Age-dependent electroencephalogram characteristics during different levels of anesthetic depth

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Research Article

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Abstract

Objective

The monitoring of anesthetic depth based on electroencephalogram (EEG) derivation is not currently adjusted for age. Here we analyze the influence of age factors on EEG characteristics.

Methods

Frontal EEG recordings were obtained from 80 adults during routine clinical anesthesia. The characteristics of EEG with age and anesthesia were observed during four kinds of anesthesia.

Results

Relative slow wave power, relative delta power, absolute slow wave power, BIS value and approximate entropy were statistically different in the adjacent anesthesia states ($P < 0.05$). Under very deep anesthesia, the relative slow wave power increases linearly with age ($R^2 = 0.1802$; $P = 0.0001$), the relative delta power decreased linearly with age ($R^2 = 0.3587$; $P < 0.0001$), the BIS value increased linearly with age ($R^2 = 0.0986$; $P = 0.005$), and the approximate entropy increases linearly with age ($R^2 = 0.0565$; $P = 0.036$). The relative slow wave power did not change in an age-dependent manner.

Conclusions

When using relative delta power, absolute slow wave power, BIS value and approximate entropy to monitor the depth of anesthesia, the influence of age should be considered, However, when using relative slow wave power, age should not be considered.

Background

Since researchers have found that the depth of anesthesia can be monitored noninvasively and reliably by electroencephalogram (EEG) information [1], more and more indicators derived from EEG information are used to monitor the depth of anesthesia [2,3]. Although these indicators bring great convenience to judge the depth of anesthesia in clinic, they are not adjusted by age, which will lead to inaccurate judgment of the depth of anesthesia and improper use of narcotic drugs [4]. EEG is formed by the summation of postsynaptic potentials synchronously generated by a large number of neurons [5]. Therefore, the changes of electroencephalogram are most significant during the initial development and final aging of neurons. In fast-growing children, the influence of age on EEG has been significantly different at different anesthesia conditions [6,7]. However, in aging adults, previous publications only described the change of EEG information with age at certain anesthesia conditions [8]. No one has studied the influence of age on EEG information at different anesthesia conditions, Therefore, it is necessary to explore the influence of age factors on EEG information at different anesthesia levels in adults, which is conducive to the use of EEG information to directly determine the depth of anesthesia in adults or the development of instruments to monitor the depth of anesthesia in the future, In order to achieve a more accurate judgment of the depth of anesthesia, and ultimately achieve the purpose of accurate use of narcotic drugs to reduce neurotoxicity [9].

The purpose of this experiment is to verify the indicators that can be used to monitor the depth of anesthesia in adults, and to explore the influence of age factors on EEG information at different anesthesia states, so as to guide the adjustment of age factors at different anesthesia states when the depth of anesthesia is determined by EEG information in the future.

Methods

Study population and anaesthetic procedure

This study was approved by the Medical Ethics Committee of the Second Hospital of Tianjin Medical University and registered as a prospective trial in the Clinical Trial Registry (NCT04760028). Written informed consent was obtained from all patients and/or their family prior to participation. Subjects comprised 40 old adult patients (range, 65 years) and 40 young adult patients (range, 65 years), all of whom were scheduled to atgo elective urological surgery. No patients had any clear neurological diseases or senile dementia, airway difficulties or known or potential airway problems, and were receiving medication.

According to the instructions, a bispectral index (BIS) sensor (Quatro sensor; Aspect Medical Systems, Natick, MA) consisting of electroencephalographic electrodes was on the patient's forehead. The Quatro sensor was connected to an A-2000 BIS® monitor (version 4.0; Aspect Medical Systems) and BIS monitor-derived parameters and raw EEG data were continuously collected for offline analysis. Anaesthesia was induced using propofol (1–2 mg kg^{-1}) combined with remifentanil which plasma target concentration of 4 ng ml^{-1} in Minto mode, facilitated by cisatracurium, and maintained using sevoflurane and 40% oxygen, combined with remifentanil. Respiratory parameters were adjusted to maintain normocapnia. Cisatracurium was administered to obtain sufficient muscle relaxation during surgery. In the process to end anaesthesia, when the main operation procedure was completed, the end-tidal concentration of sevoflurane was lowered from 1.4 minimum alveolar concentration (MAC, the minimum alveolar concentration that prevents movement in 50% of patients exposed to surgical incision) to 0.7MAC and 0.3MAC in a stepwise manner [10], while maintaining remifentanil at the same concentration as the induced concentration. Each target concentration was deliberately kept constant for 15 min, ensuring that the end-tidal partial pressure of sevoflurane in the brain was in equilibrium with that in the arterial blood [12]. Mean arterial blood pressure and heart rate were maintained at > 55 mmHg and > 45 beats min^{-1}, respectively, using phenylephrine and atropine as required.

Data acquisition and calculation

Electrode impedance was checked every 5 min and maintained at < 5 kΩ throughout the study using the A-2000 BIS monitor. The following time points were recorded: (1) The patient entered the room quietly and closed his eyes for 5min. (2) Sevoflurane concentration reached 1.4MAC at the end of respiration and remained stable for 15 minutes. (3) Sevoflurane concentration reached 0.7MAC at the end of respiration and remained stable for 15 minutes. (4) Sevoflurane concentration reached 0.3MAC at the end of respiration and remained stable for 15 minutes. The four time points were divided into four anesthetic states, and 2- minute raw EEG segments was collected at each anesthetic state for off-line processing. EEG segments were selected at four different states of anaesthesia: awake, light anaesthesia, deep anaesthesia, and very deep anaesthesia.

The raw EEG was analyzed by MATLAB software, and the clean EEG within 0.1Hz-45Hz was obtained by trapping, filtering and manual denoising. For each segment, we calculated the mean value from the chosen EEG data segments, to define overall power, the relative and absolute slow wave (0.1Hz-1Hz), delta (1Hz-3Hz), theta (3Hz-8Hz), alpha (8Hz-13Hz), beta (13Hz-25Hz) and gamma (> 25Hz) band powers, as well as the parameters such as approximate entropy, permutation entropy and sample entropy.

Statistical analysis

SPSS and MATLAB software were used for data analysis. Results are expressed as arithmetic mean ± SD for patient characteristics. Kolmogorov-Smirnov test among the four anesthetic states showed that the index values of each measure at each anesthetic state were not normally distributed, so we used Kruskal-Wallis test and multiple comparison test to estimate the significant differences among the four anesthetic states. The linear regression model between age and different anesthetic depth was established by least square method. $P < 0.05$ was considered statistically significant.

Results

Patient characteristics

Data was collected over a period of 6 months, from September 2020 until March 2021. During this period, four patients changed their anesthetic regimen and dropped out, and 80 patients eventually completed the trial. Patient characteristics are summarized in Table 1.

Table 1
Patient characteristics for different age groups.

	Young patients	**Old patients**
Patient characteristics	65years (N = 40)	65years(N = 40)
Age [years]	50 ± 5.22	72 ± 4.51
Gender [male / female]	19/21	20/20
BMI [kg/m^2]	24.34 ± 2.30	24.25 ± 3.02
Anaesthesia duration [min]	145 ± 5.60	150 ± 2.60

EEG changes related to level of anaesthesia

The relation between the relative power of the EEG and the state of anesthesia is shown in Figure. 1. Relative slow wave power and relative delta power can distinguish different anesthetic states in any age group. Relative theta power in any age group can only distinguish between deep anesthesia and very deep anesthesia. Relative alpha power can only distinguish between light and deep anesthesia and between deep and very deep anesthesia in the young group. Relative beta power can distinguish between different anesthetic states in the old group and between awake and light anesthesia as well as between light and deep anesthesia in the younger group. Relative gamma power can distinguish between different anesthetic states in the young group, awake and light anesthesia as well as deep anesthesia and very deep anesthesia in the old group.

The relationship between the absolute power of the EEG and the state of anesthesia is shown in Figure. 2. Absolute slow wave power can distinguish between different anesthetic states in any age group. Absolute delta power can distinguish between awake and light anesthesia, and between awake and light anesthesia, deep anesthesia and very deep anesthesia in the young group. Absolute theta power can distinguish between different anesthetic states in the younger group, between light and deep anesthesia and between deep and very deep anesthesia in the old group. The absolute alpha power differed between awake and light anesthesia and between light and deep anesthesia in both young and old groups. The absolute beta power can distinguish between awake and light anesthesia in the younger group, and between awake and light anesthesia, as well as between deep anesthesia and very anesthesia in the old group. The absolute gamma power can distinguish between awake and light anesthesia in the younger group, and between awake and light anesthesia and between deep and very deep anesthesia in the old group.

The relationship between total power and BIS and the state of anesthesia is shown in Figure. 3. Total power can distinguish between awake and light anesthesia in the younger group, and between awake and light anesthesia and between deep and very deep anesthesia in the old group. The BIS value can distinguish between different anesthetic states in any age group.

The relationship between approximate entropy, permutation entropy, sample entropy and anesthesia is shown in Figure. 4. Approximate entropy can distinguish different anesthetic states in any age group. In any age group, the permutation entropy can distinguish between awake and light anesthesia and between light and deep anesthesia. Sample entropy can distinguish between light and deep anesthesia and between deep and very deep anesthesia in any age group.

Age-related EEG changes

The relation of the relative power of the EEG to age is shown in Figure. 5. The relative slow wave power increased significantly with age at very deep anesthesia (R^2 = 0.1802; P = 0.0001). The relative delta power decreased with age at both deep and deep anesthesia, and the decrease was most significant at very deep anesthesia (R^2 = 0.3587; P < 0.0001). The relative alpha power decreased with age at deep anesthesia and very deep anesthesia. The relative beta power increased with age at light anesthesia, deep anesthesia, and very deep anesthesia, and the increase was most significant at deep anesthesia (R^2 = 0.1678; P = 0.0001). The relative gamma power increased with age at very deep anesthesia.

The relation of EEG absolute power to age is shown in Figure. 6. The absolute delta power decreased with age at deep anesthesia and very deep anesthesia, and the decrease was most significant at very deep anesthesia (R^2 = 0.3634; P < 0.0001). the absolute theta power decreases with age at very deep anesthesia. The absolute alpha power decreased with age at both deep anesthesia and very deep anesthesia, and the decrease was most significant at very deep anesthesia (R^2 = 0.1704; P = 0.0001). The absolute beta power decreases with age at very deep anesthesia. The absolute gamma power decreases with age at very deep anesthesia.

The relationship between total power and BIS value and age is shown in Figure. 7. Total power decreases with age at deep anesthesia and very deep anesthesia. The BIS value increases with age at very deep anesthesia.

The relationship between approximate entropy, permutation entropy, sample entropy and age are shown in Figure. 8. Approximate entropy increases with age at very deep anesthesia. Permutation entropy increased significantly with age at very deep anesthesia (R^2 = 0.1942; P < 0.0001).

Discussion

In this study, the relative slow wave power, relative delta power, absolute slow wave power, the BIS value and approximate entropy can be used to distinguish different anesthesia, but relative slow wave power, the BIS value and approximate entropy increase with age at very deep anesthesia, relative delta power decline with the age at very deep anesthesia. The relative slow wave power did not show age-dependent changes in any of the anesthetic states observed.

The decreasing trend of absolute power with age reflected in our experimental results is similar to the previous experimental results [12]. Although the changing trend of absolute slow wave power in the resting state is different from the previous studies [13], this may be related to our different definition of the awaking state. The change of relative beta power decreases with age, and the approximate entropy and sample entropy increase with age, which is consistent with the previous results [14]. The difference between this experiment and the previous experiments is that different anesthetic states are distinguished in this experiment, and the trend of change is shown only when the anesthetic depth reaches a certain level.

Our experimental results are explained as follows: As the body's aging, significant changes have taken place in the morphology of neurons in the brain [15−17], this change can be reflected EEG information, but the difference simply by aging, at normal circumstances may not be obvious, when the central nervous system is affected by the anesthetic at the same time, weakening the brain's response to the anesthetic is also changed [18,19], These age-induced changes are relatively magnified and appear more pronounced on the EEG, but the age-induced changes are not identical across the frequency range of the EEG[20].

In this experiment, we distinguish different anesthetic states in adult patients to observe the influence of age factors on EEG at each anesthetic state, which is the biggest innovation of this experiment. Since all the data were collected during the operation, which is a deficiency of this experiment, all the cases we selected were of the same type of operation. Since our data were collected in clinical practice, we believe that the results of the analysis can better reflect the real clinical situation.

Conclusions

From this experiment, we can know that when choosing different EEG indicators to judge the depth of anesthesia in clinical practice, it is necessary to consider whether these indicators are affected by age. For example, when we monitor the depth of anesthesia using relative delta power, absolute slow wave power, BIS value and approximate entropy, the influence of age factors should be considered. Age does not need to be considered in monitoring the depth of anesthesia with relative slow wave power.

Abbreviations

EEG electroencephalogram

BIS bispectral index

MAC minimum alveolar concentration

Declarations

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Author Contributions

Feixiang Li: data collection, study design, data analysis and writing up of the first draft of the paper. Yunchun Lu: study design, data collection, data analysis. Yaoyao Dang: data collection, data analysis. Huiming Chen: data collection. Huanhuan Lv: data collection. Jian Sun: data collection.

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Availability of data and materials

The dataset generated and analyzed during the current study is available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was registered as a prospective trial in the Clinical Trial Registry (NCT04760028).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

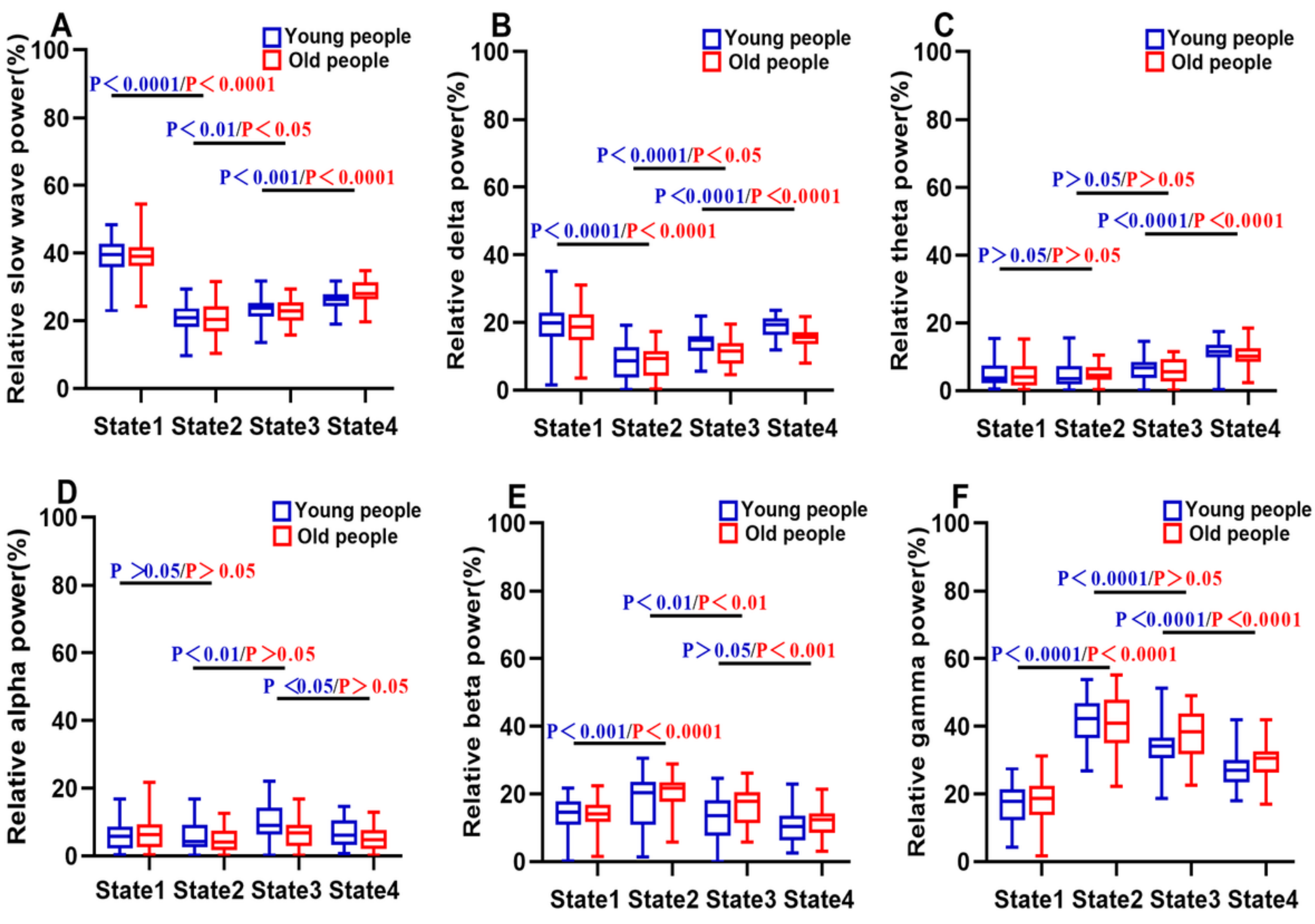

Figure 1

Relationship between relative power of electroencephalogram and state of anesthesia. A: Relationship between relative slow wave power and anesthetic status in the elderly and young groups. B: Relationship between relative delta power and anesthetic status in the elderly and young groups. C: Relationship between the relative theta power and the state of anesthesia in the elderly and young groups. D: Relationship between the relative alpha power and the state of anesthesia in the elderly and young groups. E: Relationship between relative beta power and anesthetic status in the elderly and young groups. F: Relationship between the relative gamma power and the state of anesthesia in the elderly and young groups.

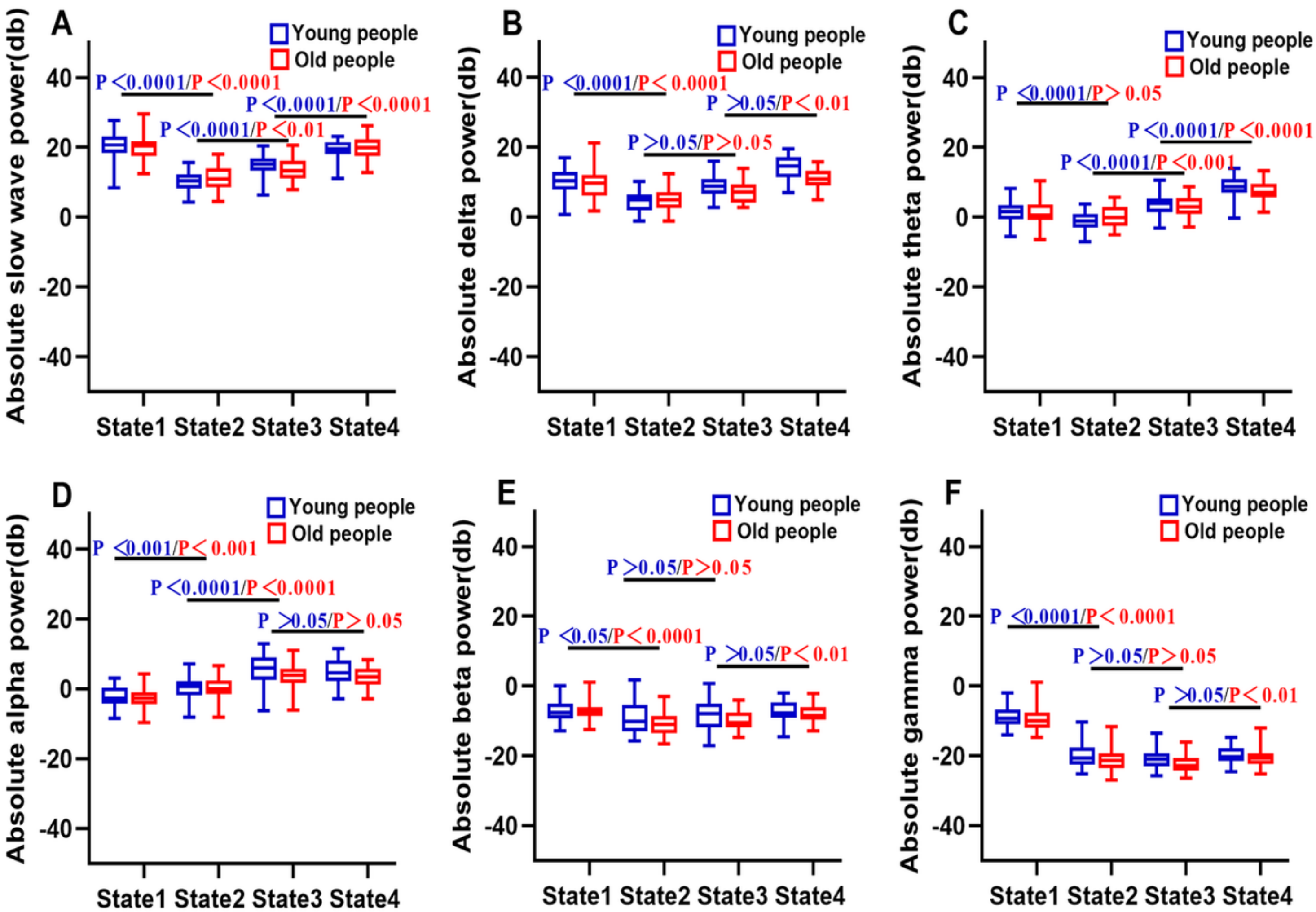

Figure 2

Relationship between absolute power and state of anesthesia. A: Relationship between absolute slow wave power and anesthetic state in the elderly and young groups. B: Relationship between absolute delta power and the state of anesthesia in the elderly and young groups. C: Relationship between absolute theta power and anesthetic state in the elderly and young groups. D: Relationship between absolute alpha power and the state of anesthesia in the elderly and young groups. E: Relationship between absolute beta power and anesthetic status in old and younger groups. F: Relationship between absolute gamma power and the state of anesthesia in the elderly and young groups.

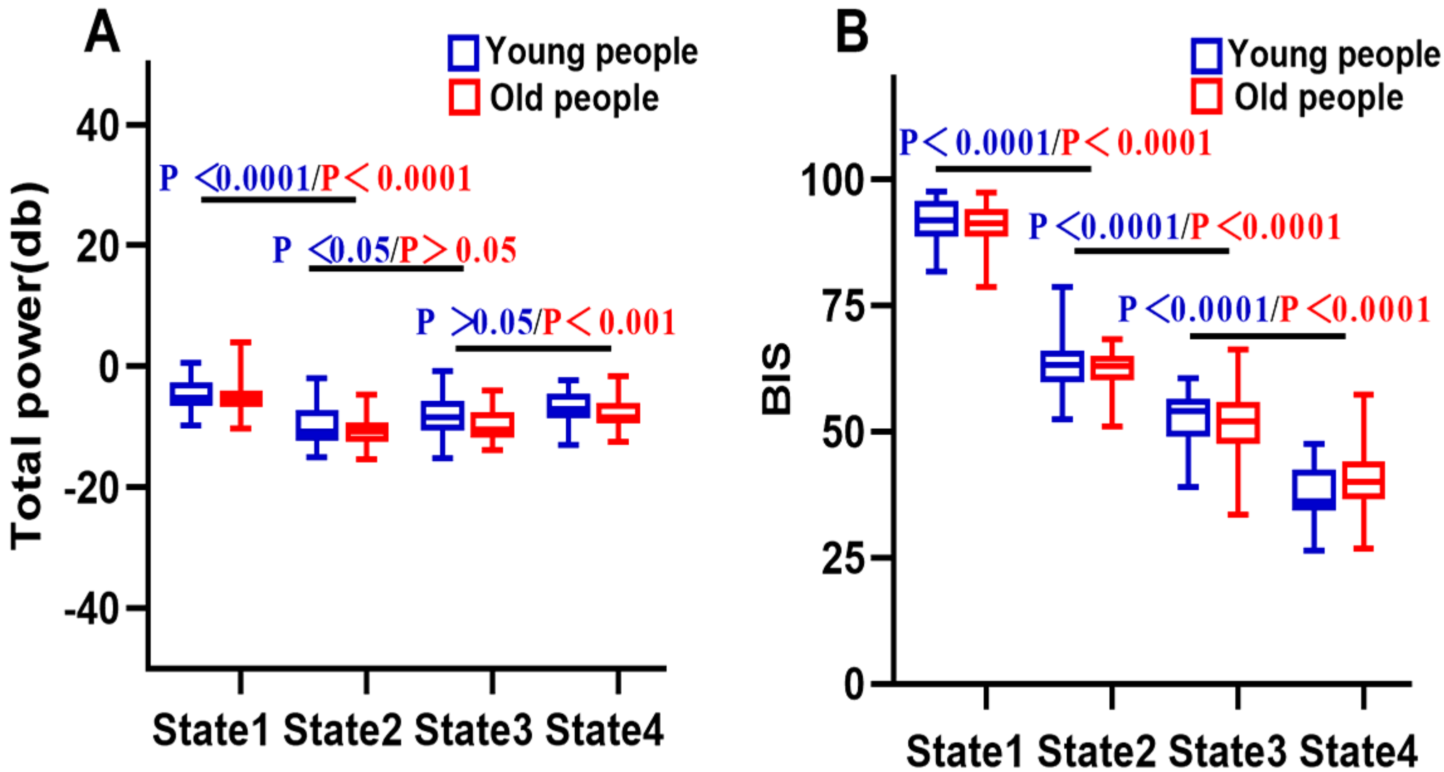

Figure 3

Relationship between total power and BIS and the state of anesthesia. A: Relationship between the total power and the state of anesthesia in the old and younger groups. B: Relationship between BIS and anesthetic status in the old and younger groups.

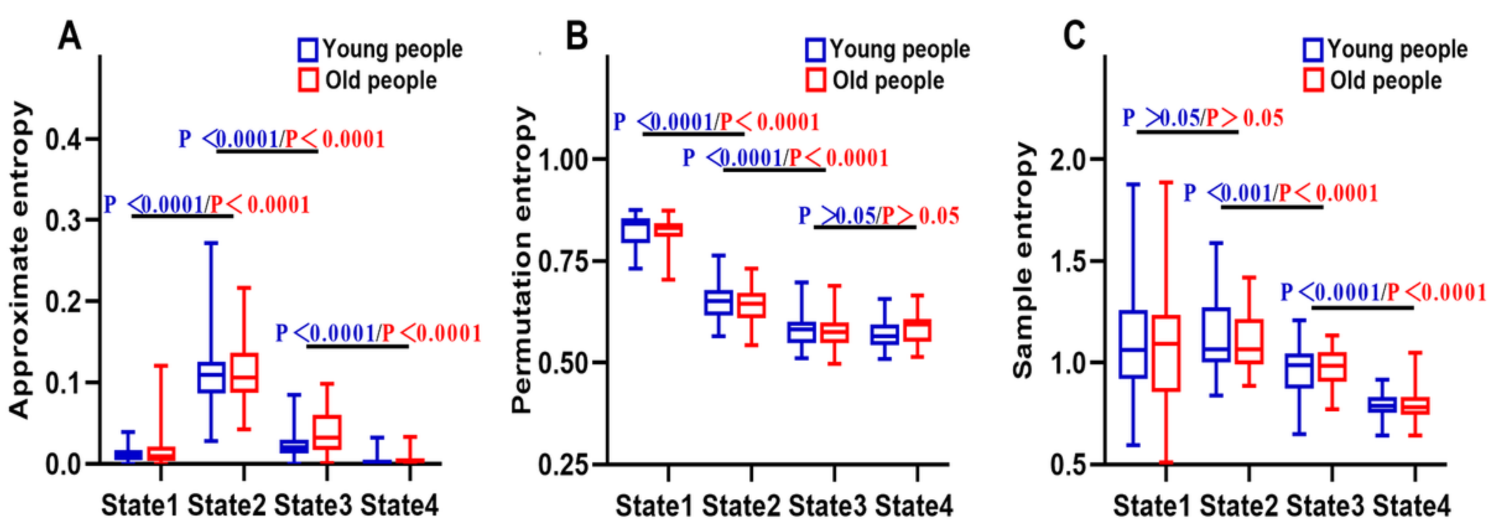

Figure 4

Relationship between approximate entropy, permutation entropy, sample entropy and anesthesia state. A: Relationship between approximate entropy and anesthetic state in the old and younger groups. B: Relationship between the permutation entropy of the elderly group and the young group and the state of anesthesia. C: Relationship between sample entropy and anesthetic state in the old and younger groups.

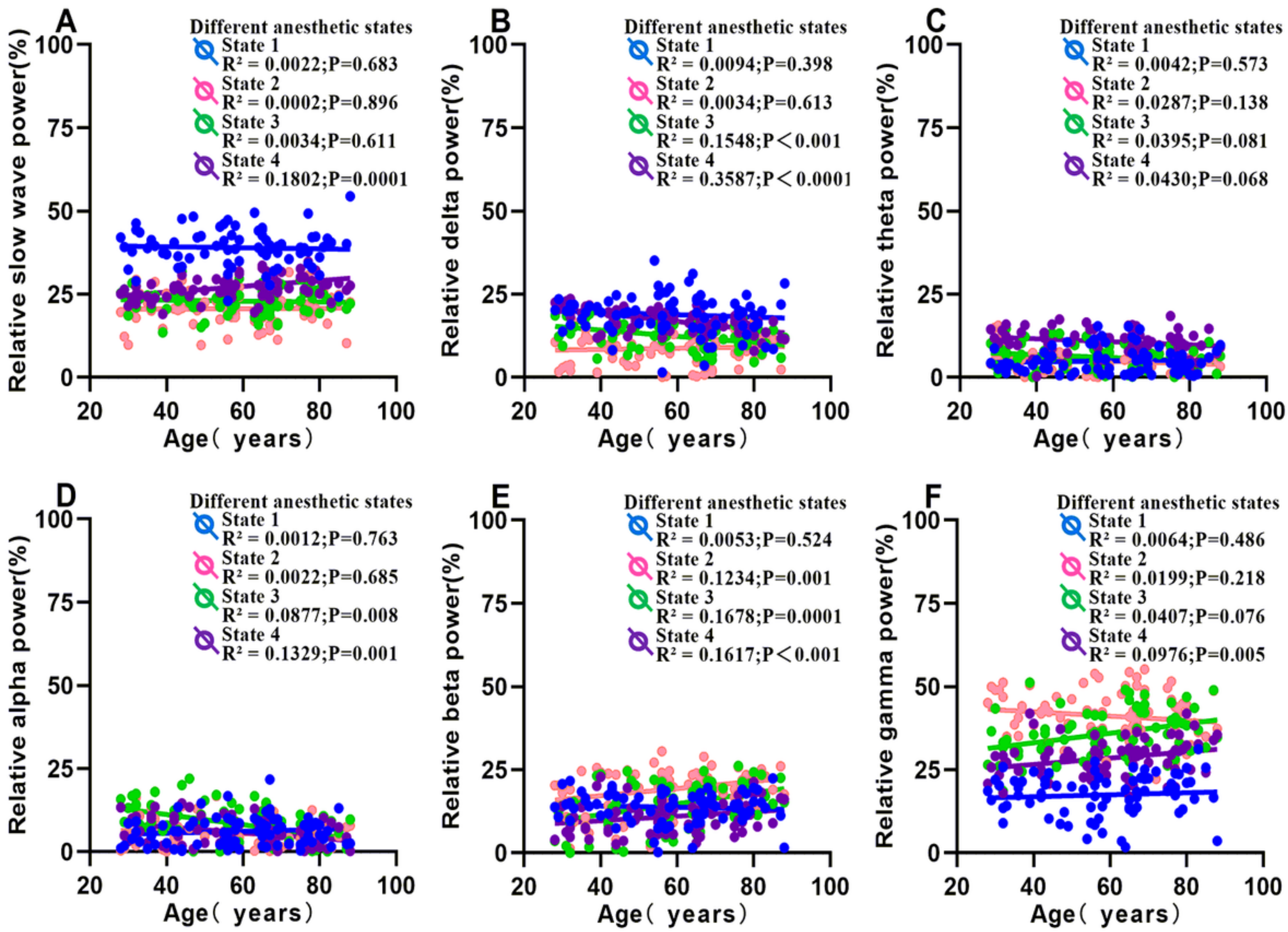

Figure 5

Relative power changes with age at different anesthetic conditions. A: Changes in relative slow wave power with age at four anesthetic conditions. B: Changes in relative delta power with age at the four anesthetic conditions .C: Changes in relative theta power with age at the four anesthetic conditions. D: Changes in relative alpha power with age at the four anesthetic conditions. E: Changes in relative beta power with age at four anesthetic conditions. F: Changes in relative gamma power with age at the four anesthetic conditions.

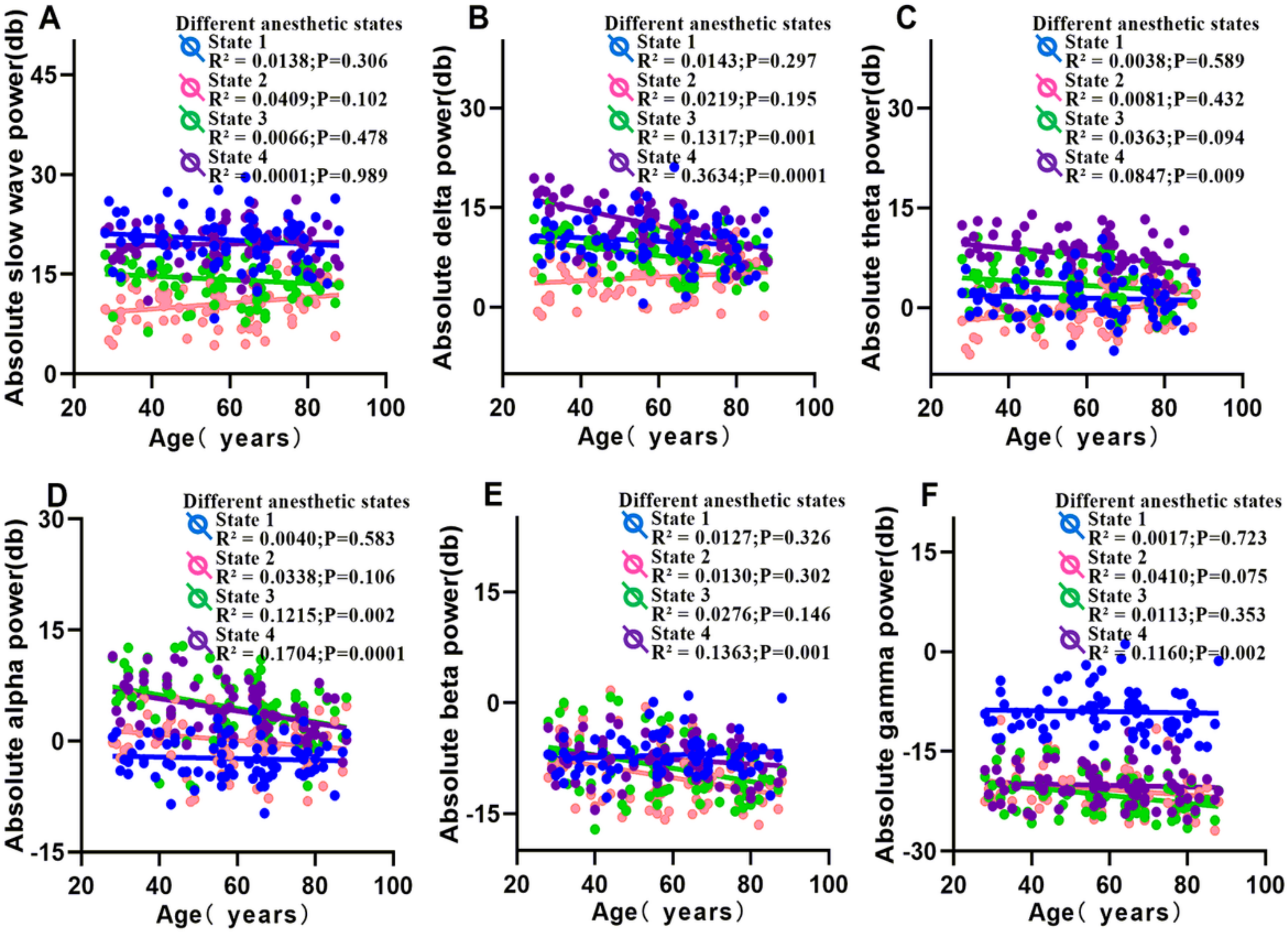

Figure 6

Changes of absolute power with age at different anesthetic conditions. A: Changes in absolute slow wave power with age at four anesthetic conditions. B: Changes in absolute delta power with age at the four anesthetic conditions. C: Changes in absolute theta power with age at the four anesthetic conditions. D: Changes in absolute alpha power with age at the four anesthetic conditions. E: Changes in absolute beta power with age at the four anesthetic conditions. F: Changes in absolute gamma power with age at the four anesthetic conditions.

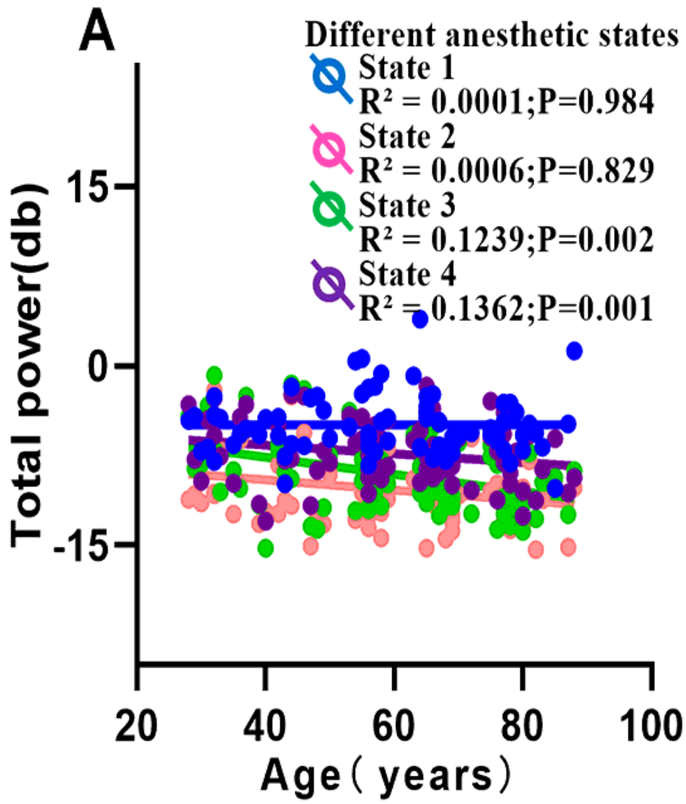

Figure 7

Total power, BIS and age change. A: Changes in total power with age at the four anesthetic conditions. B: Changes in BIS with age at the four anesthetic states.

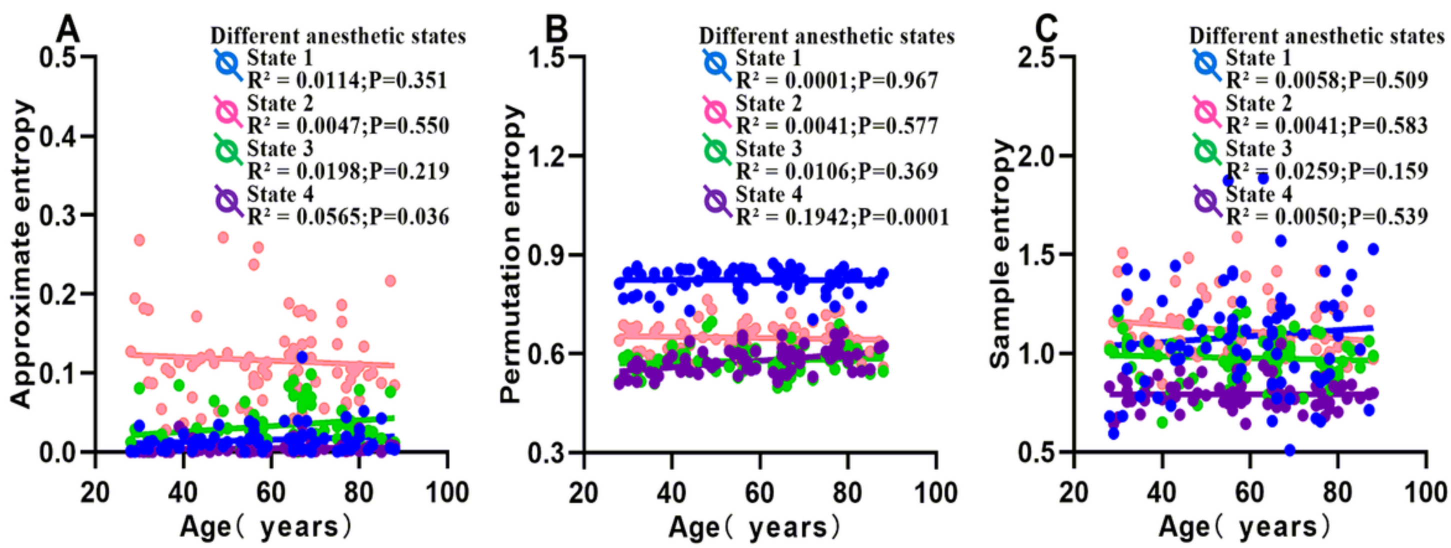

Figure 8

Changes of approximate entropy, permutation entropy, sample entropy and age. A: Changes in approximate entropy with age at four anesthetic states. B: Changes in permutation entropy with age at the four anesthetic states. C: Changes of sample entropy with age at the four anesthetic states.