Lifespan associated global patterns of coherent neural communication

Bikash Sahoo[1][**]; Anagh Pathak[1][**]; Gustavo Deco[2], Arpan Banerjee[1]*;

Dipanjan Roy[1]*

[1] Cognitive Brain Dynamics Lab National Brain Research Centre (NBRC), NH8 Nainwal Mode

122051 Manesar, Haryana, India

[2] Institució Catalana de la Recerc Estudis Avançats (ICREA), Universitat Pompeu Fabra,

Passeig Lluís, Companys 23, Barcelona, 08010, Spain

** Equal contributions

*corresponding authors

dipanjan.nbrc@gov.in; arpan@nbrc.ac.in

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17   **Abstract**

18   Healthy ageing is accompanied by changes to spontaneous electromagnetic oscillations. At the
19   macroscopic scale, previous studies have quantified the basic features, e.g., power and
20   frequencies in rhythms of interest from the perspective of attention, perception, learning and
21   memory. On the other hand, signatures and modes of neural communication have recently been
22   argued to be identifiable from global measures applied on neuro-electromagnetic data such as
23   global coherence that quantifies the degree of togetherness of distributed neural oscillations and
24   metastability that parametrizes the transient dynamics of the network switching between
25   successive stable states. Here, we demonstrate that global coherence and metastability can be
26   informative measures to track healthy ageing dynamics over lifespan and together with the
27   traditional spectral measures provides an attractive explanation of neuronal information
28   processing. Finding normative patterns of brain rhythms in resting state MEG would naturally
29   pave the way for tracking task relevant metrics that could crucially determine cognitive flexibility
30   and performance. While previously reported observations of a reduction in peak alpha frequency
31   and increased beta power in older adults are reflective of changes at individual sensors (during
32   rest and task), global coherence and metastability truly pinpoint the underlying coordination
33   dynamics over multiple brain areas across the entire lifespan. In addition to replication of the
34   previous observations in a substantially larger lifespan cohort than what was previously reported,
35   we also demonstrate, for the first time to the best of our knowledge, age related changes in
36   coherence and metastability in signals over time scales of neuronal processing. Furthermore, we
37   observed a marked frequency dependence in changes in global coordination dynamics, which,
38   coupled with the long held view of specific frequency bands sub-serving different aspects of
39   cognition, hints at differential functional processing roles for slower and faster brain dynamics.

40

Introduction:

A comprehensive understanding and characterization of the process of healthy aging are essential to treat age-associated neurological changes such as the decline in working memory, processing speeds, and executive cognitive functioning. Over the years, converging lines of evidence have successfully demonstrated the role of neural oscillations in many cognitive domains. Specific neuronal oscillatory patterns observed in EEG/ MEG data are essential markers of cognition (Buzsaki 2011), and researchers overwhelmingly agree on the use of field potential to tap neuro-cognitive processes associated with human brain function (Pesaran et al., 2018). Accordingly, several recent studies have tried to track age-related changes in the brain's oscillatory profile using spectral estimation techniques. For example, the amplitude of resting and motor-related beta-band oscillations (16-25 Hz) is typically found to be higher in the older population compared to the younger population. Similarly, a substantial number of reports have highlighted that spontaneous peak alpha frequency (8-12 Hz) is lower in older people as compared to younger participants.

While age-related alterations in sensor specific features like power and frequency are fairly well-reported, very few studies have looked at changes in global patterns of frequency-specific synchronization in the context of healthy aging. We argue that much information about the mechanisms of aging is to be found in studying patterns of coherent activity across the lifespan. The relevance of this assumption can be assessed from the existing literature. For example, the theory of communication through coherence (CTC) posits that message passing across spatially distant neural assemblies demands coordinated fluctuations in their respective excitabilities (Fries, 2005). The importance of global coherence in the context of cognitive functioning is underscored by the essential need for efficient message passing in bringing about cognition. Even though the original CTC proposal was formulated in a task context, recent work has drawn out its repercussions for spontaneous brain dynamics, a.k.a resting-state activity (Deco et al.,2016). According to this formulation, resting brain activity frequently traverses across different functional configurations to maintain a state of maximal readiness in anticipation of external stimuli, which, when presented, collapses the state of the brain to whichever configuration is deemed most relevant in the stimulus context. In other words, resting-state brain activity must demonstrate metastable dynamics, whereby the brain fluidly recapitulates varied patterns of coherent activity (Deco et al.,2016). In line with this view, global metastability is found to be associated with

74   cognitive flexibility and information processing in the brain. Therefore, tracking changes in

75   coherence and metastability is crucial, given the fact that aging is marked by distinct cognitive

76   changes that are, in turn, orchestrated by coherent neural oscillations.

77

78   The fundamental objective of this article is to track lifespan associated patterns of global

79   coherence and metastability from neurophysiological recordings. As a necessary confirmation

80   step, we first replicate the already well-established results in the field of aging neuroscience- the

81   observations of reduced peak alpha frequency and an increase in average beta power with age

82   on the current dataset. In doing so, we successfully establish the validity of earlier observations

83   on a substantially larger dataset across the age continuum - a feature lacking in many previous

84   studies. We then utilize a standard measure of global coherence to characterize band-specific

85   lifespan trends. Finally, we apply a proxy for metastability - the standard deviation of the Kuramoto

86   order parameter to characterize age-related alterations in frequency-specific metastable brain

87   dynamics. Resting-state magnetoencephalogram (MEG) recordings from the Cambridge-Ageing

88   Neuroscience (Cam-CAN) group for our purposes. Since this analysis has been carried out on a

89   large cohort of an aging population (cross-sectional) consisting of 650 participants across an age

90   range of 18-88 years we can consider them as a normative pattern of temporal structure of brain

91   rhythms associated with ageing. The relevance of the global network metrics we further evaluated

92   vis-à-vis performance in visual short term memory (VSTM) tasks over lifespan. Thus, we could

93   summarize the organization of band specific coordinated brain dynamics over lifespan.

Methods

Participants

Cam-CAN is a multi-modal, cross-sectional adult life-span population-based study. The study was approved by the Cambridgeshire 2 Research Ethics Committee, and all participants have given written informed consent. The data presented here belonged to Stage 2 of the study. In Stage-1, 2681 participants had been home-interviewed and had gone through neuropsychological assessments and been tested for vision, balance, hearing and speeded response. Participants with poor vision (< 20/50 on Snellen test), poor hearing (threshold greater than 35 dB at 1000 Hz in both ears), past history of drug abuse, with any psychiatric illness such as bipolar disorder, schizophrenia, with neurological disease e.g. epilepsy, stroke, traumatic brain injury, or a score less than 25 in Mini-Mental State Examination were excluded from further behavioral and neuroimaging experiments. 700 participants had been screened from Stage 1 to Stage 2, of which Magnetoencephalogram (MEG) data from 650 subjects were available.

Data acquisition

Data used in the preparation of this work were obtained from the CamCAN repository (available at http://www.mrc-cbu.cam.ac.uk/datasets/camcan/) (Taylor et al., 2016, Shafto et al., 2015). For all the subjects, MEG data were collected using a 306-sensor (102 magnetometers and 204 orthogonal planar magnetometers) VectorView MEG System by Elekta Neuromag, Helsinki, located at MRC-CBSU. Data were digitized at 1 kHz with a high pass filter of cutoff 0.03 Hz. Head position was monitored continuously using four Head Position Indicator coils. Horizontal and vertical electrooculogram were recorded using two pairs of bipolar electrodes. One pair of bipolar electrodes were used to record electrocardiogram for pulse-related artifact removal during offline analysis. The data presented here consisted only of resting state, where the subject sat still with their eyes closed for a minimum duration of 8 minutes and 40 seconds.

Data preprocessing

Preprocessed data was provided by Cam-CAN research consortium, where for each run temporal signal space separation was applied to remove noise from the environment, from Head Position Indicator coils, line noise and for the detection and reconstruction of the signal from noisy sensors. All the data had been transformed into a common head-position. More details about data

127   acquisition and preprocessing have been presented elsewhere (Taylor et al., 2017; Shafto et al.,
128   2014).

129

130   **Data analysis**

131   **Welch spectrum**

132

133   Fieldtrip toolbox (Oostenveld et al.,2011) was used to read the data provided in '.fif' format. For
134   each individual, data were downsampled from 1 kHz to 250 Hz. First, we sought to investigate
135   age-specific changes in the spectral densities of the raw MEG signals.

136

137   Time series corresponding to the 102 magnetometers, resulted in a matrix X of size $102 \times T$,
138   where T corresponds to the number of time points. Power spectral density for each sensor c's time
139   series $x_c(t)$ was estimated using Welch's periodogram method. Each time series was divided into
140   segments of 20 seconds without any overlap between segments. Spectrum was estimated for
141   each segment after multiplying the time series segment with a Hanning window. Spectrums of all
142   the segments were finally averaged.

143

144   We estimated a global spectrum, representative of each subject i.e. $S_I(f)$ by taking a grand
145   average across the spectrums belonging to all magnetometers.

$$S_I(f) = \sum_c s_I(c, f) \qquad \textbf{(1)}$$

147

148   ***Quantification of spatial overlap between sources of alpha and beta activity in the sensor***
149   ***space***

150

151   For each subject, the sensor map of alpha and beta activity were normalized separately.

$$\hat{\alpha}_I(c) = \frac{\alpha_I(c) - \langle \alpha_I \rangle}{\sigma_{\alpha(I)}} \qquad \textbf{(2)}$$

$$\hat{\beta}_I(c) = \frac{\beta_I(c) - \langle \beta_I \rangle}{\sigma_{\beta(I)}} \qquad \textbf{(3)}$$

154

155   where $\sigma_{\alpha(I)}$ and $\sigma_{\beta(I)}$ are the standard deviations of alpha and beta band respectively.

156   Separation between the normalized sensor level representation $\hat{\alpha}_I$ and $\hat{\beta}_I$ was indexed by the
157   cosine angle between the two multidimensional vectors.

158
$$\hat{\theta}(\alpha,\beta) = cos^{-1}\left(\frac{\hat{\alpha}_I.\hat{\beta}_I}{|\hat{\alpha}_I||\hat{\beta}_I|}\right) \qquad \textbf{(4)}$$

159

160 The angular separations across age were statistically analyzed using Spearman rank correlations

161 and t-tests.

162

163 **Global coherence**

164

165 We calculated band-specific global coherence to measure the covariation of neural oscillations

166 on a global level (Cimenser et al., 2008; Kumar et al.,2016). Global coherence among sensors at

167 any frequency f is measured as the percentage of variance explained by the first eigenvector of

168 the cross spectral density matrix at f.

169

170 In an individual subject's data, for each sensor, the time series $x(t)$ was divided into N non-

171 overlapping windows of 5seconds duration each i.e. $y(t)$. This resulted in an average of 112

172 (median, Interquartile range 1, range 70-220) windows for each subject. We employed 3

173 orthogonal discrete prolate spheroidal sequences (Slepian tapers) to avoid leakage in spectral

174 estimates into nearby frequency bands. The time-bandwidth product was taken to be 2, which

175 resulted in a bandwidth of 0.4Hz.

176

177 Before computing FFT, each data segment was detrended i.e. from each data segment $y(t)$ the

178 best straight line fit was regressed out.

179
$$\hat{y}(t) = y(t) - \underline{y}(t) \qquad \textbf{(5)}$$

180

181 where $\underline{y}(t)$ is the straight line fit of $y(t)$. Each segment was multiplied with a set of 3 orthogonal

182 Slepian tapers and fast fourier transform was applied to the tapered segments.

183 Computing the complex FFT (for T tapers) at frequency f for each segment n of sensor c resulted

184 in a complex matrix Y of dimension $F \times C \times N \times T$. We utilized the chronux (Bokil et al., 2010)

185 library to perform the global coherence analysis.

186

187 Cross spectral density between two sensors was estimated from $\hat{Y}$ by using the formula

188
$$S_f(i,j) = \frac{1}{N}\sum_n \sum_T conj\left(\hat{Y}(f,i,n,T)\right)\hat{Y}(f,j,n,T) \qquad \textbf{(6)}$$

189   where i and j are the channel indices, f is the frequency index n is the segment index and T is the

190   taper.

191

192   Singular value decomposition was applied to the cross spectral density matrix S_f for each

193   frequency value f.

$$S_f = USU^T \qquad \textbf{(7)}$$

194

195   Diagonals of S would be proportional to the explained variance by the orthogonal set of

196   eigenvectors U. The values of S were normalized so that each entry denote the percentage of the

197   net variance explained in S_f.

$$\hat{S} = \frac{S}{\sum_i S_i} \qquad \textbf{(8)}$$

198

199   The first entry of $\hat{S}$ is defined as the global coherence. Global coherence was computed for each

200   frequency value f, resulting an array G of length F.

201   **Metastability**

202

203   We calculated the metastability measure for all participants across all magnetometer sensors.

204   Metastability is defined as variability of the Kuramoto Order parameter, $R(t)$, which is given as,

$$R(t)e^{i\psi(t)} = \frac{1}{N}\sum_{n=1}^{N} e^{i\varphi_n(t)} \qquad \textbf{(9)}$$

205

206   Where φ_n is the phase of the nth oscillator and ψ is the mean phase of the system of oscillators.

207   In this analysis, every MEG sensor is conceptualized as a coupled oscillator, summarized by its

208   instantaneous phase $\phi(t)$. At any given point of time, the phase of each oscillator is extracted

209   and projected onto a polar coordinate system, as a unit vector ($e^{i\varphi_n(t)}$). The length of the resultant

210   vector, obtained from averaging all the unit vectors is interpreted as the Kuramoto Order

211   parameter, $R(t)$. The temporal variability of $R(t)$ is measured by the standard deviation $\sigma(R(t))$,

212   and defined as metastability (Deco et.al.,2017).

213

214   As a first step, the pre-processed resting state time series was band-pass filtered so as to obtain

215   filtered time series. Instantaneous phase of each filtered band was estimated from the filtered

216   data for metastability calculation. The pass band for the band-pass filtering step was kept narrow

217   so that the resulting phase is readily interpretable.

218

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220 filtered time series. Instantaneous phase of each filtered band was estimated from the filtered
221 data for metastability calculation. The pass band for the band-pass filtering step was kept narrow
222 so that the resulting phase is readily interpretable. For this analysis, each time series was filtered
223 in the following frequency bands- 2-4 Hz, 3-7 Hz, 8-12 Hz. Since valid phase estimation requires
224 narrow pass bands, the beta band was further split into 2 sub-bands-16-20Hz and 20-25Hz and
225 the respective metastability averaged. As mentioned earlier, the choice of frequency bands was
226 dictated by phase considerations. An additional criterion was to chunk the frequency bands so
227 that they map onto well-known frequency bands such as delta, theta, alpha and beta. As
228 mentioned earlier, we restricted our analysis to below 40 Hz due to presence of HPI noise.
229
230 FieldTrip toolbox (ft_preproc_bandpassfilter.m) was used to band-pass filter each signal in the
231 appropriate frequency bands. This routine was used to implement a finite impulse response (FIR),
232 two-pass filter that preserves phase information of the time series.
233
234 Subsequently, instantaneous phase was estimated by using built-in MATLAB implementation of
235 the Hilbert transform (hilbert.m). The resulting phase time series for each channel and participant
236 was used to calculate band and subject specific metastability.
237
238 Similar to the preceding analysis, metastability analysis was performed by 1.) treating age as a
239 continuous variable 2.) binning participants in the following age brackets - 18-35 years (Young
240 Adults), 36-50 years (Middle Age), 51-65 years (Middle Elderly) and 66 -88 years (Elderly).
241
242 For the region-wise analysis, the brain was segmented into 5 non-overlapping regions (frontal,
243 centro-parietal, occipital, left and right temporal). Metastability index was calculated individually
244 for all regions separately by randomly sampling 14 sensors from each region. Metastability was
245 tracked as a function of age by calculating the Spearman rank correlations.
246

Statistical Analysis

248

Continuous and categorical analysis of aging data

250

251 In order to bring all aspects of age-associated neural communication we performed both
252 continuous and categorical analysis of the aforementioned brain measures with age as an

253 explanatory variable. The primary goal of the continuous analysis was to capture the pattern

254 change over lifespan (e.g., whether changes of the patterns are increasing/ decreasing). For this

255 analysis we divided the whole cohort into bins of 5 years starting from 18 years. The bins were

256 non-overlapping and the center of each bin was considered as the representative age value of

257 the bin.

258

259 On the other hand, in the categorical analysis decomposing the whole data into cohorts with age

260 ranges 18-35, 36-50, 51-64 & 66-88 allowed us to get finer and accurate insights in each stage

261 of the adult span which has been well-documented in the fMRI literature (Chan et al., 2014) as

262 well as the results obtained here can be contextualized with previous studies. The age ranges

263 were unequally chosen because of the limitations posed by the CAM-CAN data set where different

264 numbers of samples in each age group are available. However, in order to keep a reasonable

265 number of samples > 120 in each cohort we chose the bins accordingly.

266

267 **Regression analysis**

268

269 Linear regression analysis was performed by separately considering each of the 5 estimated

270 measures (Power, Global Coherence, Metastability, PAF and Topographical segregation Index)

271 as response variables, while keeping age as the explanatory(continuous) variable.

272

273 $$y = \beta_0 + \beta_1 * Age \qquad (11)$$

274

275 Linear regression was performed using the fitlm.m matlab procedure, which yielded an omnibus

276 F-statistic, regression coefficients and goodness of fit(R^2) and log-likelihood(L). The regression

277 coefficient was taken to represent effect size. Additionally, we also considered 2nd and 3rd

278 order polynomial fits such as-

279

280 $$y = \beta_0 + \beta_1 * Age + \beta_2 * Age^2 \qquad (12)$$

281 $$y = \beta_0 + \beta_1 * Age + \beta_2 * Age^2 + \beta_3 * Age^3 \qquad (13)$$

282

283 Akaike Information Criteria was used for model selection and was calculated as-

284 $$AIC = -2L + 2K \qquad (14)$$

285 Where K is the number of model parameters including the intercept.

286

287   For the analysis that report spearman correlations, Effect sizes were computed using cohen's d

288   $$d = \left| \frac{2r}{\sqrt{1-r^2}} \right|$$ (15)

289

290   (Reported in Supplementary Material in detail)

291

292   **Categorical Analysis**

293

294   To systematically evaluate the relationship between age and brain measures Power, Coherence,
295   metastability, PAF and Topographical segregation we used Spearman correlation analysis
296   following what was described at Khan et al., 2018. Except for the logarithm of power, the other
297   measures are not guaranteed to be following a Gaussian or normal distribution, hence a common
298   non-parametric test, Spearman correlation was chosen to evaluate all correlations in this article.

299

300   In brief, pairwise comparisons between groups were performed using permutation testing. In each
301   iteration the groups were collapsed and random draws were made to form random groups.
302   Difference of means was calculated for the random group assignments and the procedure
303   repeated for 10000 iterations to construct a surrogate distribution. Finally, significance was
304   estimated using the surrogate distribution. The statistics were reported in terms of p-values, effect
305   sizes and difference of means.

306

Results

308 Our analysis strategy was two-fold. First, we conducted a categorical analysis by chunking the

309 age-continuum into discrete groups (see Table 1). We have divided the age values of total N=650

310 subjects into four age groups: Young Adults (YA), Middle Elderly (ME), Middle Late (ML), Older

311 Adults (OA), for which the demographic information has been provided in **Table 1.** Earlier studies

312 have done similar grouping (Chan et al 2014) and care was taken such that we have sufficient

313 number of participants in each age group > 120. Subsequently, we considered age to be a

314 continuous variable with bins consisting of 5 years between 18-88 and performed linear and

315 polynomial regression to estimate age associated trends. The bins were non-overlapping and the

316 center of each bin was considered as the representative age value of the bin.

317

318 **<u>Age trajectories in MEG resting state brain dynamics</u>**

319

320 We studied the effect of healthy ageing on the fundamental properties of the endogenous band-

321 limited neural oscillations such as amplitude and center frequency. Since the Head Position

322 Indicator (HPI) coil related noise can be unreliable at higher frequencies, we concentrated our

323 analysis between 0-40Hz which fully contains the neural oscillations in the **Delta** (1-3Hz), **Theta**

324 (4-8Hz), **Alpha** (8-12Hz), and **Beta** (16-25Hz) frequency bands.

325

326 **Band limited power**

327 An omnibus ANOVA that considers age as the explanatory variable yielded significance for all

328 measures tested (**details reported in Supplementary material**). Our analysis revealed that

329 spectral power in **Delta** ($\beta = 0.008, p = 0.1$), **Theta** ($\beta = 0.004, p = 0.46$) and **Alpha** ($\beta =$

330 $0.0002, p = 0.76$) bands did not vary with age (**see Fig 1**). In contrast, beta band power varied

331 significantly with age ($\beta = 0.03, p < 0.0001$). Visual inspection of **Fig. 1d** seemed to suggest 18-

332 22 to be an outlier group, so we additionally removed that group and compared linear and 2nd

333 order polynomial fits for the beta band and found the 2nd order polynomial fit to be better (AIC

334 linear = 2722, AIC quadratic = 2718). Alpha band power was estimated by averaging the

335 estimated spectral values within 8-12 Hz. We further quantified age-effects in the beta band using

336 a categorical approach and found significant differences in group means between YA vs ME, YA

337 vs ML, YA vs OA and ME vs OA groups.

338

339

340   Peak alpha frequency (PAF) shifts with age

341

342   The center frequency in the alpha band (8-12 Hz) has long been studied in the context of healthy

343   and pathological aging (**see Fig 2**). Here, we sought to quantify age related variations in PAF by

344   averaging the center frequency across the 102 sensors and correlating the global mean with age

345   as a variable. The regression analysis confirmed age-related reduction in PAF ($\beta = -0.01, p <$

346   0.0001). Frequency value at which there was maximum activity in the alpha band i.e. 8-12 Hz for

347   a subject, was taken to be the peak alpha frequency of that subject. **Fig 1B** is an age-spectrogram

348   which shows variation in the power spectral density in the alpha band with age.

349   Next, we split the age-range into discrete categories and performed permutation tests to estimate

350   group differences across age groups. YA was found to differ significantly with ME, ML and OA

351   whereas the ME group differed from OA in terms of the sample means (effect sizes reported in

352   Supplementary Materials).

353

354   Topographical distribution alpha and beta band power

355

356   Next, we investigated the spatial topographies of whole brain networks corresponding to age-

357   related difference along slow and fast time scales of neuronal signal using subspace analysis

358   borrowed from linear algebra. We quantified the overlap between the two sensor topographies by

359   the angle between their respective vector representations (**See Fig 2**). Larger angles indicated

360   more separation and less topological overlap between sensor groups. The topographical

361   separation between the sensor−wide distribution of alpha and beta power was found to increase

362   with age ($\beta = 0.003, p < 0.0001$) (**Fig 2A**). **Fig 2B** shows the average topographical map of alpha

363   activity at the center alpha frequency and average beta activity in 16-25 Hz for the youngest and

364   oldest age groups.

365

366   Although we observed similar patterns of difference between the oldest and youngest age groups

367   for global alpha band power and beta band power, there seemed to be a qualitative difference in

368   the overlap of sensors representing alpha and beta band activity. The categorical analysis

369   revealed that sample means in YA group differed from ME, ML and OA. ME differed from ML and

370   OA whereas ML was different from OA (effect sizes reported in Supplementary Material).

371

372   **Age trajectories in band-specific global network measures: coherence and metastability**

373

374   **Global Coherence over lifespan**

375

376   Presence of large-scale functional brain networks was investigated using global coherence across

377   all MEG sensors at different frequencies for each subject (Cimenser et al,2011; Kumar et al.

378   2016). Whole-brain coherence was summarized as the ratio of the principal eigenvalue to the sum

379   of all eigenvalues of the inter-sensor coherence matrix (see Materials and methods).

380

381   Global coherence at all the frequency values within a frequency band were averaged to generate

382   a representative value for the corresponding frequency band in four age groups, YA, ME, ML, OA

383   (**Fig 3A**). Representative global coherence in age bin was averaged for the continuous analysis

384   and standard error was computed for each age bin (**Fig 3B**). Global Coherence in the delta and

385   theta band was found to increase with age – delta ($\beta=0.0005, p < 0.0001$), theta ($\beta=0.0002, p =$

386   0.009). In contrast, global coherence in the alpha band varied inversely with age ($\beta=-0.0008, p <$

387   0.001) while Beta band global coherence did not display an age effect ($\beta\sim0, p = 0.86$) (See **Fig**

388   **3B).**

389

390   **Metastability and aging**

391

392   We estimated the variability of neuronal communication states using metastability as a function

393   of age and frequency. We observed a dichotomous pattern in metastability as a function of

394   frequencies in all age groups - a sharp decrease with increasing frequencies till 12 Hz and a

395   gradual increase in the metastability indices across frequencies between 12 – 40 Hz (**Fig 3C**).

396   Qualitatively, we found metastability to be higher for delta, theta and beta bands as compared to

397   the alpha band. Interestingly, in all age categories, the variation of metastability with frequencies

398   was consistent, essentially a U-shaped profile. From the continuous analysis we could establish

399   that band-specific metastability increased with age across all frequency bands- Delta

400   ($\beta=0.0004, p < 0.0001$), Theta ($\beta=0.0004, p < 0.0001$), Alpha ($\beta=0.0003, p < 0.0001$), Beta

401   ($\beta=0.0001, p < 0.0001$).

402

403   **Region-wise analysis of metastability reveals differential trends**

404

405   In order to track changes in metastability in specific brain areas we segmented the sensors in 5

406   groups - Frontal, Centro-Parietal, Occipital, Left Temporal and Right Temporal regions. The
407   region-wise analysis consisted of 14 randomly sampled sensors to compute metastability in each
408   brain region. Next, we tracked the region-wise metastability with aging. Spearman rank correlation
409   was performed to characterize trends in band and region specific metastability and effect sizes
410   quantified using Cohen's d. Delta and Theta oscillations either stayed invariant or reduced as a
411   function of age in the occipital, left temporal and right temporal regions. Beta band metastability
412   showed the highest age correlation (using Spearman rank test) in the centro-parietal sensors
413   while staying invariant in the occipital and temporal sensors. The following Spearman rank
414   coefficients and effect sizes (Cohen's d) were obtained for delta band - frontal ($c = 0.2499, d = 0.249, p < 0.001$), centro-parietal ($c = 0.1629, d = 0.3302, p < 0.001$), occipital ($c = -0.0686, d = -0.13, p = 0.0805$), left temporal ($c\sim0, p = 0.92$), right temporal ($c = -0.1428, d = -0.28, p < 0.001$). The corresponding values for alpha band were frontal($c = 0.2161, d = 0.44, p < 0.001$), centro-parietal ($c = 0.1808, d = 0.36, p < 0.001$), occipital ($c = 0.1348, d = 0.27, p < 0.001$), left temporal ($c = 0.2030, d = 0.414, p < 0.001$), right temporal ($c = 0.2070, d = 0.42, p < 0.001$). For theta band- frontal ($c = 0.1725, d = 0.35, p < 0.001$), centro-parietal ($c = 0.2049, d = 0.416, p < 0.001$), occipital ($c = 0.1141, d = -0.2, p < 0.001$), left-temporal ($c = -0.04, d = -0.08, p < 0.2396$), right-temporal ($c = 0.0457, d = -0.08, p < 0.2443$) were obtained. We tracked metastability in the beta band for two frequency bands (β_1, β_2) using similar statistical methodology. Centro-parietal sensors showed the highest age- related positive correlations ($c = 0.2046, 0.2542, d = 0.418, 0.51, p < 0.001$ for the two bands respectively) (Fig 4).

Relationship of between global network measures and performance metrics over lifespan

In order to evaluate the relationship of normative brain rhythms over lifespan we computed the correlations between global network measures and the performance metric of precision in a visual short-term working memory (VSTM, previous used by Zhang et al 2008) task available with the Cam-CAN cohort. We observed a significant correlation at 95% confidence levels between global coherence in the alpha band and precision in VSTM task after regressing out the effect of age ($\rho = 0.09, p = 0.0143$, **Fig 5**). The global coherences and metastability computed in other frequency band were not significantly correlated with precision (**detailed statistics reported in Supplementary Materials**).

Discussion

Neuronal communication is the backbone of basic human brain functions and supports a myriad of cognitive functions at various scales of nervous system organization (Mesulam 1990). While spectral estimates attempt to link neural oscillations with cognition (Henry et al. 2016, see Pesaran et al. 2018 for a nice review), very few studies are available that provide normative mapping of neuronal oscillations across healthy lifespan aging. We observed a significant age-related decline in peak alpha frequency (PAF) at the sensor level as well as increase in broadband beta power in a healthy cohort consisting of 650 human participants from the CAMCAN repository (Fig 1). Out of all sensor specific spectral features such as frequency and amplitude of oscillations in narrowband and broadband, PAF and beta power varied exclusively with age in opposite ways (Fig 1). Subsequently we could track the global subspace that sculpts the alpha and beta topographies, and their corresponding overlap over lifespan. Interestingly the angular separation between the alpha and beta topographies increase with age indicative of segregation of underlying generators over lifespan (Fig 2). Integrative mechanisms operational at the macroscale of whole-brain MEG sensor-space were captured by two complementary mathematical frameworks – global coherence spectrum that parametrizes the strength of band specific synchronization in different frequencies over a set of network nodes (MEG sensors for the purpose of this paper), and metastability that captures the degree of intermittency that exists between two successive synchronization states (Fig 3). Together, the two measures along with the spectral estimates quantifies the dynamic repertoire of the state variables. We observed an emerging dichotomy with aging in pattern of global coherence across slow and fast time scales (Fig 3A, B). The global alpha coherence decreases over lifespan followed a linear relationship whereas global beta coherences are unaffected by aging. The global coherences in slower frequencies - delta and theta on the other hand, are unaffected by aging up to a critical age of around ~45-50 years (Fig 3B). Thereafter, the global coherence shows an increase with age up to ~70 years and decrease further upon reaching a peak value. While alpha global coherence could be fitted best with a linear curve, theta and delta variation over age was non-linear. Concurrently, metastability exhibited a monotonically increasing relationship over lifespan in all frequencies (best fitted by a linear curve), with a visible saturation for elderly (~70 years) (Fig 3C, D). Interestingly, while increase in metastability in alpha band was truly global, increases in metastability in other bands were region-specific (Fig 4). Furthermore, while global coherence may be reflective of task performance, metastability, which is essentially a measure of phase variability was uncorrelated with task performance (Fig 5). In summary, we present a

471   comprehensive account of the temporal properties of neuro-electromagnetic signals over lifespan

472   aging that can be further interpreted in relation to recent and established findings in the literature

473   to develop a neurodynamic explanation of several important observations in healthy aging (Fig 1-

474   5). Furthermore, we argue that our results are extremely helpful for understanding the pathological

475   aging scenarios (e.g. Alzheimer's and Dementia) beyond the standard model of "accelerated

476   ageing" (Toepper 2017)

477   The decrease in PAF, prominently observed in our study, has been reported to be a biomarker of

478   normal and pathological aging process, especially for dementia, mild cognitive impairment, and

479   Alzheimer's disease (Scally et al., 2018; Dickinson et al., 2018; Osipova et al., 2005; Jeong,

480   2004). Patients with Alzheimer's disease show a significant decrease in PAF compared to age-

481   matched control group (Osipova et al., 2005; Jeong, 2004). Parkinson's patients with dementia

482   have a lower PAF compared to age-matched controls (Soikkeli et al., 1991). Interestingly,

483   developmental changes in spontaneous electrocortical activity is associated with an increase in

484   PAF from early to late childhood (Miskovic et al., 2015). While the mechanistic explanation of this

485   dichotomy still remains elusive, several computational attempts have suggested a link between

486   the thalamocortical circuitry responsible for alpha rhythmogenesis and age-related morphological

487   differences in thalamocortical circuits to explain slowing down of PAF. In fact, PAF may carry the

488   signature of an ending of rapid neurodevelopmental process of human beings, behaviorally

489   observed as trait developments from adolescence to young adults. Concurrently, cognitive task

490   relevant EEG/MEG studies have linked PAF with scores on cognitive paradigms such as working

491   memory (Clark et. al 2004) and visual acuity (Samaha et. al 2015) suggesting a crucial role of

492   PAF with age associated changes in attention and memory from YA to OA. Consistent with extant

493   literature, power in the beta band was found to increase with age. Increase in the band-limited

494   beta power in older population compared to younger population has been reported both in the

495   context of resting state and sensory-motor tasks (Rossiter et al., 2014; Heinrichs-Graham et. al,

496   2016), where beta oscillations have been regarded as an index of motor inhibition and volitional

497   movement (Heinrichs-Graham et. al 2016). Subsequently, we depart from some earlier studies in

498   key respects. Firstly, we find that band-limited power (spectral feature independent of frequency

499   in our study) in the delta, theta and alpha bands does not vary with age. Second, the angular

500   overlap decrease between the alpha and beta bands topographies with age reflects a segregation

501   of function which can emerge from neuro compensatory functional mechanisms or possibly

502   structural decline e.g., myelination degradation. Neurodegenerative pathologies like AD and

503   Parkinson's share many similarities with healthy aging, due to which many have speculated

504 whether neurodegeneration is an accelerated aging process (Toepper 2017). Remarkably, the
505 two sets of features, PAF and band-limited beta power exhibits different age associated
506 trajectories. While decline of PAF is best described with a linear model, the band limited beta
507 power trend is best described by a quadratic curve across age continuum. Thus, our results throw
508 in the possibility that while PAF decrease observed in pathological scenarios may be a non-
509 specific marker of disease, other features like beta power increase may be more relevant
510 candidates to tag preservation of function via neuro compensatory mechanisms.

511 A key contribution of our study is the archival of global network measures over lifespan,
512 particularly that are relevant for the neural information processing time scales. Few recent studies
513 using M/EEG have further emphasized that patterns of age-dependent segregation for beta and
514 gamma mediated networks differed substantially during maturation (Miskovic et al., 2015; Khan
515 et al., 2018). A recent study by Khan et al., 2018 further reports that beta band mediated networks
516 become more locally efficient, i.e. tending towards clustering and more connections with adjacent
517 regions with age, while gamma band mediated networks become more globally efficient, i.e.
518 tending towards shorter overall path lengths and thus faster communication across larger cortical
519 distances, with age during maturation. However, how do such large-scale and local
520 communication organize and orchestrate across different sensors and in different bands during
521 various stages of healthy adult lifespan remains largely unknown. In our study, we attempt to
522 quantify the band specific normative values as features during resting state borrowing the concept
523 from Communication Through Coherence (CTC) hypothesis. CTC operationally defines neuronal
524 communication as generation of coherent activity across neuronal assemblies. This view holds
525 that interareal coherence presents windows of excitability where communication channels
526 between brain regions are maximally utilized (Fries, 2005). Resting state brain activity is said to
527 reflect the brain's tendency to engage and disengage these channels of communication
528 spontaneously (Deco et. al, 2011). From a dynamical systems perspective, spontaneous brain
529 activity must exhibit metastable brain dynamics, whereby the global brain dynamic stays clear of
530 the two extremes of constant synchronization and desynchronization and instead, periodically
531 shuttles back and forth between coherent and incoherent regimes. More formally, global
532 coherence indexes the average phase and amplitude correlation across sensors whereas
533 metastability measures the variability in phase relationships of sensors across time. The
534 complimentary, yet related nature of global coherence and metastability offers unique insights
535 into the mechanistic underpinnings of global brain dynamics. An example of this is a recent
536 computational study by Vasa et al. which describes how local lesioning in nodes with high

537 eigenvector centrality leads to a simultaneous decrease in global synchrony along with an
538 increase in metastability (Vasa et al., 2015). For a review of the complementary nature of global
539 coherence and metastability, see (Hellyer et al. 2015, Vasa et al. 2015, Deco et al. 2017). The
540 global coherence decreases in alpha band (8-12 Hz) with concomitant increase of metastability
541 over lifespan indicates the transformative role of alpha over the aging process. This would strongly
542 suggest that alpha can be a possible mode of neural communication associated with neural
543 compensation whereas slower frequencies like delta and theta may reflect a critical juncture in
544 adult lifespan at certain age ranges. Interestingly the critical age ranges from where delta and
545 theta global coherence start peaking (~45-50) is a critical phase of life in terms of performance
546 where ability to learn new skill starts diminishing (Janacsek et al. 2012). We argue while alpha
547 coherence decrease may be associated with neuro compensatory mechanisms, they may not
548 have a direct bearing on performance for which delta and theta may be more informative. Studies
549 have demonstrated that theta rhythms are crucial for information processing underlying sequence
550 learning (Sauseng et al. 2009, Koene and Hasselmo 2009) which is clearly a relevant metric for
551 skill learning observed by Janaccsek et al. 2012.

552 Our earlier work has proposed that a way to implement the CTC hypothesis, that is, optimal
553 exploration of the dynamical repertoire inherent in the brain structural connectivity, is by
554 maximization of metastability (Deco et. al., 2016). Here, we interpret metastability as a measure
555 of the variability of the states of phase configurations with time. Thus, metastability should
556 decrease with the introduction of external stimulation and task conditions. In terms of dynamical
557 systems, resting brain to exhibit maximal metastability, refining and providing evidence in favor of
558 the synergetic hypothesis of Haken (Corning 1995) (later further explored by Tognoli and Kelso
559 2014). We observe an age-related increase in global metastability across all frequency bands and
560 the trend is best fitted by a linear model. This result can be contextualized from two opposing
561 theories of healthy aging. The method of neuro-compensation argues that age-related changes
562 in brain dynamics suggest a compensatory mechanism by which function gets restored in
563 response to structural decline (Naik et al. 2017). In this regard, it is interesting to note that
564 Alzheimer's disease and traumatic brain injuries (TBI) are associated with a reduction in global
565 metastability (Córdova-Palomera et al., 2017; Hellyer et al., 2015). Since metastability is a direct
566 measure of the functional capacity of the brain and has been shown to confer cognitive flexibility
567 in task-switching, information-processing and logical memory (Hellyer et al. 2015), this would
568 argue in favor of a compensatory explanation of the global increase in metastability with aging.
569 However, the neural noise hypothesis of aging would suggest a different interpretation. This

570 theory argues that age-related cognitive decline is best explained as a consequence of an
571 increase in the noisy baseline activity of the brain (Voytek et al., 2015; Dave et al., 2018).
572 According to this framework, global phase inconsistencies as we observe here is an obligatory
573 change resulting from change in underlying scaffold dictated by gradual change in white and grey
574 matter volume that shifts the baseline and result in an unspecific lifespan-associated increase in
575 neural noise. Within this framework, changes in global metastability and coherence reflect an
576 epiphenomenon that occurs due to an increase in neural noise. Future efforts should focus on
577 resolving this debate. One possible direction would be to study brain signals through measures
578 of signal complexity using source reconstructed EEG/MEG, to elucidate the role of specific brain
579 regions in bringing about metastable patterns of activity. More direct estimates of metastable state
580 switching from electrophysiological data could be employed to disentangle the effects of noise.
581 Recent works in this direction have proposed ways to directly estimate metastable switching
582 between synchrony states. For example, Vidaurre et.al. 2016 propose a Hidden Markov Model
583 (HMM) based method to decompose electrophysiological time series into recurrent, quasi-
584 stationary phase-locked regimes. This involves fitting source reconstructed time series with
585 multivariate autoregressive models and modelling state switches through the HMM approach.
586 Another promising avenue would be to invoke whole brain computational models which
587 incorporate neural plasticity mechanisms that operate at time scales that are relevant to aging
588 (Vattikonda et al., 2016; Abeysuriya et al., 2018). This is also necessary to reconcile the region
589 specific metastability patterns we observe across frequency bands, with alpha band metastability
590 increase being truly global versus region-specific enhancement and decrease of metastability in
591 other frequency bands over lifespan (Fig 4).

592 An ongoing research direction in the neuroimaging community is to relate resting state dynamics
593 to performance measures also sometimes referred to as behavioral phenotypes (Nomi et al 2017,
594 Liegeois et. al 2019). While the slow time-scale of fMRI has been primarily used for this purpose
595 to argue about cognitive flexibility from resting state functional connectivity (FC) metrics (Naik et
596 al 2017, Nomi et al 2017, Liegos et al 2019), the variation of the global coherence and
597 metastability from MEG presented us an opportunity to investigate the relationships between
598 global network properties and task performance in the neural times-scale. The CAM-CAN dataset
599 has the Verbal short-term memory task (VSTM) in which the accuracy is anti-correlated linearly
600 with increase in age. Interestingly only the global coherence in alpha band was correlated with
601 precision when the age effects were corrected, while the global coherence in other frequency
602 bands are uncorrelated with VSTM performance (Fig 5). On the other hand, metastability has no

603   bearing on performance accuracy once the effects of ageing were considered for any frequency.
604   Thus, except the global network captured by alpha global coherence, the others are non-specific
605   measures of neurophysiological processing. In other words, measures like global coherence/
606   metastability quantifies the overall shift global information processing rather than being relevant
607   for a specific task.

608   An important caveat of our study was due to limitation posed by the Cam-CAN data set particularly
609   because of the presence of harmonics of lower frequencies being present in higher frequencies,
610   a systematic analysis of gamma band was not possible. The gamma frequencies in the resting
611   state did not show any statistically significant differential change with ageing at least in the low
612   gamma range (30-40 Hz), although the task data showed interesting patterns. However, such
613   discussions remain out of scope of this paper. Another limitation is that in spite of large sample
614   size the current analysis is restricted to the sensor level, our results are so far only indicative of
615   activity at the neural level. Source reconstruction may provide a direct estimate of global
616   coherence at the level of neural assemblies and help in elucidating its relationship with sensor
617   level global coherence and metastability, the efforts toward which will be presented elsewhere in
618   future. Caution is also required in interpreting the results due to the modest effect sizes involved
619   in certain measures. Similarly, caution is warranted in interpreting global coherence and
620   metastability measures. Due to the way it is constructed, global coherence may give misleading
621   information under some circumstances. For example, it is possible to obtain spuriously high
622   values of global coherence even when the underlying signals are independent when most of the
623   power is concentrated in a few sensors. In this study, the almost evenly distributed scalp
624   topographies (Fig.3) would preclude that possibility. Future work is underway to address some of
625   these issues and limitations. The other limitation of the present study is the use of simple statistical
626   models to explain spectral features as a function of age, but more complicated component models
627   can be used in future (e.g., in Liegeois et al. 2019). A multidimensional analysis by estimating FC
628   dynamics corresponding to different performance measures using big data techniques can further
629   shape the understanding of rest and task

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Disclosure Statement

The authors declare no conflicts of interest.

Acknowledgements

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890

891 # Table and Figure Legends

892

893 **Table1.** Sample size and gender statistics in each representative age group

894

895 **Figure 1. Relation between global spectral activity and age. A.** Plots of mean power spectral
896 density for 4 non-overlapping age groups i.e. 18-35, 36-50, 51-65 and 66-88. Shaded region
897 denote standard error of mean. **B.** Variation of alpha activity with aging. Center frequency in the
898 alpha band for each age bin has been plotted as solid circles and solid black line is the linear fit
899 of these points (labels indicate effect sizes, significance and correlation function) **C.** Spectra in
900 the delta, theta and alpha bands as a function of age. **D.** Beta spectra as a function of age

901

902 **Figure 2.** Segregation of sensor level topographies with aging. **A.** Angular separation between
903 alpha and beta bands(in radians) as a function of age. **B.** Boxplot for the distribution of angles
904 between the sensor topographies of center alpha power and average beta power for the four age
905 groups. Blue line denotes the median of the distribution and the notch indicates 95% confidence
906 interval of the median. Inset:Sensor topographies of alpha power at center frequency and average
907 beta power for the two extreme age groups.

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909

910 **Figure 3. Differential changes in global coherence with aging**. **A.** Plots of mean global
911 coherency for the four age groups. Shaded region denotes s.e.m. **B.** Differential variation of
912 global coherence for frequency bands. **C.** Metastability for four age groups in delta, theta, alpha
913 and beta bands.

914

915 **Figure 4: Region-wise increase and decrease in global metastability. A.** Shows the results
916 for the region-wise metastability analysis. Colors indicate the direction of the age-related trend as
917 measured by the spearman rank correlation coefficients. 14 sensors were chosen at random from
918 each of the 5 anatomical areas- frontal, centro-parietal, occipital, left and right temporal. **B.** Vector
919 View magnetometer layout.

920

921 **Figure 5: Correlation of VSTM precision with global coherence and metastability. Center:**
922 Scatterplot of precision with age. **Left:** Scatterplot of band-specific global coherence with
923 precision in VSTM task. **Right:** Scatterplot of band-specific global coherence with precision in
924 VSTM task.

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Age group	N	% Female
YA (18-35)	126	55
ME (36-50)	159	49
ML (51-65)	149	50
OA (66-88)	216	46

933

934   **Table1.** Sample size and gender in each representative age group

935

Fig 1.

A.

B.

$R^2 = 0.87$, p < 0.001
y = -0.021x + 10.665

C.

D.

Fig 2.

DELTA THETA ALPHA

BETA(16-20) BETA(20-25Hz)

Increase

Decrease

No Change

MEG 0521 MEG 0811 MEG 0911
MEG 0511 MEG 0551 MEG 0821 MEG 0921
MEG 0311 MEG 0551 MEG 0941
MEG 0541 MEG 0931 MEG 1211
MEG 0121 MEG 0611 MEG 1011 MEG 1021 MEG 1411
MEG 0111 MEG 0341 MEG 0321 MEG 1231 MEG 1221 MEG 1421
MEG 0331 MEG 0641 MEG 0621 MEG 1031 MEG 1241
MEG 0131 MEG 0211 MEG 0221 MEG 0411 MEG 0421 MEG 0631 MEG 1041 MEG 1111 MEG 1121 MEG 1311 MEG 1321 MEG 1441
MEG 0141 MEG 1431
MEG 0231 MEG 0441 MEG 0431 MEG 0711 MEG 0721 MEG 1141 MEG 1131 MEG 1341
MEG 1511 MEG 0241 MEG 1331 MEG 2611
MEG 1541 MEG 0741 MEG 0731 MEG 2241 MEG 2221
MEG 1541 MEG 1811 MEG 1321 MEG 2411 MEG 2621
MEG 1611 MEG 1621 MEG 2421
MEG 1521 MEG 183 MEG 2241 MEG 2231 MEG 2641
MEG 1841 MEG 2441
MEG 1631 MEG 2011 MEG 2021 MEG 2431
MEG 1531 MEG 1641 MEG 2311 MEG 2531
MEG 1721 MEG 1911 MEG 2521
MEG 1941 MEG 2041 MEG 2031 MEG 2321
MEG 1711 MEG 1731 MEG 1921 MEG 2111 MEG 2341 MEG 2511 MEG 2531
MEG 1931 MEG 2121 MEG 2331 MEG 2541
MEG 1741
MEG 2141 MEG 2131

GLOBAL COHERENCE

METASTABILITY

LIFESPAN PERFORMANCE

Delta
Theta
Alpha
Beta

Fig S1. Boxplot of distribution of band limited power in the beta band (16-25 Hz). Blue line indicates the median of each distribution. Notch denotes 95% confidence interval of the median
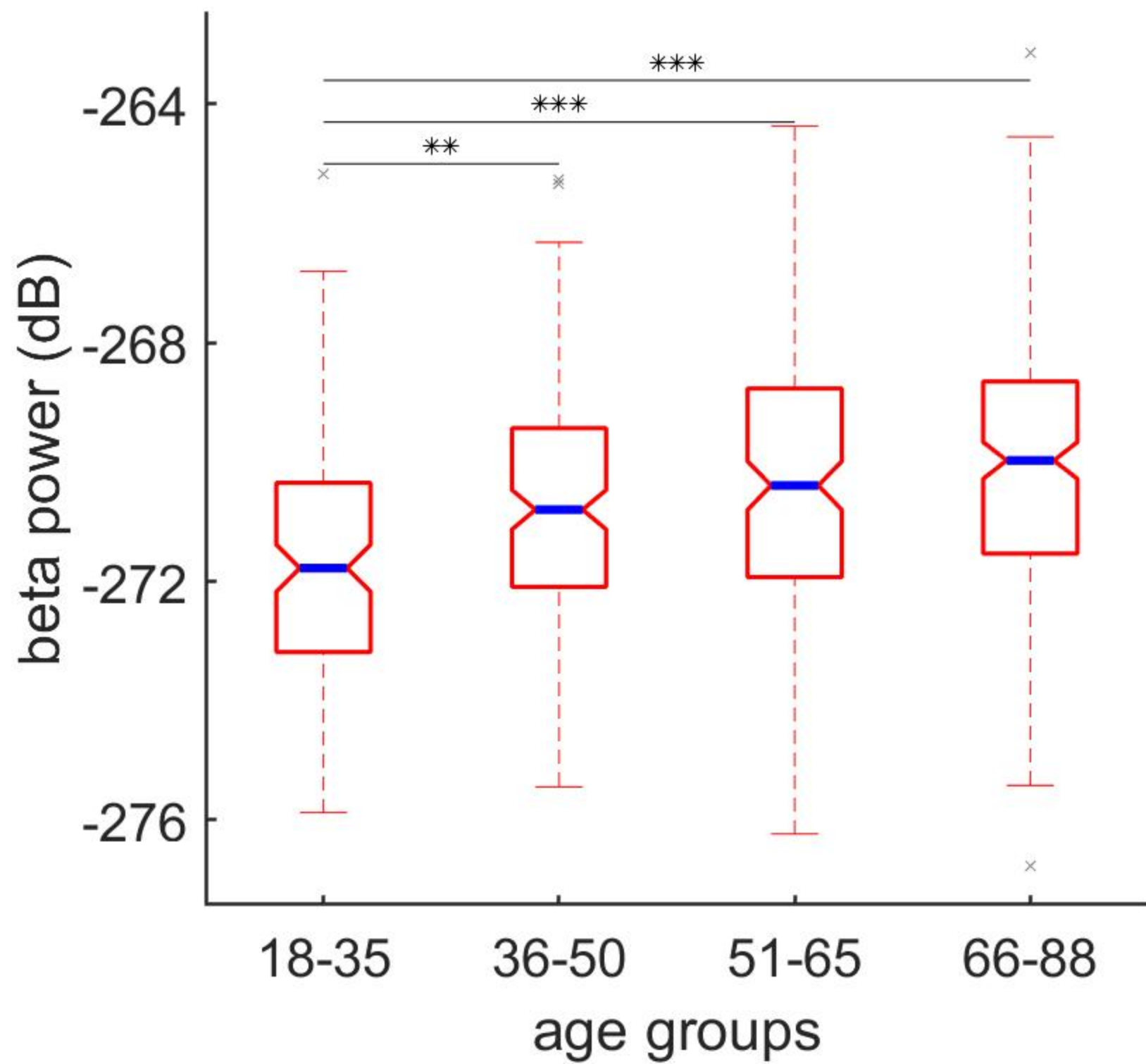
S2.
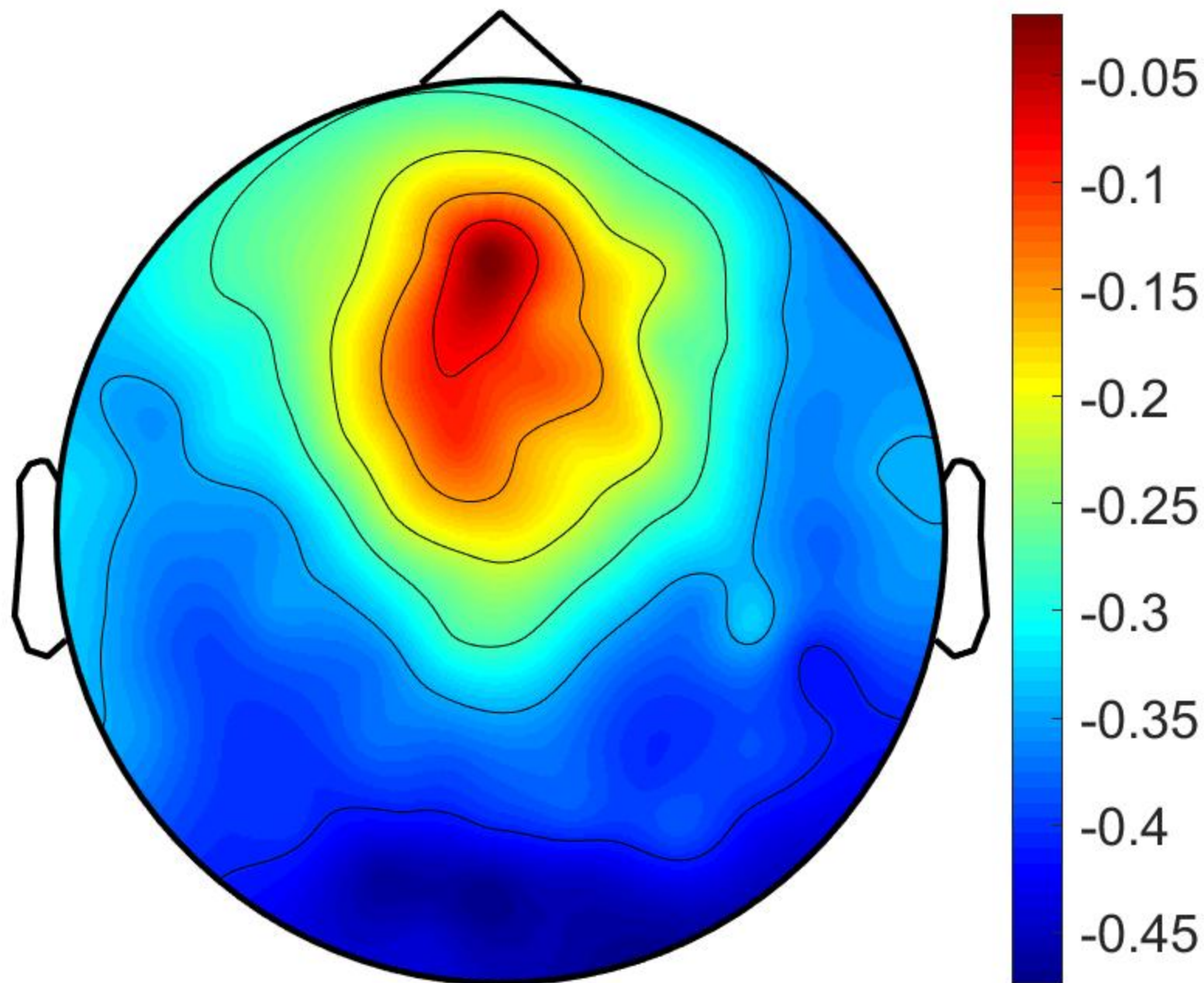
Fig. S2 represents Sensor topography of correlation between peak alpha frequency and age. Colorbar represents Spearman's rank correlation value.

Supplementary Table 1.

	Measure	F(1,648)(p=value)	beta1	R^2
	Delta Power	**2.61(0.1)**	0.008(0.1)	0.004
	Theta Power	**0.546(0.46)**	0.004(0.46)	0.0008
	Alpha Power	**0.08(0.76)**	0.0002(0.76)	0.0001
POWER	**Beta Power**	**41.3(<0.0001)**	**0.03(<0.0001)**	0.06
	Global Coherence(Delta)	**22(<0.0001)**	**0.0005(<0.0001)**	0.03
	Global Coherence(Theta)	**6.76(<0.0001)**	**0.0002(<0.009)**	0.01
	Global Coherence(Alpha)	**60(<0.0001)**	**-0.0008(<0.0001)**	0.084
COHERENCE	**Global Coherence(Beta)**	**0.03(0.86)**	~0(0.86)	~0
	Metastability(Delta)	**95(<0.0001)**	**0.0004(<0.0001)**	0.128
	Metastability(Theta)	**105(<0.0001)**	**0.0004(<0.0001)**	0.139
	Metastability(Alpha)	**77.5(<0.0001)**	**0.0003(<0.0001)**	0.107
METASTABILITY	**Metastability(Beta)**	**21.6(<0.0001)**	**0.0001(<0.0001)**	0.032
	Peak Alpha Frequency	**109(0.0001)**	**-0.01(<0.0001)**	0.144
	Alpha-Beta topographical segregation index	**65.7(<0.0001)**	**0.003(<0.0001)**	0.09

T1. Statistical table for power, coherence and metastability measures. F-values, beta coefficients and goodness of fit for linear regression based analysis are reported.

Supplementary Table 2.

Beta Power	YA	ME	ML	OA
YA		<0.001, -0.48, -0.9679	<0.001, -0.61, -1.28	<0.001, -0.83, -1.73
ME			<0.21, -0.14, -0.3	<0.0016, -0.34, -0.76
ML				<0.06, -0.19, -0.4496

T2. Tabulates the between group test for beta power. 10000 iterations were performed to generate surrogate data for each comparison. Reported values correspond to p-values, effect size, group difference in means in that order.

Supplementary Table 3.

Peak Alpha Frequency(PAF) Categorical Analysis

PAF	YA	ME	ML	OA
YA		0.02, 0.2674, -0.193	<0.001, -0.61, -1.28	<0.001, -0.83, -1.73
ME			0.21, -0.14, -0.3	0.0016, -0.34, -0.76
ML				0.06, -0.19, -0.4496

*p-value, effect size, group difference in means

T3. Tabulates the between group test for peak alpha frequency(PAF). 10000 iterations were performed to generate surrogate data for each comparison. Reported values correspond to p-values, effect size, group difference in means in that order.

Supplementary Table 4.

Alpha-Beta Topographical segregation

ANG_SEP	YA	ME	ML	OA
YA		0.03 ,-0.25, -2.81	<0.001, -0.47, -5.55	<0.001, -0.77, -9.06
ME			0.03 ,-0.24, -2.7	<0.001, -0.55, -6.24
ML				0.0064, -0.289, -3.5

T4. Tabulates the between group test for alpha-beta segregation measure. 10000 iterations were performed to generate surrogate data for each comparison. Reported values correspond to p-values, effect size, group difference in means in that order.

Supplementary Table 5. Global Coherence Categorical Analysis

Delta	YA	ME	ML	OA
YA		0.88 ,-0.01, 0.0006	0.24, -0.15 -0.006	0.0003, -0.48, -0.02
ME			0.21 ,-0.14, -0.006	<0.001, -0.43, -0.02
ML				0.011,-0.28, -0.01

Theta	YA	ME	ML	OA
YA		0.6 ,-0.06, 0.001	0.43,0.09,0.002	0.05, -0.25, -0.009
ME			0.8,0.02, 0.0009	0.01,-0.26,-0.011
ML				0.01,-0.29,-0.01

Alpha	YA	ME	ML	OA
YA		0.1 ,0.18, 0.01	<0.001, 0.63,0.03	<0.001, 0.73, 0.03
ME			0.0002 ,0.43, 0.02	<0.001, 0.52, 0.02
ML				0.4, 0.08, 0.003

Beta	YA	ME	ML	OA
YA		0.36,0.1,0.002	0.03, 0.25, 0.005	0.78,0.031, 0.0007
ME			0.16,0.15,0.003	0.52,-0.06,-0.001
ML				0.04,-0.2,-0.005

T5. Tabulates the between group test for global coherence measure. 10000 iterations were performed to generate surrogate data for each comparison. Reported values correspond to p-values, effect size, group difference in means in that order.

Supplementary Table 6. Metastability Categorical Analysis

Delta	YA	ME	ML	OA
YA		0.007,-0.32, -0.004	<0.001, -0.66, 0.01	<0.001, -1.0, -0.01
ME			0.002 ,-0.33, -0.006	<0.001, -0.74, -0.01
ML				0.0006, -0.39, -0.008

Theta	YA	ME	ML	OA
YA		<0.001 ,-0.41, -0.006	<0.001,-0.74,-0.01	<0.001, -1.15, -0.02
ME			0.003 ,-0.33, -0.006	<0.001, -0.73, -0.01
ML				<0.001, -0.4, -0.009

Alpha	YA	ME	ML	OA
YA		0.02 ,-0.27, -0.003	<0.001, -0.62, -0.009	<0.001, -0.96, -0.01
ME			0.004 ,0.32, 0.005	<0.001, -0.67, -0.01
ML				0.0003, -0.38, -0.007

Beta	YA	ME	ML	OA
YA		0.04 ,-0.24, -0.003	0.03, -0.26, -0.003	<0.001, -0.6, -0.009
ME			0.82 ,-0.025, -0.0004	0.002, -0.33, -0.006
ML				0.006, -0.29, -0.005

T6. Tabulates the between group test for metastability measure. 10000 iterations were performed to generate surrogate data for each comparison. Reported values correspond to p-values, effect size, group difference in means in that order.
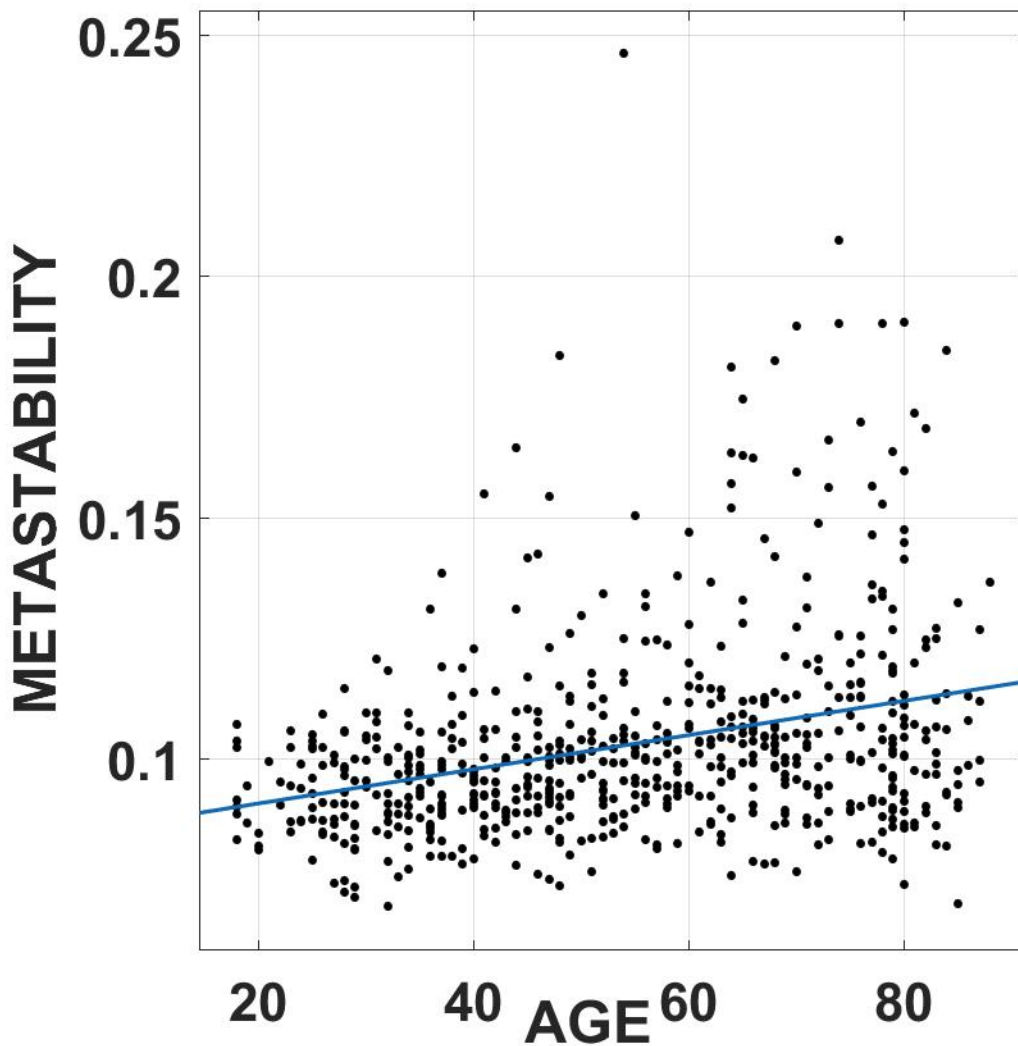
S.3
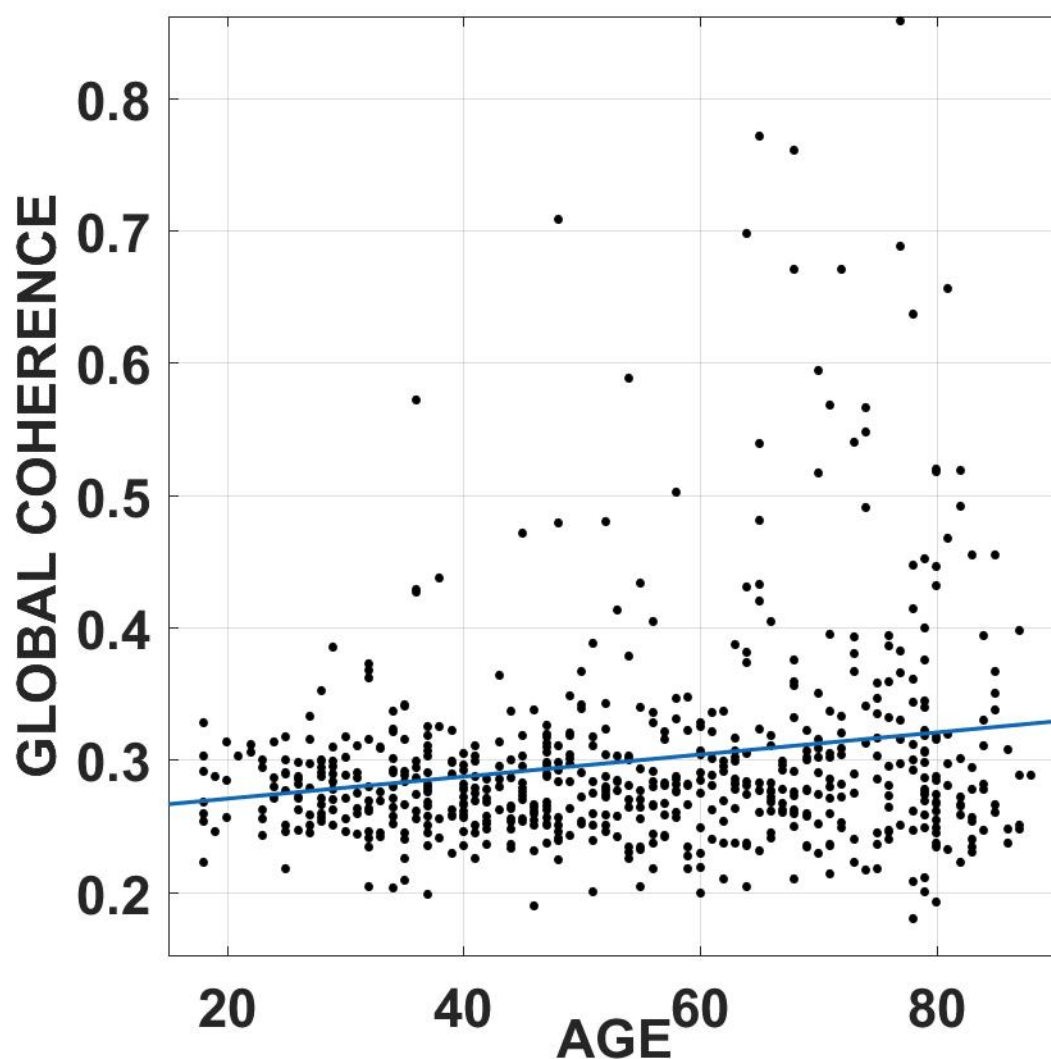
Fig S3. represents a scatter plot of Global Coherence in theta band(3-7Hz) (ICA CORRECTED) as a function of age. ECG and EOG signals were subtracted from the data using an automated ICA procedure as outlined in the main text.
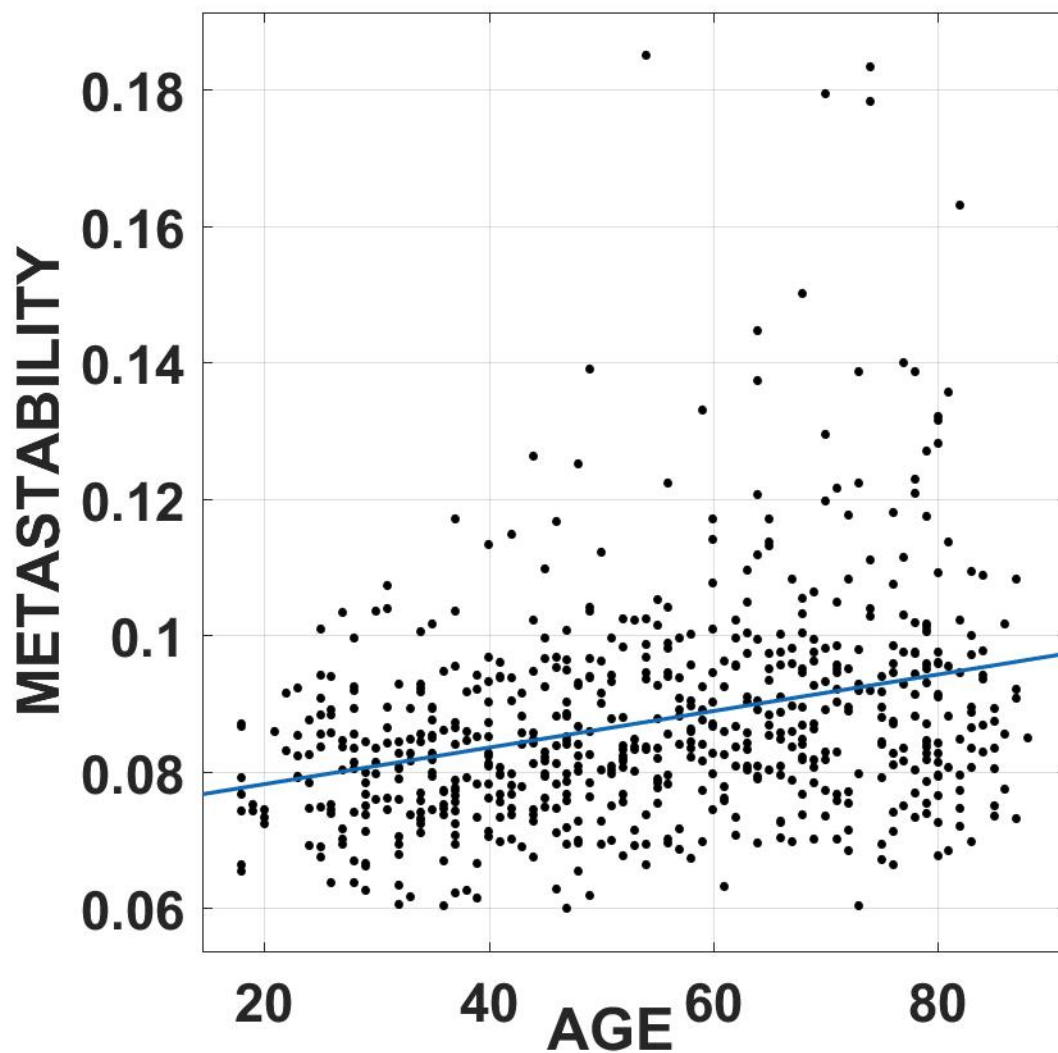
S4.
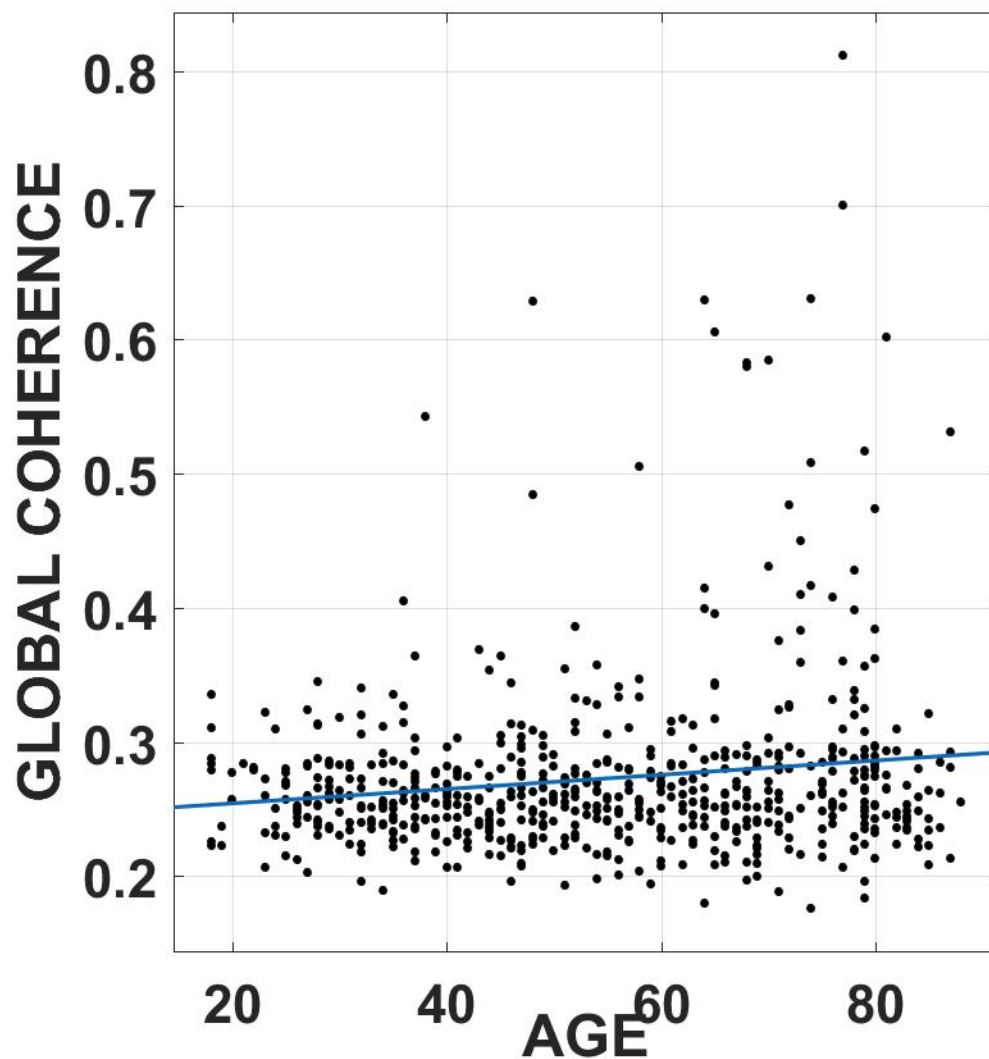
Fig.S4 represents a scatter plot of Global Coherence in alpha band(8-12Hz) (ICA CORRECTED) as a function of age. ECG and EOG signals were subtracted from the data using an automated ICA procedure as outlined in the main text.

S5.
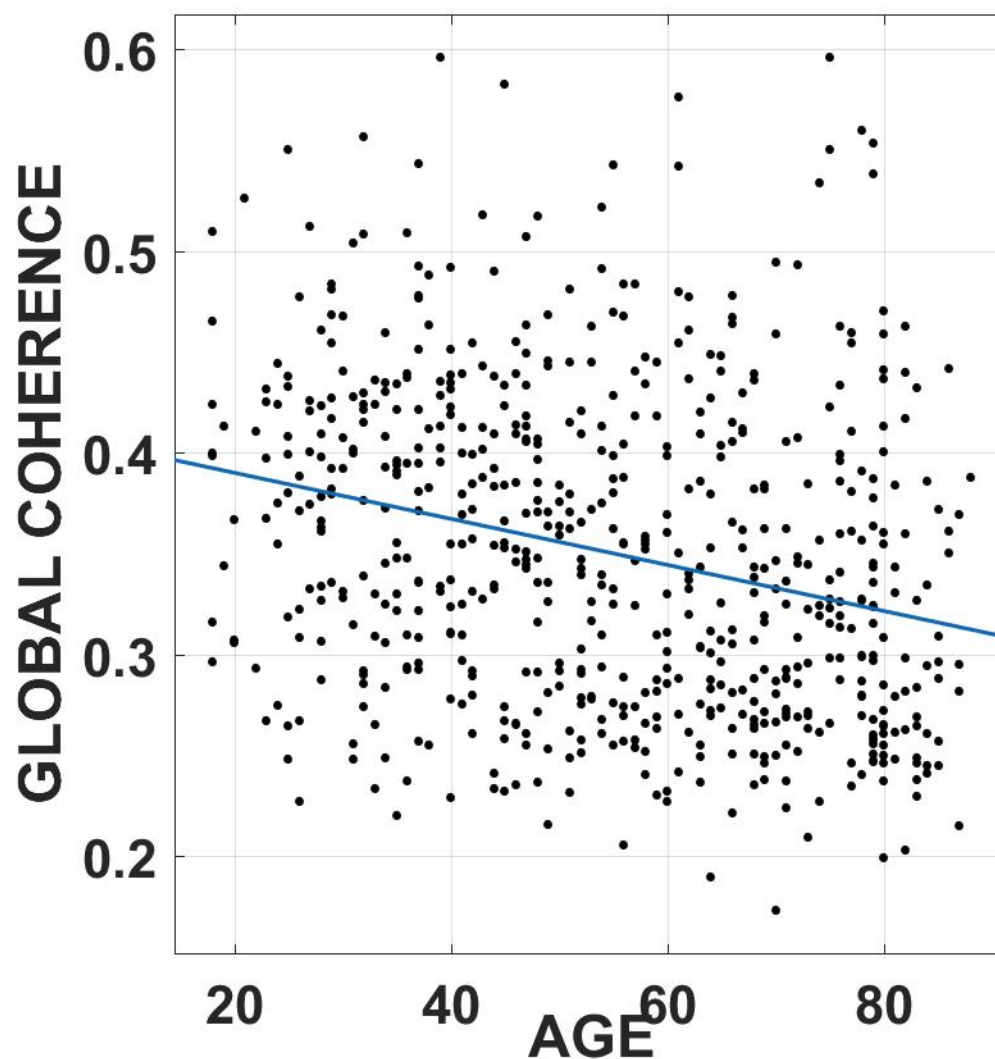
Fig.S5 represents a scatter plot of Global Coherence in alpha band(8-12Hz) (ICA CORRECTED) as a function of age. ECG and EOG signals were subtracted from the data using an automated ICA procedure as outlined in the main text.

S6.
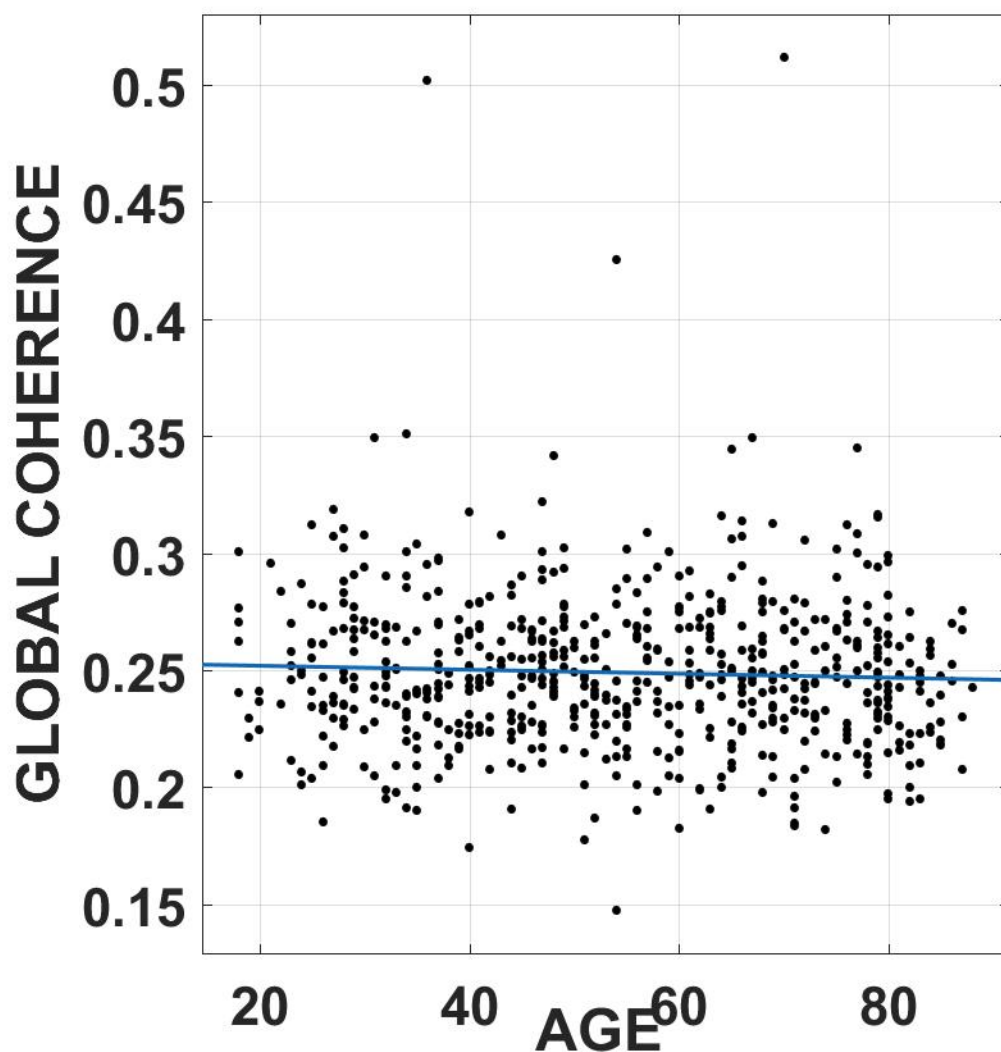
Fig.S6 represents a scatter plot of Global Coherence in beta band(16-25Hz) (ICA CORRECTED) as a function of age. ECG and EOG signals were subtracted from the data using an automated ICA procedure as outlined in the main text.

S7.

Fig. S7 Represents a scatter plot of metastability in delta band(1-3Hz) (ICA CORRECTED) as a function of age. ECG and EOG signals were subtracted from the data using an automated ICA procedure as outlined in the main text.

S8.

Fig. S8 represents a scatter plot of metastability in alpha band(8-12Hz) (ICA CORRECTED) as a function of age. ECG and EOG signals were subtracted from the data using an automated ICA procedure as outlined in the main text.

S9.
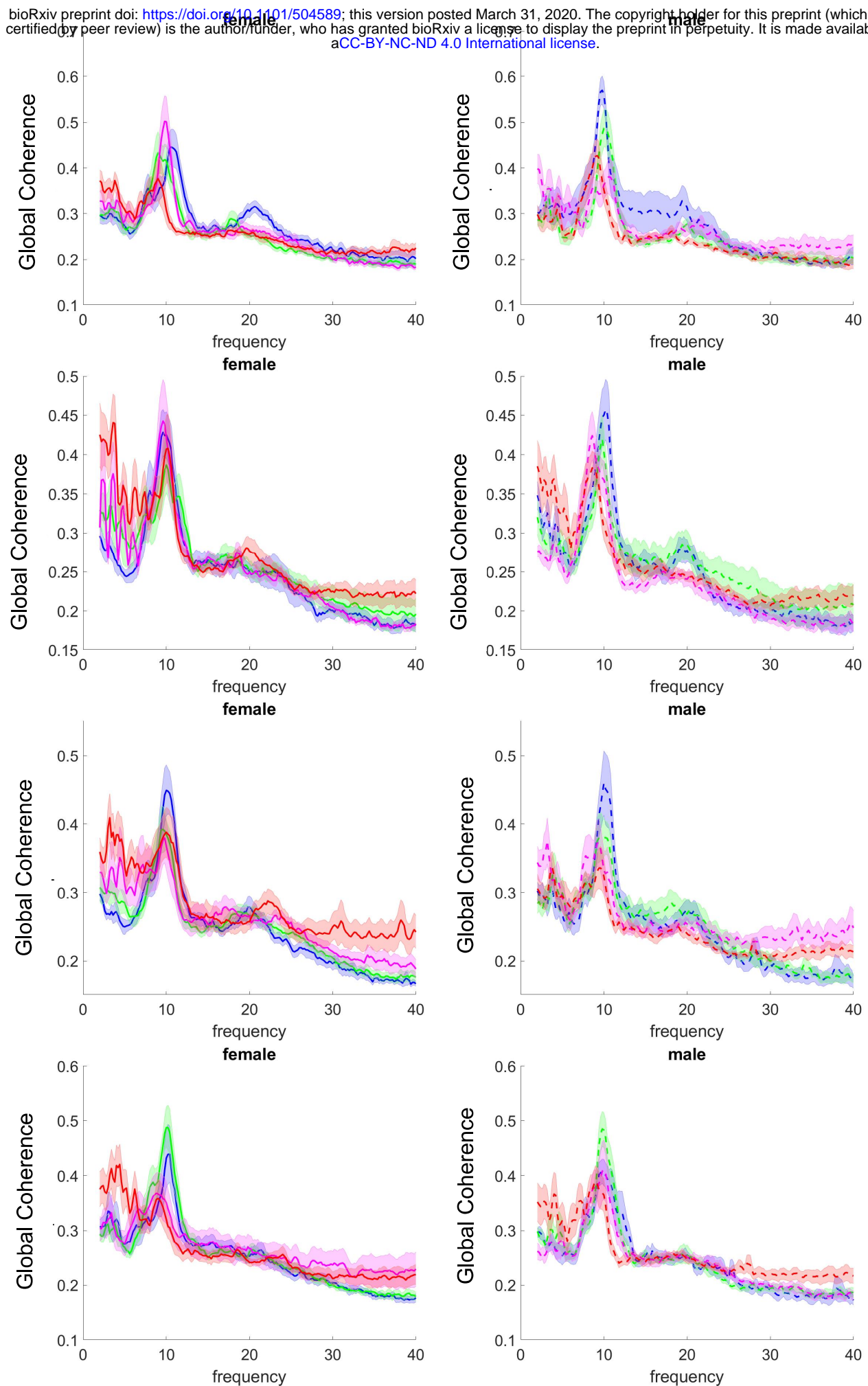
Fig. S9 represents Gender-wise comparison of randomly sampled age groups. 50 samples were drawn at random from each age-group and GC calculated.
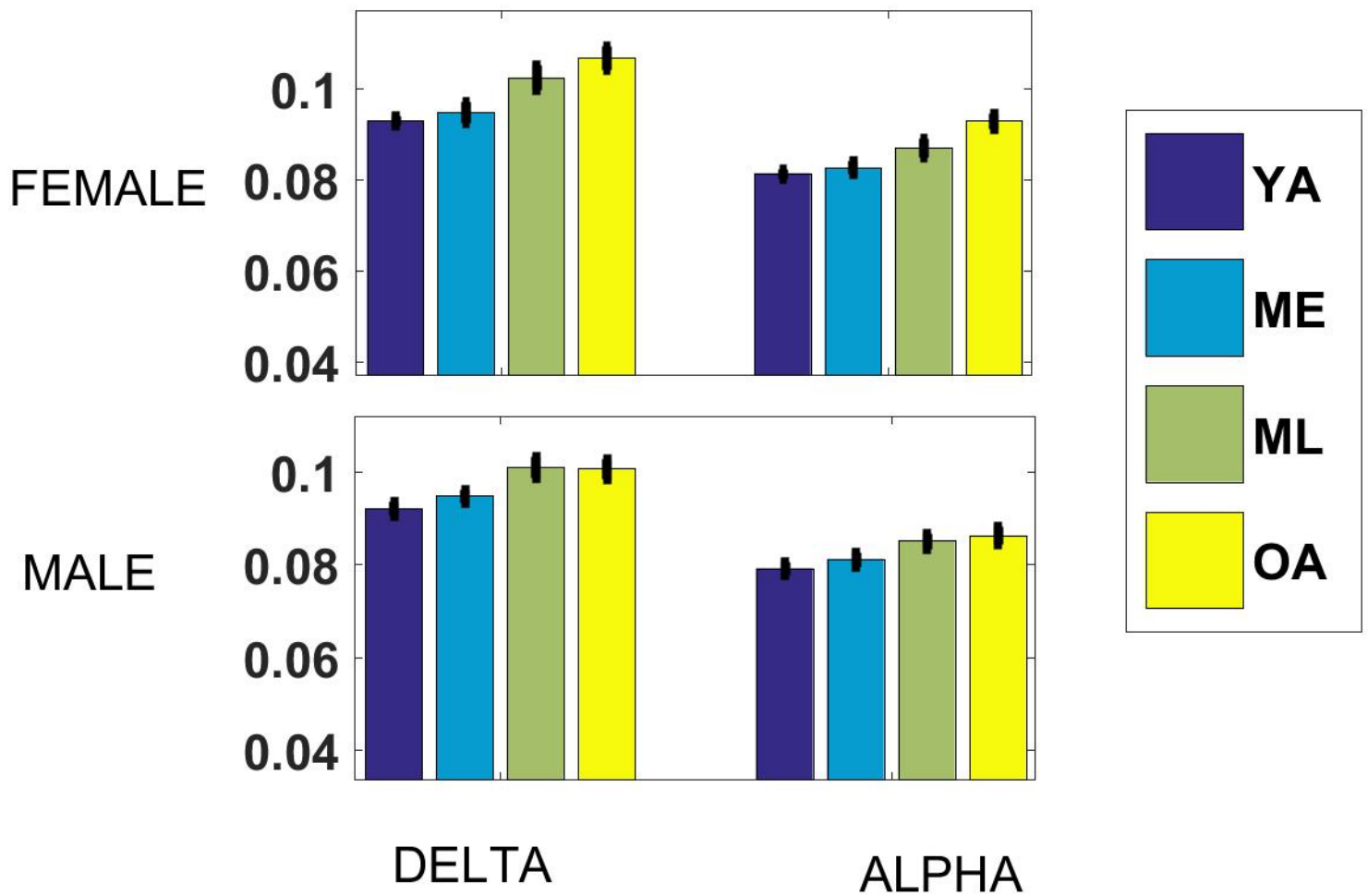
S10.

Fig. S10 Gender-wise metastability in delta and alpha band. Data consisted of 328 Males and 322 Females. Bar plots represent metastability in the delta and theta bands for the 4 age groups.

Supplementary Table 7.

GLOBAL COHERENCE		
BAND	**RHO**	**P**
DELTA	-0.0018	0.96
THETA	0.01	0.72
ALPHA	0.09	0.01
BETA	0.08	0.06
METASTABILITY		
BAND	**RHO**	**P**
DELTA	0.04	0.27
THETA	0.04	0.24
ALPHA	0.03	0.03
BETA	0.01	0.79

T7. Rho and P-val for partial correlation between precision in VSTM task and frequency-specific coherence and metastability(age regressed out).