Analysis of MEG Activity across the Life Span Using Statistical Complexity

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Abstract—**The aim of this research was to analyze the changes in magnetoencephalographic (MEG) activity across the life span. For this task, 220 healthy subjects with ages ranging from 7 to 84 years were enrolled in the study. A statistical complexity measure based on the Shannon entropy and the Euclidean distance were used to assess changes in MEG oscillations during brain development. An increasing quadratic relationship between entropy and age was found, whereas the opposite behavior was observed between statistical complexity and age. Entropy and statistical complexity significantly increased and decreased, respectively, as a function of age from childhood to adolescence ($p < 0.0071$; Mann-Whitney *U*-test, Bonferroni corrected). Our results suggest that brain development is accompanied by several changes in the irregularity and statistical complexity patterns. These findings provide new insights into the delimitation of 'normal behavior' of neural dynamics during maturation and ageing.**

Keywords—**Brain maturation, magnetoencephalogram, entropy, disequilibrium, statistical complexity.**

I. INTRODUCTION

The brain is likely the most complex organ of the human body. Development across the life span is accompanied by important changes in neural activity [1]. In the last decades, considerable effort has been devoted to explore electroencephalographic changes associated with brain development [2]–[4]. However, only a few works have analyzed magnetoencephalographic (MEG) recordings to study the modifications in brain activity across the life span [5], [6]. Human brain can be affected by several neurological disorders from childhood to senescence [5]. Therefore, the analysis of age-related changes in MEG activity becomes a relevant issue to accurately characterize pathological states and differentiate them from changes associated with normal aging.

During the last decades, several definitions of complexity have been proposed [7], [8]. The present study is focused on the statistical complexity, based on the Shannon entropy and the Euclidean distance. This measure, derived from information theory, provides an alternative description of neural dynamics to that provided by other complexity families, such as algorithmic, dimensional or those directly linked to irregularity [7], [9]. The statistical complexity assumes that states with maximum or minimum entropy (i.e. "randomness" or "perfect order", respectively) do not contain significant information. Therefore, they are considered "trivial" [10]. This notion of complexity introduces a useful framework to characterize complex systems where a delicate interplay between functional segregation and integration can be found, such as the brain [11].

In the present research, we want to analyze the changes in entropy, disequilibrium and statistical complexity of MEG activity during brain development. Our results will provide original insights into the definition of the 'normal behavior' of neural dynamics across the life span.

II. MATERIAL

A. Subjects

Two-hundred and twenty normal controls were enrolled in the study. They were cognitively healthy controls with no history of neurological or psychiatric disorders. Subjects' age ranged from 7 to 84 years. Statistical analyses were carried out by grouping the sample into eight age stages, which correspond to eight decades of life. Table 1 summarizes the socio-demographic data for each age stage. None of the participants were taking any drug that could affect MEG activity at the recording time. All volunteers gave their informed consent to participate in the study, which was approved by the local Ethics Committee.

B. MEG Recordings

Five minutes of spontaneous MEG activity were recorded from the 220 participants using a 148-channel whole-head magnetometer (MAGNES 2500 WH, 4D Neuroimaging, San Diego, USA) placed in a magnetically shielded room at MEG Center Dr. Pérez-Modrego (Spain). Subjects were asked to relax, stay awake and with their eyes closed to avoid blinking and moving. Subjects' behavior and consciousness level were monitored during the recording. The sampling frequency was 678.17 Hz and a hardware band-pass filter of 0.1-200 Hz was applied. MEG recordings were decimated by a factor of 4 (169.549 Hz). Visual inspection and independent component analysis were performed to minimize the presence of artifacts. A mean of 17.8 ± 10.1 artifact-free epochs of 5 s per subject were selected. Finally, epochs were filtered between 1 and 65 Hz.

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III. METHODS

A. Spectral Analysis

Measures from information theory are usually computed from a probability distribution function (PDF) that describes the physical processes of the system under study [8]. Previous studies have found that the dynamics associated to brain activity can be characterized using a PDF based on its spectral content [9], [12]. In the present work, the dynamics of MEG activity will be analyzed using the normalized power spectral density function, $PSD_n = \{p_j, j=1,\ldots,N\}$, with N the number of frequency bins between 1 and 70 Hz. PSD_n was calculated for each 5 s artifact-free epoch (848 samples).

B. Entropy

Entropy is a thermodynamic parameter useful to characterize the disorder of a system [8]. Although several entropy definitions can be found, this study is focused on the canonical formulation of statistical mechanics (i.e. the Shannon's entropy, H_S). In the context of signal processing, H_S has been adapted to quantify the irregularity of a signal, based on its power spectrum [12]. Hence, H_S is an information measure that characterizes the uncertainty associated to the physical processes described by PSD_n.

$$H_S[PSD_n] = -\frac{1}{\ln(N)} \cdot \sum_{j=1}^{N} p_j \cdot \ln(p_j), \qquad 0 \le H_S \le 1. \quad (1)$$

Eq. 1 includes a normalization by the factor ln(N). This is the maximum value of H_S, which is obtained when our "ignorance" of the underlying process described by PSD_n is maximized (i.e. all the spectral components are equally probable, $P_e = \{ p_j^e = 1/N, j=1,\ldots, N\}$) [10].

C. Disequilibrium

A statistical complexity measure is based not only in the concept of "disorder" or "information", but also in the distance from the given PDF to the PDF that represents the equilibrium (i.e. the uniform distribution, P_e). Thereby, the disequilibrium would detect if there exist "privileged" states among the accessible ones [8]. In the context of the current research, the disequilibrium would reflect if there are "more likely" spectral components in the PSD_n. Certainly, the disequilibrium can be computed using several distances. Nevertheless, the Euclidean norm was selected on the basis of the results obtained in previous MEG studies [9].

$$Q_E[PSD_n] = \sqrt{\frac{N}{N-1}} \cdot \left[\sum_{j=1}^{N} \left(p_j - p_j^e\right)^2 \right]^{1/2}, \quad 0 \le Q_E \le 1. \quad (2)$$

Table 1 Summary of the socio-demographic data of the sample

Age stage	N	Age (years)	Gender
		Mean ± SD	Males:Females
I (<9 years)	9	8.3 ± 0.9	5:4
II (10-19 years)	20	15.0 ± 3.6	7:13
III (20-29 years)	43	24.4 ± 3.0	20:23
IV (30-39 years)	36	33.0 ± 2.6	18:18
V (40-49 years)	19	44.3 ± 3.1	12:7
VI (50-59 years)	21	55.9 ± 3.0	11:10
VII (60-69 years)	40	64.9 ± 2.7	11:29
VIII (>70 years)	32	75.1 ± 4.1	15:17

It should be noted that Eq. 2 is normalized by the factor $\sqrt{N - 1/N}$. This is the maximum possible value of the Euclidean distance, which is reached between P_e and a PDF with only one component different from zero [10].

D. Statistical Complexity

Statistical complexity measures reflect the interplay between the amount of information stored in a system and its disequilibrium [8]. Thereby, two extreme states can be considered as non-informative: (i) maximum foreknowledge (i.e. "perfect order") and maximum ignorance (i.e. "maximum randomness") [10]. In the present study, statistical complexity is defined in terms of H_S and Q_E,

$$C_S^E[PSD_n] = H_S[PSD_n] \cdot Q_E[PSD_n]. \quad (3)$$

C_S^E is not a trivial function of entropy, since it depends on two different PDFs: the one associated to the MEG activity (PSD_n) and the uniform distribution (P_e) [8].

E. Statistical Analysis

An exploratory data analysis was initially performed. Data did not meet parametric test assumptions. Hence, statistical differences between consecutive pairs of age groups (i.e. I vs. II, II vs. III, and so on) were assessed by means of Mann-Whitney U-tests adjusted for multiple comparisons by a Bonferroni correction ($\alpha = 0.05/7 = 0.0071$).

All computations and statistical analyses were performed using Matlab (version 7.14; Mathworks, Natick, MA).

IV. RESULTS

Initially, H_S and Q_E were computed for each 5 s artifact-free MEG epoch. Results were averaged over all channels to obtain a quantitative measure per subject. The evolution across the life span of H_S and Q_E is displayed in Fig. 1. In both cases curve fitting with quadratic models have been included. As depicted in Fig. 1, H_S seems to increase until a

certain maximum, decreasing after that value. The opposite behavior can be observed for Q_E.

C_S^E was computed from H_S and Q_E. Fig. 2 illustrates the boxplots corresponding to mean C_S^E values for each age stage. It can be observed that C_S^E shows a decreasing trend until the seventh decade of life and slightly increases during the eight decade. Statistically significant differences were only achieved between the first and second decade of life (i.e. between age stages I and II) for H_S (Z = -2.8991, p-value = 0.0037) and C_S^E (Z = 2.7106, p-value = 0.0067). No significant differences were found for the remaining pairwise comparisons (p-values > 0.0071).

V. Discussion

Our findings revealed that H_S tended to increase as a function of age, whereas the opposite behavior was found with Q_E. Likewise, the trend is reversed during the last decades of life (i.e. age stage VIII). These results suggest that the irregularity of the spectral content of MEG activity progressively increases as a function of age, until it reaches a maximum around the seventh decade of life. Several maturational studies also found a quadratic relationship between age and several non-linear parameters [4], [5]. Their findings support the notion that brain activity is associated with an increasing complexity with age [3], until a certain maximum [4], [5]. On the contrary, our findings suggest that C_S^E tended to decrease as a function of age during the first seven decades of life, whereas the opposite trend was observed in later life.

Certainly, the statistical complexity should not be confused with algorithmic complexity, dimensional complexity or the definitions of complexity directly linked to irregularity [7], [9]. As previously mentioned, C_S^E considers the states of maximal order or disorder trivial (i.e. they are non-informative). This fact is illustrated in Fig. 3, where C_S^E is plotted as a function of H_S. In Fig 3.a, the bounds of C_S^E are convex curves, vanishing on global extremes. Fig. 3.b expands the region of Fig. 3.a where the C_S^E values for the 220 controls are located. Likewise, the color scale illustrates the evolution of complexity with age. Fig. 3.b shows that decreasing C_S^E values are obtained with increasing age. This fact can also be observed analyzing the grand-average values for each age group (marked as hexagrams in Fig 3.b). Nevertheless, this trend changes in the age stage VIII. Though a high C_S^E value does not necessarily reflect an optimal information processing, it represents some kind of

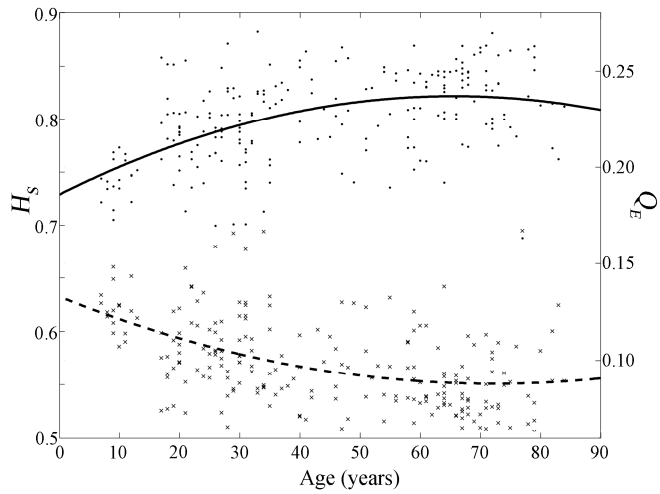

Fig. 1 Scatterplots showing age effects for H_S and Q_E. Each subject is plotted as a filled circle (HS) or a cross (Q_E), whereas fitted models represented as quadratic functions of age are plotted as solid (H_S) and dashed lines (Q_E).

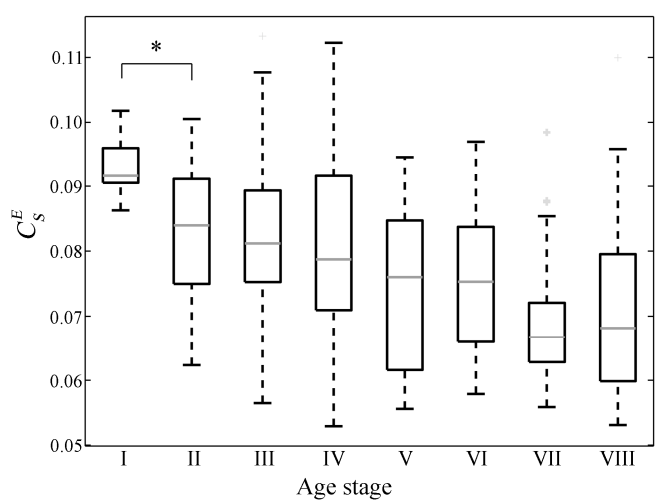

Fig. 2 Boxplots showing the distribution of C^E_S for each age stage. Statistically significant p-values are marked with asterisks (*, p < 0.0071).

highly informative processing. Hence, increasing statistical complexity values suggest that MEG oscillations were generated by a system governed by a balanced interplay between functional integration and segregation [11].

The results obtained with H_S, Q_E and C_S^E indicate that the more prominent changes in brain development can be seen between the age stages I and II. Indeed, the first and the second decades of life correspond with the maturation period. Our findings agree with previous studies that found age-related changes of neural activity, specially during

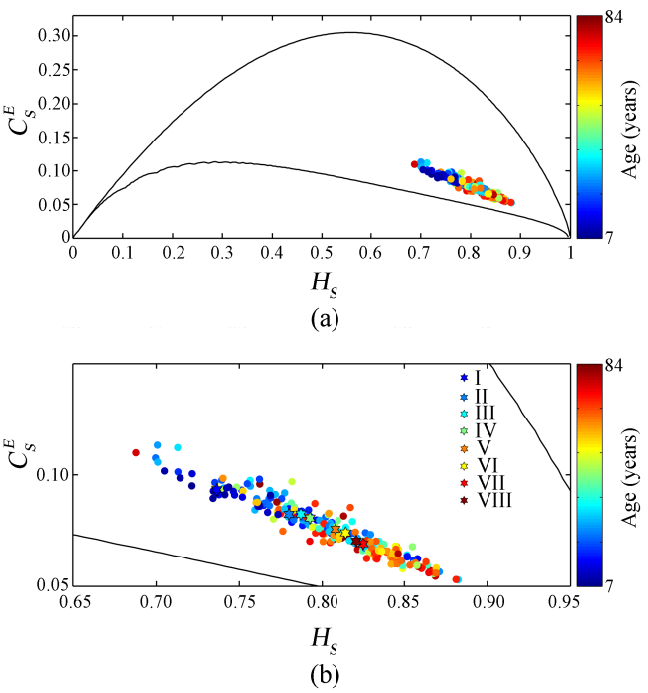

Fig. 3 Complexity *versus* entropy diagram for C^E_S and H_S, as a function of age. (a) $H_S \in [0\ 1]$. (b) $H_S \in [0.65\ 0.95]$ (grand-average values for each age stage are marked as hexagrams). Maximum and minimum possible values of C^E_S are also displayed (continuous curves).

maturation [2]–[5]. Thereby, they seem to reflect the synaptic and axonal modifications that have been reported during the transition from childhood to adolescence [13].

Several issues merit further consideration. Future work should address the assessment of the regional patterns of H_S, Q_E and C_S^E. In addition, further studies should analyze whether different definitions of entropy and disequilibrium could provide alternative statistical complexity measures. Finally, the present research was performed during a resting-state eyes-closed condition. Hence, it would be interesting to assess the neural dynamics elicited during an eyes-open resting condition or during the performance of visual or memory tasks, by means of the statistical complexity.

VI. Conclusions

Our findings support the notion that neural dynamics of MEG activity are modified across the life span. Brain development is accompanied with a progressive increase of entropy and decrease of statistical complexity until the seventh decade of life, in which a trend change can be found. Furthermore, significant changes in entropy and statistical complexity can be found during brain maturation.

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