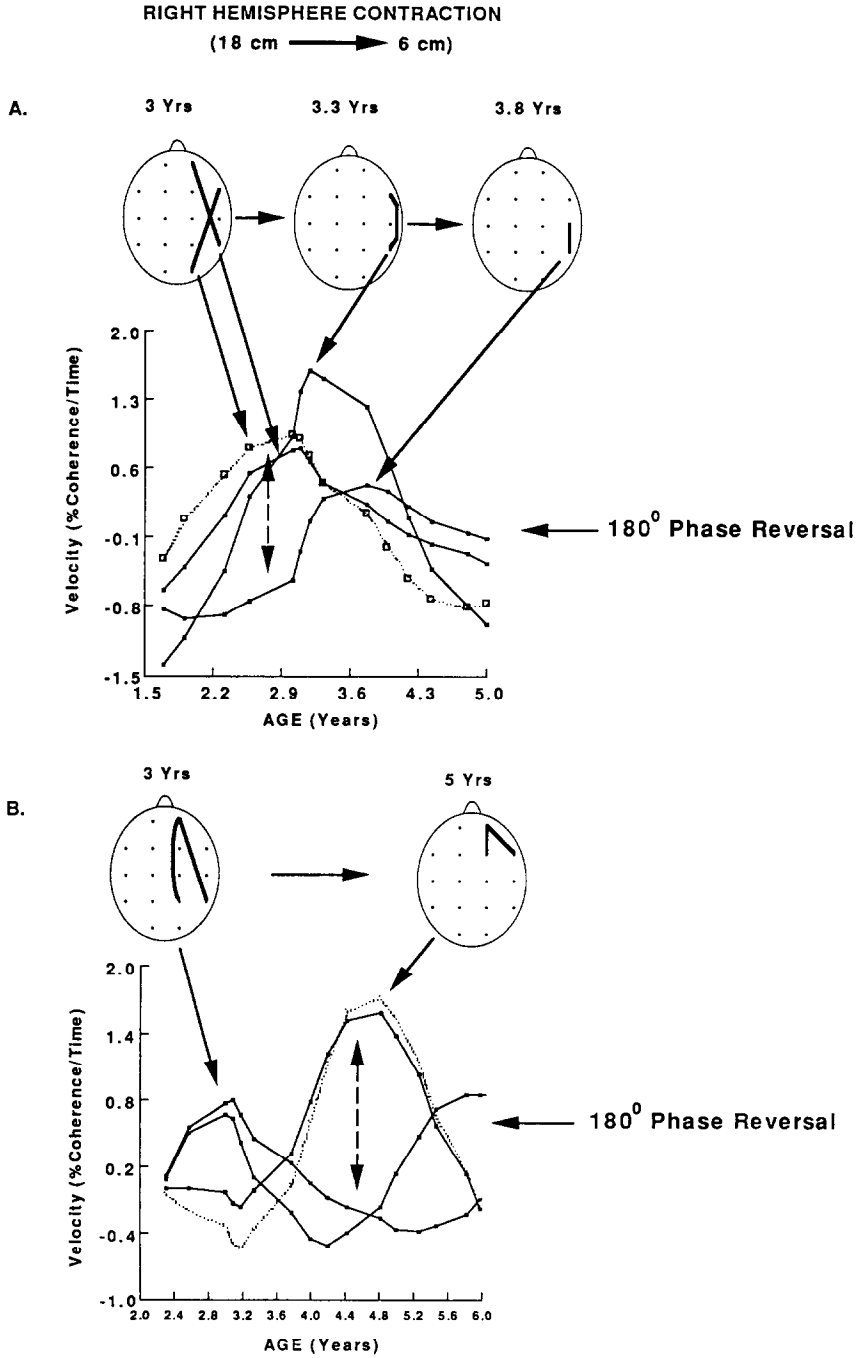
The following sections are an in-depth analysis of some of the developmental trajectories observed in Figs. 1 and 2. The purpose of these sections is to examine in detail the timing and location of growth spurts.

Expansion of Left Intracortical Connections

Figure 3A shows the sequential lengthening of left hemisphere intracortical growth spurts in EEG coherence at ages of approximately 1.5 to 3.0 years. For example, a peak in the first derivative of EEG coherence occurred in short distance parietal-to-ventral temporal leads around age 1.6 years (e.g., P3–T3, approx 6 cm), this was followed by a peak in the first derivative around 2.5 years in the parietal-to-lateral frontal (e.g., P3–F7, approx 12 cm) and this was followed by a peak in the first derivative around 3.1 years in a longer distance connection system (e.g., F7–O1, approx 21 cm).

Figure 3B shows a similar sequential lengthening of left hemisphere intracortical growth spurts during the period from 5.5 to 6.5 years. The short distance connection system of the parietal-to-lateral temporal regions (e.g., approx 6 cm) exhibited a growth spurt at approximately 5.5 years

FIG. 3. Examples of left hemisphere expansion sequences from short-distance intracortical connections to longer distance connections (see Fig. 2). (A) Sequence of expansive growth spurts in mean EEG coherence trajectories during the 1.5- to 3-year period. A peak in velocity occurred first in short distance intracortical connections (e.g., approx 6-cm interelectrode distance) in the left parietal lateral–temporal regions at age 1.6 years, was followed by a peak in the intermediate distance intracortical connections of the left parietal–lateral frontal region at 2.5 years (e.g., approx 12-cm interelectrode distance), and then, finally, was followed by a peak in velocity in the longer distance lateral frontal–occipital region at 3 years postnatal (e.g., approx 18 cm). (B) A second and iterative sequence of expansive growth spurts in mean EEG coherence trajectories during the 5.5- to 6.5-year period. A peak in velocity again occurred first in the short distance intracortical left parietal lateral–temporal region at age 5.5 years (e.g., approx 6-cm interelectrode distance), was followed by a first-derivative peak in the intermediate distance intracortical systems in the left lateral fronto–occipital region at 6.2 years (e.g., approx 12 cm), and, finally, was followed by a peak in velocity in the longer distance medial–frontal–occipital region (e.g., approx


RIGHT HEMISPHERE CONTRACTION
(18 cm → 6 cm)
A.
3 Yrs
3.3 Yrs
3.8 Yrs
Velocity (%Coherence/Time)
2.0
1.3
0.6
-0.1
-0.8
-1.5
1.5
2.2
2.9
3.6
4.3
5.0
AGE (Years)
180° Phase Reversal
B.
3 Yrs
5 Yrs
Velocity (%Coherence/Time)
2.0
1.4
0.8
0.2
-0.4
-1.0
2.0
2.4
2.8
3.2
3.6
4.0
4.4
4.8
5.2
5.6
6.0
AGE (Years)
180° Phase Reversal

and was followed by growth spurts at 18 cm (e.g., F7–O1), followed by a growth spurt at 6.5 years at approximately 24 cm (e.g., F1–O1). It should be noted that a 180° phase reversal between long distance versus short distance connection systems was observed in both Figures 3A and 3B.

Contraction of Right Intracortical Connections

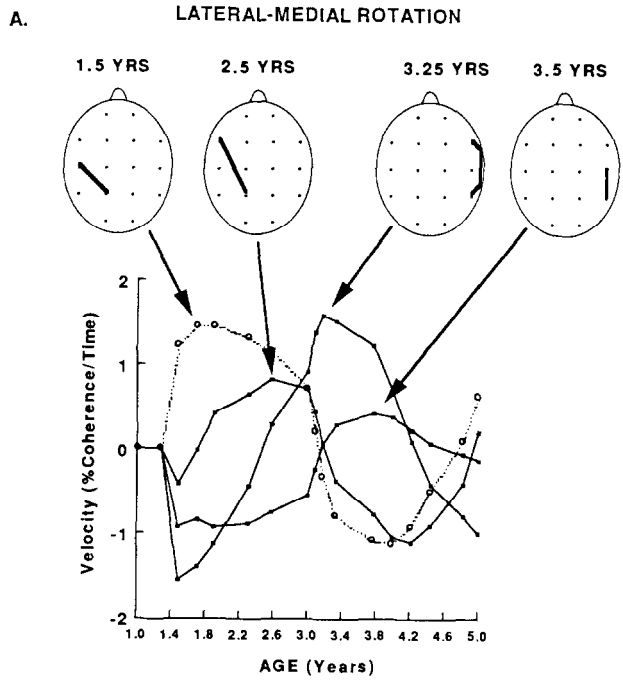
The right hemisphere pattern of contraction appeared to be the reverse of the left hemisphere pattern of expansion. As shown in Fig. 4A, between approximately 3.0 and 3.8 years, the right hemisphere exhibited a sequence of contraction or consolidation of long distance rostral–caudal intracortical growth spurts (e.g., approx 18 cm) to a shorter distance right posterior cortical growth spurt (i.e., 6 cm, right occipital–temporal). As shown in Fig. 4B, a similar contracting sequence was observed between the right frontal pole and right temporal and frontal regions between the ages of 3.0 and 5.0 years.

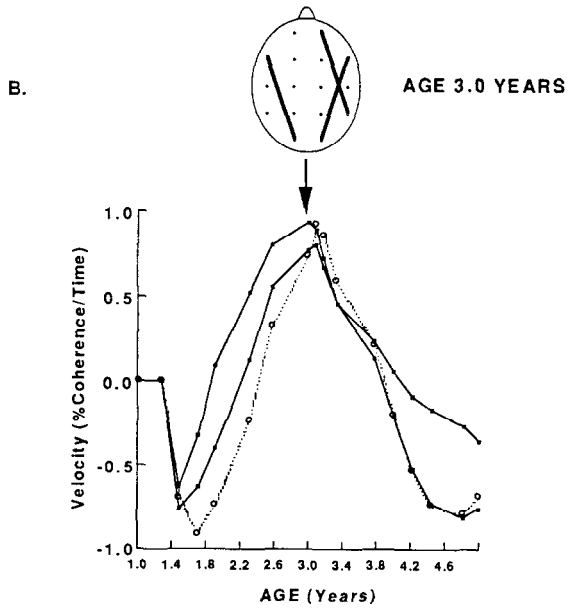
Age 3 as the North Pole in a Lateral-to-Medial Anatomical Rotation

Figure 5A shows the full sequence of left and right hemisphere growth spurts between the ages of approximately 1.5 and 3.5 years. A sequential left hemisphere expansion of intracortical growth spurts was followed by a right hemisphere sequence of intracortical contractions. This process can be visualized as a left-to-right, lateral–medial[1] rotational vector in

[1] The T3/4 and F7/8 electrodes record activity primarily from the lateral and ventral–lateral frontal regions while the F3/4 and C3/4 electrodes record activity primarily from the dorsal and dorsal–medial regions. Some prefer to refer to these electrode locations as lying along the lateral–dorsal rather than lateral–medial plane (e.g., Fox & Bell, 1990). The full dimension of neocortical evolution and ontogenesis is lateral–medial with the dorsal in between the lateral and the medial cortical regions (Lohman & Smeets, 1990; Pandya & Barnes, 1989; Smart, 1983). We prefer to emphasize the phylogenetic evolution of the two fronto–temporal systems and, therefore, use the lateral–medial nomenclature. The reader is referred to the approximate correspondence of the electrode locations to Broadman's areas as given by Homan, 1988.

FIG. 4. Examples of right hemisphere contraction sequence from long-distance intracortical connections to shorter distance connections. (A) Growth spurts in mean EEG coherence trajectories during the 3- to 4-year period. Peaks in the first derivative occurred first in long distance intracortical connection systems (e.g., approx 12- to 18-cm interelectrode distances) in the right fronto–temporal and right fronto–occipital areas at age 3.0 years, were followed by a larger amplitude peak in the shorter distance intracortical connections in the right lateral frontal–posterior temporal regions, and, finally, were followed by a peak in the lateral temporal–posterior temporal regions at 3.8 years postnatal (e.g., approx 6 cm). (B) Right frontal pole growth spurts in mean EEG coherence trajectories during the 3.0- to 5.0-year period. Peaks in the first derivative again occurred first in the long distance intracortical right fronto–temporal regions at approximately age 3.0 years (e.g., approx 18


A.
LATERAL-MEDIAL ROTATION
1.5 YRS
2.5 YRS
3.25 YRS
3.5 YRS
Velocity (%Coherence/Time)
2
1
0
-1
-2
1.0 1.4 1.8 2.2 2.6 3.0 3.4 3.8 4.2 4.6 5.0
AGE (Years)


B.
AGE 3.0 YEARS
Velocity (%Coherence/Time)
1.0
0.5
0.0
-0.5
-1.0
1.0 1.4 1.8 2.2 2.6 3.0 3.4 3.8 4.2 4.6
AGE (Years)

which the "north pole" is reached at approximately age 3. Figure 5B shows the left and right dorsal frontal growth spurts which are present at approximately age 3 years. Note that near age 3 there is an approximately 2- to 3-month phase lag between left and right hemisphere growth spurts with the left hemisphere leading the right.

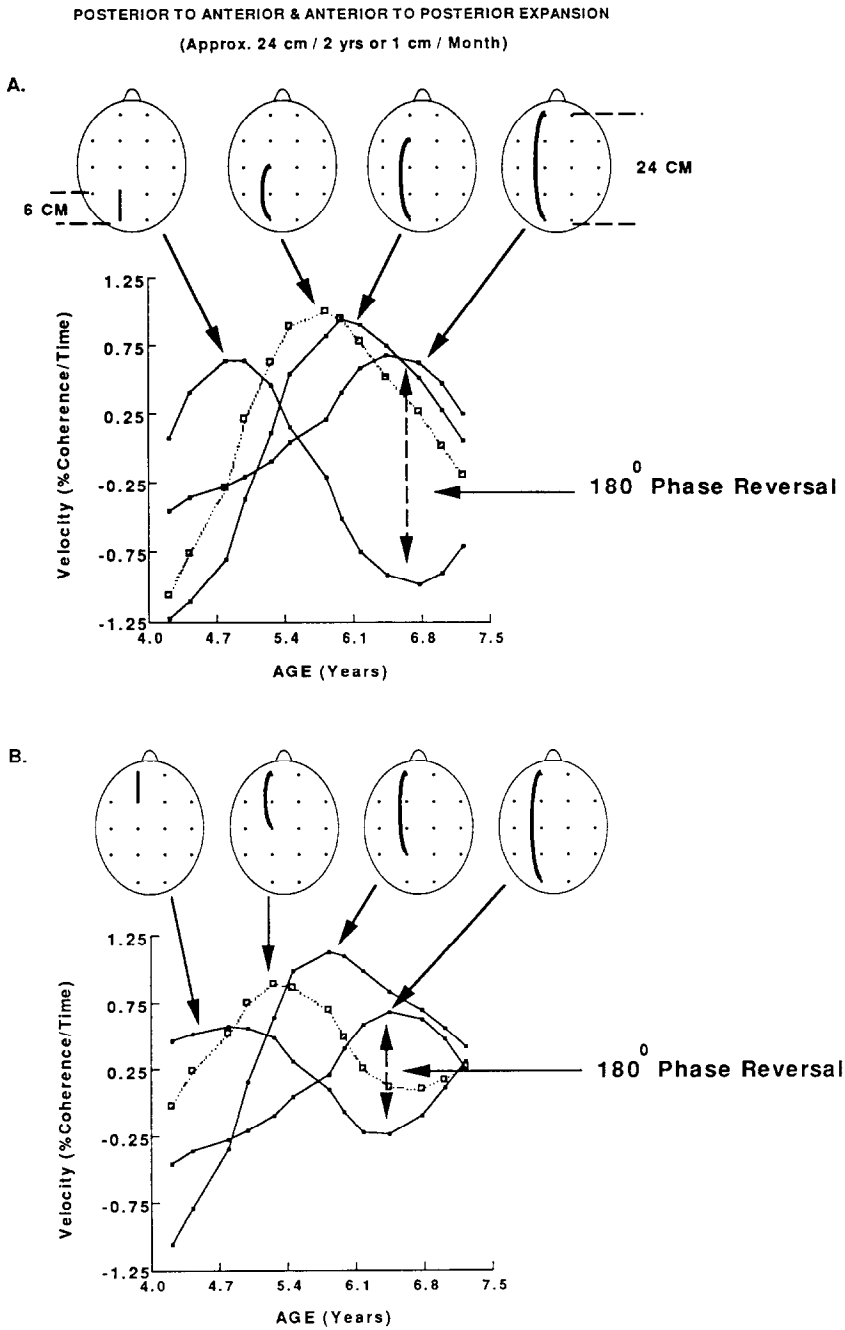
Rostral–Caudal Expansion of Intracortical Connections

Figure 6A shows a sequential posterior-to-anterior expansion in the length of intracortical growth spurts. The expansion begins around the age of 4.7 years with a growth spurt between short distance intracortical connections (i.e., O1–P3, approx 6 cm), followed by a growth spurt in longer distance connections (i.e., O1–C3, approx 12 cm), followed by a growth spurt in a longer distance connection system (i.e., O1–F3, approx 18 cm) followed, finally, by a longer distance growth spurt at age approximately 6.7 years (i.e., O1–F1, approx 24 cm). This entire process is completed in approximately 2 years and represents a sequence of growth spurts in intracortical connections that lengthens from 6 cm to 24 cm and exhibits a velocity of approximately 24 cm/2 years or ~1 cm/month.

As shown in Fig. 6B, a similar sequential lengthening of intracortical connections was observed in the anterior-to-posterior direction. This growth process occurred during the same postnatal interval of approximately 4.7 to 6.7 years as observed for the growth process in the posterior-to-anterior direction. However, the timing of growth spurts for a given interelectrode distance was somewhat different for the two directions of growth. For example, the growth spurt in the 12-cm distance in the posterior-to-anterior direction (e.g., O1–C3) occurred at approximately age 5.8 years, whereas the same distance in the anterior-to-posterior direction (e.g., F1–C3) exhibited a growth spurt at approximately 5.4 years.

A prominent feature of the rostral–caudal directional growth spurts was a 180° phase reversal between short-distance versus long-distance connections. As discussed elsewhere (Thatcher et al., 1986; Thatcher, 1992a,b) 180° phase reversals often reflect a competitive relationship, especially in dynamical nonlinear systems (Thom, 1975; Thompson and Stewart, 1986).

FIG. 5. (A) A sequence of expanding and contracting growth spurts that reflect a clockwise anatomical rotation. The process begins at age approximately 1.5 years in the left temporal–parietal region, rotates and extends at approximately age 2.5 years to the left lateral frontal–parietal region, rotates at approximately age 3.2 years to the right lateral frontal–posterior temporal region, and, finally, rotates and contracts to the right lateral temporal–posterior temporal region at age 3.5 to 4 years. (B) The long distance cortico–cortical growth spurts which are present near the dorsal medial cortex around the age of 3.0 years. Age 3.0 represents the "12 o'clock" or "north pole" of the lateral-to-medial rotational vector and is characterized by a phase lag of about .25 years between long distance


POSTERIOR TO ANTERIOR & ANTERIOR TO POSTERIOR EXPANSION
(Approx. 24 cm / 2 yrs or 1 cm / Month)
A.
6 CM
24 CM
1.25
0.75
0.25
-0.25
-0.75
-1.25
Velocity (%Coherence/Time)
4.0
4.7
5.4
6.1
6.8
7.5
AGE (Years)
180° Phase Reversal
B.
1.25
0.75
0.25
-0.25
-0.75
-1.25
Velocity (%Coherence/Time)
4.0
4.7
5.4
6.1
6.8
7.5
AGE (Years)
180° Phase Reversal

An Age 5.0 Right Frontal Pole Growth Spurt

Figure 7A shows a spatial gradient in the magnitude of a right frontal pole growth spurt around the age of 4.75 to 5.0 years. A maximum first derivative is in the short-distance right frontal pole interelectrodes of F2–F8 and F2–F4 (i.e., approx 6 cm), a smaller growth spurt is simultaneously present in the longer distance frontal pole interelectrodes of F2–T4 and F2–C4 (i.e., approx 12 cm), and no growth is present in the frontal pole to occipital electrode pairs (i.e., approx 28 cm). A comparison to the same electrode pairs in the homologous left hemisphere is shown in Fig. 7B. Only very small first derivatives were present with no spatial gradient evident.

These data suggest that a uniquely localized right frontal lobe growth spurt was present around the age of 4.5 to 5.0 years.

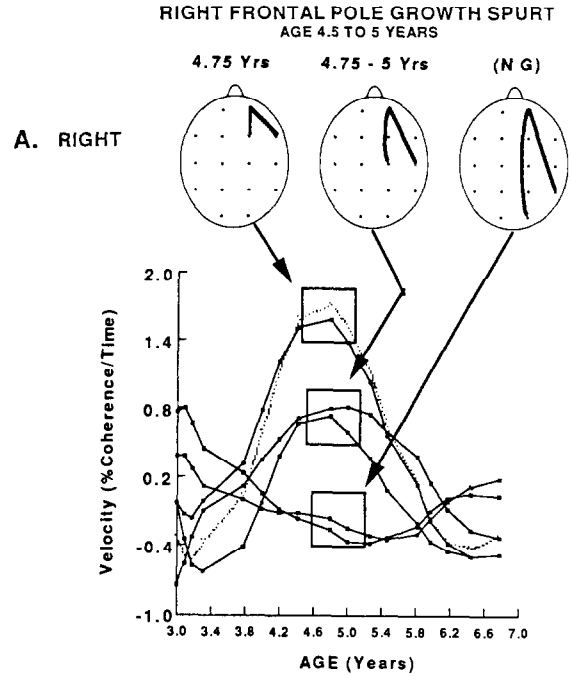
DISCUSSION

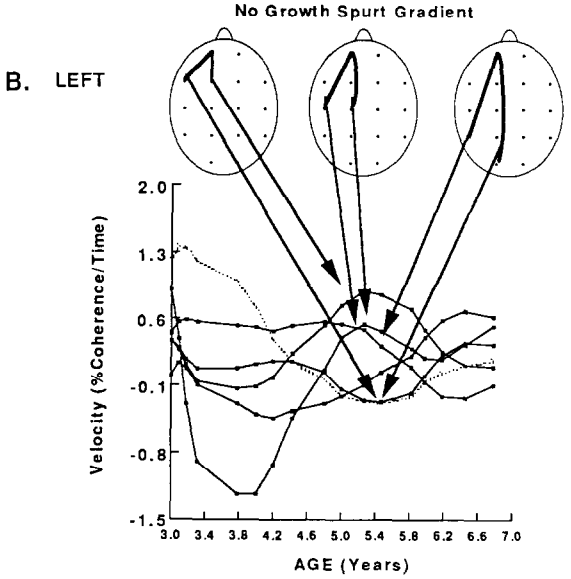
Limitations of the Study

There are several limitations of this study. One concerns the demographics of the population which, while composed of normal children, was not adequately represented by left-handed children and contained a mixture of sexes. The spatial and temporal aspects of the growth spurts may well be different for left-handed children as well as for males and females. The occurrence of EEG coherence growth spurts must be studied in different groups of children before the exact timing and anatomy of growth spurts can be considered to be accurate. Nonetheless, given the robustness of the general finding of cycles of spatial vectors of development, it is expected that all groups of children will exhibit these general phenomena.

Another limitation concerns the physiological meaning of EEG coherence. EEG coherence, while reflecting the actions of intracortical con-

FIG. 6. (A) An expanding sequence of posterior-to-anterior growth spurts which occur in the medial–dorsal plane. This process begins at approximately age 4.5 years in the left occipital–parietal region, then expands to the left occipital–central region at approximately age 5.75 years, then expands to the left occipital–dorsal frontal at approximately age 6.0 years, and, finally, expands to the left occipital–frontal pole at approximately age 6.5 years. A 180° phase reversal between the short-distance intracortical electrode pair (i.e., O1–P3) and the long distance intracortical electrode pair (i.e., O1–F1) is evident around age 6.5 years. (B) A complementary and nearly simultaneous expanding sequence to that observed in (A) but in the anterior-to-posterior direction. This process begins at approximately age 4.5 in the left frontal pole–dorsal frontal region, then expands at approximately age 5.3 to the left frontal pole–central region, then expands at age approximately 6.0 to the left frontal pole–parietal region, and, finally, expands at approximately age 6.5 years to the left frontal pole–occipital region. A 180° phase reversal between the short distance intracortical electrode pair (i.e., F1–F3) and the long distance intracortical electrode pair (i.e., F1–O1) is again


RIGHT FRONTAL POLE GROWTH SPURT
AGE 4.5 TO 5 YEARS
4.75 Yrs
4.75 - 5 Yrs
(N G)
A. RIGHT
Velocity (%Coherence/Time)
2.0
1.4
0.8
0.2
-0.4
-1.0
3.0 3.4 3.8 4.2 4.6 5.0 5.4 5.8 6.2 6.6 7.0
AGE (Years)


No Growth Spurt Gradient
B. LEFT
Velocity (%Coherence/Time)
2.0
1.3
0.6
-0.1
-0.8
-1.5
3.0 3.4 3.8 4.2 4.6 5.0 5.4 5.8 6.2 6.6 7.0
AGE (Years)

nections, fails to precisely define the mechanisms of this interaction. Equations (1) and (2) are very general and do not distinguish between basic neurophysiological processes capable of affecting intracortical interactions such as axonal sprouting, synaptogenesis, mylenation, expansion of existing synaptic terminals, pruning of synaptic connections, presynaptic changes in the amount of neurotransmitter, and changes in the postsynaptic response to a given neurotransmitter. Although all of the neurophysiological mechanisms influencing Eq. (2) cannot be distinguished using EEG coherence and phase, recent advances in digit signal analysis allow distinctions to be made between "white matter" versus "gray matter" contributions. In general, white matter axonal transmission delays are defined by a linear operator in which the signal is shifted in time without distortion. In contrast, synaptic delays and dendro-somatic integration delays of the gray matter are often nonlinear in which delay times are a function of amplitude and/or frequency. This distinction between linear white matter delays versus nonlinear gray matter delays is due to the fact that there is a relatively uniform and narrow range of cerebral axonal diameters in man and all-or-none axonal conduction velocities (approximately 2 to 9 meters/sec) within each axon, in contrast, synaptic transfers operate as low-pass filters in which the delays (.3 to 1.2 meters/sec) are frequency dependent (Lopes da Silva et al., 1989). These new technologies have not been applied to this population of children.

The method of defining the growth spurts is also an important limitation. The first derivative reflects the rate of change in mean coherence, independent of the actual mean coherence values. Thus, a 30% change in the mean can occur whether the mean is .1 or .8 and the derivative value will be identical. Thus, the relative magnitude of influence or connectivity between two brain regions is not directly represented by the first derivative. Nonetheless, the first derivative is valuable as a definition of growth since it normalizes "growth" by providing a precise definition of the point in time when there is a maximum rate of change. Another limitation is that only positive first-derivative values were counted as growth spurts. As mentioned previously, this was decided based upon Eq. (2) and the fact that postnatal synaptogenesis often involves the production of a surplus of synapses followed by a pruning of synapses. The positive first-derivative peaks presumably correspond to the over production phase

FIG. 7. (A) A right frontal pole growth spurt around the age of 4.5 to 5.0 years. Right frontal pole localization of the growth spurt is demonstrated by the spatial gradient in the decline of the first derivative from right frontal pole electrode pairs at approx 6 cm (i.e., F2–F4/F8) to longer distance frontal pole electrode pairs at approx 12 cm (i.e., F2–C4/T4) to no growth (NG) at approximately 18 to 24 cm (i.e., F2–O2/T6). (B) First-derivative values from the homologous left frontal pole as those shown in (A). No spatial gradient was evident and only minor first-derivative values were observed.

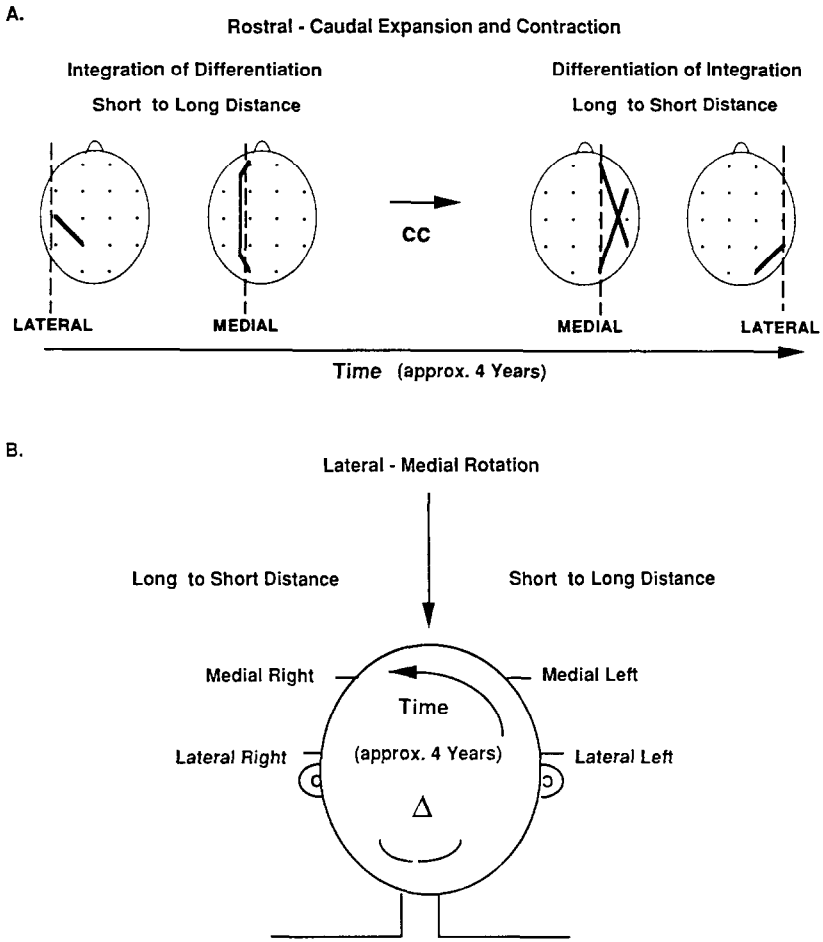


FIG. 8. (A) A diagramatic representation to illustrate the rostral–caudal sequence of development in the left and right hemispheres. The left hemisphere exhibited a sequential lengthening of intracortical connection systems, described as a developmental process of integrating differentiation. The right hemisphere exhibited a sequential shortening of the intracortical connection systems, described as a developmental process of differentiating integration (see Figs. 3, 4, and 5). (B) A diagramatic representation to illustrate the lateral–medial sequence of development. The sequence begins at left lateral cortex then intrahemispherically expands to left dorsal medial cortex, then projects through the corpus callosum to the right dorsal medial cortex, and then intrahemispherically contracts in the right lateral cortex (see Figs. 3, 4, and 5).

while the negative peaks correspond to the pruning phase. Further, whether a statistical criteria (e.g., $P < .05$) or an absolute positive derivative value was used (e.g., $>.5$ or rate of increase at 20% or greater per year, etc.) did not significantly alter the general finding of a left-to-right hemisphere sequence of expanding and contracting growth spurts

with rostral–caudal and lateral–medial vectors. Finally, a limitation was the use of the factor analysis with >.80 loadings to determine which developmental trajectories to examine. This criteria is relatively conservative since it minimizes the contribution by rare and spurious processes. However, while some type II errors may have been introduced, this procedure tended to minimize type I errors and provide a more reliable assessment of the dynamics of the growth spurts. For example, of the over 400 interelectrode combinations, 9 to 11 factors accounted for greater than 90% of the variance (Thatcher, 1991). It is this basic and stable structure, involving spatially synchronized activity, upon which the growth spurts were based.

Left versus Right Hemispheric Development

It is not surprising that the left and right hemispheres develop at different rates, since this is consistent with the neuropsychological literature. However, a new finding is that there are anatomical poles of postnatal cortical development and spatial gradients which operate differently for the two hemispheres. The developmental sequence of the left hemisphere, from short distance differentiated subsystems to long distance integration of the subsystems, mirrors the adult functional differences between the two hemispheres. For example, left hemisphere development can be likened to a process that functionally integrates differentiated subsystems. In contrast, the development of the right hemisphere, from long distance connections to short distance subsystems, can be likened to a process of functional differentiation of a previously integrated system. These observations suggest that the complementary functions of the left and right hemisphere are established early in human development through complementary developmental sequences. These complementary developmental sequences of the left and right hemisphere appear to recapitulate the differences in hemispheric function observed in the adult. For example, the adult left hemisphere is specialized for analytical and sequential processing which involves a high degree of local differentiation (Kinsbourne, 1974). However, differentiated subsystems require coordination and integration to operate efficiently. The developmental sequence of the left hemisphere is from differentiation to integration and this order may play an important role in the eventual maturation of left hemisphere analytical and sequential processing observed in the adult. In contrast, the specialized functions of the right hemisphere involve holistic and integrative information processing (Kinsbourne, 1974). Accordingly, the developmental order of the right hemisphere begins from an integration of distributed subsystems and then converges to differentiated or specialized subsystems. Presumably, this iterative sequence reflects a consolidation of the holistic functioning of the right hemisphere to relatively localized regions of the right parietal and right temporal lobes. Figure 8 is a sum-

mary of the specialized integration–differentiation distinctions of the two hemispheres.

In addition to the complementary directions of development, there appear to be at least two specialized and qualitatively unique differences in hemispheric development. One is the unique right frontal pole growth spurt around the age of 4.5 years (see Fig. 7) in which there was a spatial gradient of first-derivative values with a maximum at the right frontal pole. A similar growth spurt was absent in the homologous left frontal pole. This localized right frontal pole growth spurt occurs near the end of the first medial-to-lateral right hemisphere growth cycle (i.e., 4 years) and just prior to the beginning of the second lateral-to-medial left hemisphere growth cycle around age 5. A behavioral developmental landmark which occurs around the age of 4 to 4.5 years is referred to as "perspective taking" (Flavel, 1977) or the "Theory of Mind" (Perner & Wimmer, 1985) in which children develop the ability to represent what other people think about other people's thoughts. This is also a period of self development in which the child clearly separates him or herself from others in representational and social terms (Fischer & Pipp, 1984). The second unique feature of right hemispheric development is the differentiation of the right temporal lobes in the rostral–caudal plane. That is, the end of the medial-to-lateral right hemisphere growth cycle is marked by a differentiation between right temporal frontal and right temporal occipital and parietal subsystems. A similar bifurcation into subsystems is not observed in the homologous left hemisphere. The differentiation of the temporal lobes marks the end point of the first cycle of differentiation of integration (e.g., age 3 to 5) and presumably reflects the consolidation of integrated function within specialized subsystems of the right hemisphere.

Competition and Cooperation between Cortico–Cortical Connection Systems

Competition in EEG coherence is reflected by 180° phase reversals between different electrode pairs, whereas cooperation is reflected by in-phase (or nearly in phase) developmental trajectories (Thatcher et al., 1986; Thatcher, 1991). A common finding in the present study was that competition was maximal between long distance versus short distance intrahemispheric electrode pairings (see Figs. 3, 4, and 6). This finding is consistent with anatomical analyses demonstrating developmental remodeling of short distance axonal distributions through a process referred to as "collateral elimination" (Innocenti, 1981; O'Leary, Stanfield, & Cowan, 1981; Ivy & Kallackey, 1982; O'Leary, 1987). According to this process "local" synaptic connections to a given neuron are pruned or lost, while more "distant" synaptic connections to that same neuron are maintained or increased (O'Leary, 1987).

Speculation as to why synaptic competition is most prevalent between local versus long distance connections is that such a process may be a developmental strategy which increases connectional diversity at the expense of regional specificity (O'Leary, 1987). That is, if there is a limited and finite amount of dendritic surface on which synaptogenesis may occur, then an optimal developmental strategy would be to shift neural control from a highly specialized and differentiated system to a more globally integrated system. In the present study, the global integration of long distance connections is not a random network process, but rather one that specifically favors frontal to posterior cortico–cortical connection systems. The functional consequence of such a developmental process would be to bring local neural networks in posterior cortical regions under increasing control of frontal regions.

Lateral versus Medial Frontal Lobe Development: Assimilation and Accommodation Revisited

A central and unifying concept of Piaget's various developmental stages (i.e., sensory–motor, preoperational, operational, and formal) is that a child willfully acts upon the world in which he or she finds himself. A given motor act is created through motivation, perception, and goal-directed plans. At birth a child has a limited ability to act upon the world. As the child grows this ability evolves from simple sensory–motor units of behavior to complicated temporal organizations of behavior which involve the integration of motor acts that depend upon the bridging of substantial discontinuities between perception and action. Many neuroscientists agree that the frontal areas of the neocortex participate to some degree in the temporal organization of behavior and that the most anterior regions, e.g., the prefrontal cortex, are especially crucial for the bridging of the gap between perception and action (see reviews by Fuster, 1980; Goldberg, 1985; Brown, 1977; and Pribram, 1991).

Especially germane to the present paper is the recent evidence that there are two independent and parallel sources involved in the phylogenetic development of the frontal lobes (Dart, 1934; Abbie, 1940; Sanides, 1971; Pandya & Barbas, 1985; Pandya & Barnes, 1989). One is the olfactory bulbs and amygdala, which form the lateral frontal lobes, and the other is the hippocampus and cingulum, which form the medial frontal lobes. Among many anatomical differences, the medial frontal regions, with their center at the supplemental motor area, interhemispherically connect through the corpus callosum, whereas the lateral frontal regions, with their center at the lateral premotor area, are not connected through the corpus callosum (Goldberg, 1985).

A parallel can be drawn between Piaget's concepts of assimilation and accommodation and the functions of the lateral versus medial frontal systems. For example, the lateral system relies on short-term memory and

is influenced more by emotion and motivation, while the medial system relies more upon logical structure to form abstractions and higher levels of action patterns. The medial system is concerned with the representation of space and is essential for extended, predictive, and projected action. This system is more concerned with navigating the limb through space than with perceiving and accurately identifying objects in space (Fuster, 1980, 1981; Goldberg, 1985). In contrast, the lateral system is concerned with perceiving and recognizing external inputs and imparting to them motivational significance. The lateral system is involved in the production of actions responsive to the immediate environment, whereas the medial system is more involved in anticipatory or predictive actions that are guided by how the world will be in the future (Goldberg, 1985; Rizzolatti, Matelli, & Pavesi, 1983; Paillard, 1982; Fuster, 1980). The lateral system is uniquely connected to the limbic system through the temporal lobe–archicortical–amygdaloid pathway and is involved in the retrospective evaluation of movements through short-term memory, whereas the medial system is uniquely connected to the limbic system through the cingulate–paleocortical–hippocampal system and is involved in the prospective aspect of anticipating or predicting future actions. It is consistent with the analyses of Fuster (1980, 1981) and others (Goldberg, 1985; Rizzolatti et al., 1983; Fox & Bell, 1990; Pribram, 1991) to postulate that assimilation and accommodation are interactively reflected in the operations of these two evolutionary and architectonically separate frontal lobe systems, that is (1) through the temporally retrospective process of short-term memory and motivation mediated by the lateral system and (2) through the temporally prospective process of prediction and anticipation mediated by the medial system.

Cyclic Convergence as a Process that Narrows the "Gap" between Structure and Function

The data from the present study indicate that various intracortical connection systems iteratively exhibit growth spurts on an approximately 2- to 4-year cycle. The dominant patterns of the developmental trajectories of EEG coherence over the period from 1.5 years to age 7 indicate "poles" of development from which there are spatial gradients of organizational structure. The left–right, rostral–caudal, and lateral–medial poles of development reflect the three major anatomical axes of the cerebral cortex. That is, the major dimensions of anatomical differentiation, as manifested in differences in neocortical cytoarchitecture and intracortical connections, are along these three axes (Bayer & Altman, 1991). Furthermore, gross anatomical differentiation along the three major axes is largely established prenatally and is certainly complete by the second year of life (Salamon, Raynaud, Regis, & Rumeau, 1990; Rakic, 1985). However, at age 2 there

is a large disparity between structure and function in that adult anatomical differentiation is established early while adult functional differentiation only slowly emerges during the postnatal period (Piaget, 1971, 1975; Fischer & Pipp, 1984; Fischer, 1980; Fischer & Farrar, 1987; Case, 1985, 1987). Thus, the iterative growth spurts and patterns of development during the postnatal period may reflect a convergence process which narrows the disparity between structure and function by slowly sculpting and shaping the brain's microanatomy to eventually meet the demands and requirements of an adult world. According to this notion, an individual's gross anatomical structure is established early in development and the postnatal iterative sculpting process is used to fine tune anatomical structure to meet the needs of diverse and unpredictable environments. The sculpting process unlocks or tailors the functional potential of the stable gross anatomy according to individual needs and environmental demands.

Presumably, the cyclical patterning reflects a dialectic process which iteratively and sequentially reorganizes intracortical connection systems. This process can be described as a spiral staircase in which intracortical connection systems are reorganized each time the spiral sweeps around, forming successively higher levels of integration. However, precisely what is this spiral process and what are the mechanisms by which spatial and temporal growth is governed? Preliminary population dynamic models have recently been developed to fit the data and to simulate some of the critical features of the development of EEG coherence (Thatcher, 1989, 1992b,c). While these studies are still preliminary they utilize spatial population models of predatory–prey behavior and spatial models of two species competing for a common food supply. The species are two intracortical connection systems competing for synaptic binding sites on the dendrites of cortical pyramidal cells. A growth wave, involving propagation of a nerve growth factor, is postulated to arise from lateral cortical regions and to rotate clockwise at a rate from approximately 1.0 to 0.5 cm/month (i.e., assumes 24-cm excursion in the rostral–caudal and/or lateral–medial directions over a 2- to 4-year period). Each periodic wave front involves the local production of a surplus of synaptic connections followed by a pruning of excess connections. It is postulated that environmental factors, such as use and need of specific connections, largely determine which synaptic connections will survive and which will be pruned.

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