

1 Article

2 Assessment of cognitive aging using an SSVEP-based 3 Brain Computer Interface System

4 Saraswati Sridhar ^{1*} and Vidya Manian ²

5 ¹ Southwestern Educational Society; 21038@sesolion.com

6 ² University of Puerto Rico at Mayaguez, Dept. of Electrical and Computer Engineering;
7 manian@ece.uprm.edu

8 * Correspondence: Correspondence: 21038@sesolion.com

9

10 **Abstract:** Cognitive deterioration caused by illness or aging often occurs before symptoms arise,
11 and their timely diagnosis is crucial to reducing its medical, personal, and societal impacts. Brain-
12 Computer Interfaces (BCIs) stimulate and analyze key cerebral rhythms, enabling reliable cognitive
13 assessment that can accelerate diagnosis. The BCI system presented analyzes Steady-State Visually
14 Evoked Potentials (SSVEPs) elicited in subjects of varying age to detect cognitive aging, predict its
15 magnitude, and identify its relationship with SSVEP features (band power and frequency detection
16 accuracy), which were hypothesized to indicate cognitive decline due to aging. The BCI system was
17 tested with subjects of varying age to assess its ability to detect aging-induced cognitive
18 deterioration. Rectangular stimuli flickering at theta, alpha, and beta frequencies were presented to
19 subjects, and frontal and occipital EEG responses were recorded. These were processed to calculate
20 detection accuracy for each subject and calculate SSVEP band power. A neural network was trained
21 using the features to predict cognitive age. The results showed potential cognitive deterioration
22 through age-related variations in SSVEP features. Frequency detection accuracy declined after age
23 group 20-40 and band power, throughout all age groups. SSVEPs generated at theta and alpha
24 frequencies, especially 7.5 Hz, were the best indicators of cognitive deterioration. Here, frequency
25 detection accuracy consistently declined after age group 20-40 from an average of 96.64% to 69.23%.
26 The presented system can be used as an effective diagnosis tool for age related cognitive decline.

27 **Keywords:** brain-computer Interface; cognitive aging; steady-state visual evoked potential, neural
28 network; detection accuracy; band power

29

30 1. Introduction

31 Cognitive decline via deterioration of key neural networks can be caused by normal aging
32 and/or illness (i.e. Alzheimer's Disease), and often occurs before symptoms can be noted. It is well
33 known that age significantly increases one's risk of acquiring Alzheimer's Disease (AD), a severe
34 neurodegenerative illness affecting 46.8 million people worldwide^[1].

35 Cognitive deterioration has been explored through EEG signaling, which enables monitoring
36 of electrical activity in the brain with a high temporal resolution^[2]. For example, Taillard et al
37 indicates that aging is associated with characteristic changes in EEG waveforms collected during
38 Non-REM sleep^[3]. Furthermore, McBride et al uses regional spectral and complexity features in EEG
39 signals to discriminate between Amnesic Mild Cognitive Impairment (aMCI) and Alzheimer's
40 Disease (AD)^[4]. Ishii et al shows that aging is characterized by significant changes in resting state

41 oscillatory activity, Event-Related Potentials (ERPs) elicited by cognitive tasks, functional
42 connectivity between cerebral regions, and signal complexity^[5]. Miraglia et al discusses the use of
43 EEG functional network studies in order to build network topology models that could help better
44 understand changes in brain architecture throughout an individual's lifespan^[6]. Additionally,
45 Horvath et al examines EEG and ERP bioindicators of Alzheimer's Disease^[7] and Pagano et al
46 examines EEG subitization in healthy elderly subjects during working memory and attention-related
47 tasks^[8].

48 Steady-state visually evoked potentials (SSVEPs) are elicited by steadily oscillating visual
49 stimuli are commonly employed in studies of visual perception due to their high Signal to Noise
50 Ratio (SNR) and analytical simplicity^[9]. Most importantly, studies^[10] have shown that SSVEP features
51 have strong correlation with the topology of the networks they elicit. SSVEP amplitude and SNR has
52 strong positive correlation with efficiency and connectivity of their corresponding networks and
53 strong negative correlation with their length, making them accurate standards of neural efficacy^[11].
54 Such parameters affect the size of the SSVEP response generated because more efficient topological
55 organizations of neural networks are associated with larger responses. However, few studies have
56 focused on the effects of aging on SSVEP features; one study employs LED lights to extract Fourier
57 Amplitude and feature detection accuracy using an SSVEP-based Brain-Computer Interface (BCI) in
58 ALS patients and subjects of varying age^[16]. SSVEPs, which primarily entrain visual pathways
59 throughout the brain, are a promising source of biomarkers of cognitive aging because the pathways
60 stimulated by them extend throughout the entire brain. Studies examining a plethora of visual
61 biomarkers have shown promising levels of correlation with age^[13]; one prominent example is critical
62 flicker fusion, examined by Mewborn et al; which is the frequency (flicker speed) at which the flicker
63 of light can no longer be perceived. Critical flicker fusion, which provides insights into visual
64 processing mechanisms, showed strong negative correlation with age^[12].

65 SSVEP signals have a frequency range of 3.5-75 Hz; they can be categorized into particular
66 bands, depending on their frequency. The Theta, Alpha, and Beta bands, which are easiest to detect,
67 are comprised of frequencies 4-8 Hz, 8-13 Hz, and 14-30 Hz, respectively. The Theta band is generated
68 in the frontal midline during deep relaxation and can be activated by rational thinking. It is also
69 correlated with visualization or dreaming, memory, and cognitive control. The Alpha band is
70 generated in a state of relaxed alertness; their power is diminished by open eyes or increased attention
71 levels. This rhythm, which often dominates EEG recordings, increases in prevalence and amplitude
72 at age 7-20 and undergoes an overall decrease with age. The Beta band, prevalent in the frontal lobe,
73 is generated during a state of active concentration and is associated with problem solving, judgement,
74 and decision-making. This band is not usually clear in EEG recordings of healthy subjects^[14].

75 SSVEPs are commonly employed in Brain-Computer Interfaces (BCIs), which allow direct
76 interaction between an enhanced human brain and computerized device without the necessity of
77 conventional output pathways. BCIs typically translate signals into meaningful commands for
78 external devices, by restoring, at least partially, motor and communicative capabilities to individuals
79 with compromised neural tracts. It can also facilitate interactions between humans and speech
80 synthesizers, neural prostheses, and other assistive appliances^[15]. They are also used to study
81 different types of brain activity while the user induces a particular mental state or performs a
82 particular task. BCIs analyze different types of EEG signals, such as P300, Event Related
83 Synchronization or Desynchronization (ERS/ERD), Slow Cortical Potentials (SCPs), Sensorimotor
84 Rhythms (SMR), and Steady-State Evoked Potentials (SSEPs)^[9].

85 The objective of this study is to develop an SSVEP-based Brain-Computer Interface System that
86 employs flickering light of 10 different frequencies (4, 6.6, 7.5, 8.57, 10, 12, 15, 20, 25, 30 Hz) to collect

87 SSVEP responses from 16 subjects spanning from age group 10-20 to >60. These responses were then
88 epoched and analyzed to identify trends between SSVEP features and age. A predictive neural
89 network was trained to identify level of cognitive age using these features. Section 2 presents
90 materials and methods, Section 3 presents the results, and Section 4 presents the discussion and
91 conclusions.

92 2. Materials and Methods

93 The setup consisted of 5 electrodes (4 frontal and 1 occipital), positioned on a headband that the
94 subject wears. The stimuli were presented on a laptop. Data was collected from the Cyton Biosensing
95 board, which received the signals from the electrodes placed on the subject's scalp in the EEG
96 headband and wirelessly transmitted it to a USB dongle placed in a laptop computer.

97 I. Visual Stimulus Presentation

98 In this study, a single rectangular flickering stimulus (12.7 X 17.78 cm) was implemented to
99 evoke SSVEPs in the frontal and occipital regions. This stimulus, which flickers at 4, 6.6, 7.5, 8.57, 10,
100 12, 15, 20, 25, and 30 Hz was programmed using MATLAB's Psychophysics toolbox and presented
101 on a laptop. The flickering was produced by flipping between a black screen display and the texture
102 drawing routine of PsychToolbox, which produced the white rectangle. The amount of flips is
103 determined by the stimulus frequency; for example, a stimulus frequency of 4 Hz will result in 4 flips
104 between the background screen and rectangle. Each frequency was encoded with a distinct binary
105 matrix, in which '0' encoded the black screen display and '1' encoded the white rectangle. Each
106 stimulus frequency was presented once per subject, for 26 seconds. An intermission of 2 minutes was
107 provided between each presentation, to minimize visual fatigue. EEG data collection was stopped 1
108 second after stimulus presentation.

109

110 II. Data Acquisition

111 EEG responses to the flickering visual stimuli was collected using OpenBCI software, via 4
112 frontal electrodes (Fp1, FpZ, Fp2, F4, and Oz), situated on a wearable headband, and 1 occipital
113 electrode (Oz), arranged according to the International 10/20 System, which is one of the electrode
114 placement systems. After the headband was fastened around the head of the subject, the occipital
115 electrode (dry comb type) was taped (masking tape) to the back of the head and fastened under the
116 headband. A measuring tape and marker was used to locate the electrode positions on the scalp. 2
117 auricular electrodes, which served as ground and reference locations, were fastened onto the subjects'
118 ears. Conductive gel was applied to the electrodes when necessary, in order to reduce signal
119 impedance (<100 μ V). The electrode pins from the 7 electrodes were connected to a Cyton Biosensing
120 Board, which relayed the EEG signals to a USB dongle connected to a laptop computer. The USB
121 dongle enables the signals to be viewed and adjusted in the OpenBCI graphical user interface. The
122 experimental setup is shown in **Figure 1**. Bandpass filters were applied to EEG data to filter out
123 artifacts and noise caused by eye blinks, the presence of skin and hair, and equipment errors, among
124 others. These filters only allowed EEG data in the range 1-50 Hz to be transmitted. The sampling rate
125 for EEG signals collected was 250 Hz.

126 EEG data was collected from human subjects pertaining to age groups 10-20, 20-40, 40-60, and
127 >60, each age group comprising 4 subjects, totaling 16 subjects. All subjects possessed normal or
128 corrected-to-normal vision and if subjects had major treatments or medical issues regarding their eye
129 health, they did not participate in this study. These subjects were covered by the Institutional Review
130 Boards (IRB) of the University of Puerto Rico, and adequate consent and approval was obtained from
131 all subjects. In order to control sources of variation in the data, the experiments were conducted at
132 roughly the same time of day in a darkened room where the subjects were comfortably seated about
133 30.48 cm. away from the computer monitor.

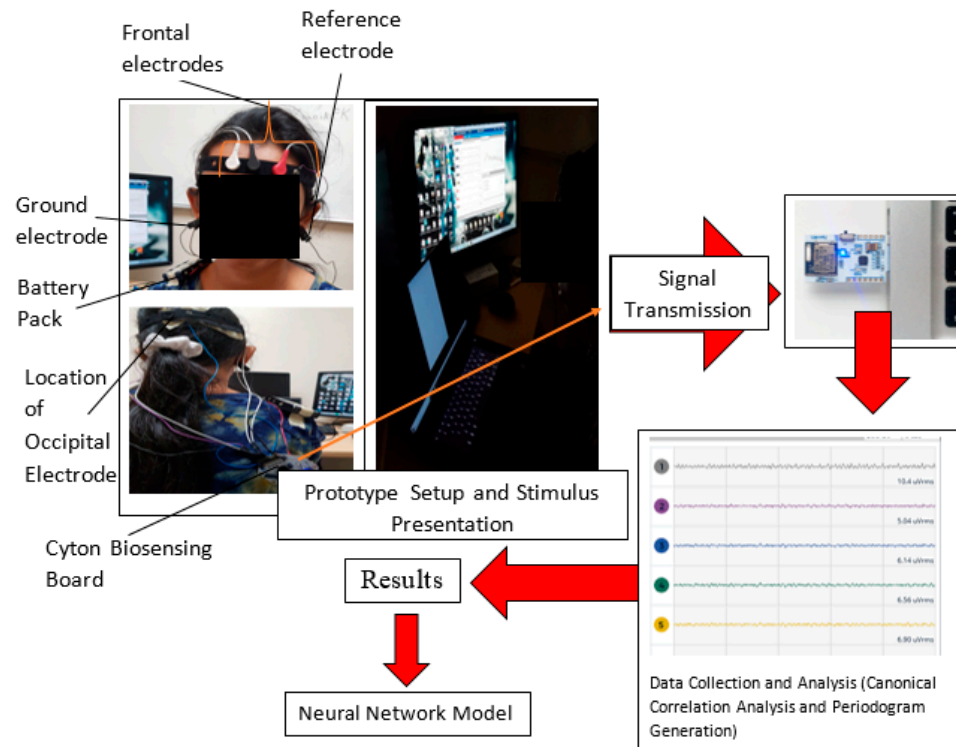


Figure 1. BCI equipment setup and experimentation.

134

135

136 III. Signal Processing and Feature Extraction

137 The EEG data, which is contained in ASCII files, was converted to a MATLAB-readable format,
 138 where it is represented by a 5-column matrix (5 data channels) with 6,540 samples or rows of points
 139 (signal amplitudes) on the EEG time-series plot (amplitude vs. time). The '.mat' file was then saved
 140 under a MATLAB variable.

141 Canonical correlation analysis (CCA) was used to compute a correlation coefficient between the
 142 SSVEP signals recorded at stimulus frequencies and reference signals generated at the same
 143 frequencies^[3]. Reference sinusoidal signals were generated for each stimulus frequency; each signal
 144 comprised 2 harmonics and was generated using the same sampling rate (250 points/sec) and number
 145 of points as the EEG signal. CCA was used to determine the reference signal that had the greatest
 146 correlation with the EEG signal; this in turn, was used to determine which frequencies were elicited
 147 in the SSVEP. The EEG signal was processed using differing averaging intervals (2, 3, 4, and 5 s), in
 148 order to divide it into differing amounts of epochs (10, 7, 5, and 4 epochs, respectively), or trials (4160
 149 in total). CCA was performed to determine which stimulus frequency had the greatest level of
 150 correspondence with the SSVEP in each epoch. This was used to determine intra-group detection
 151 accuracies of all 10 stimulus frequencies for each subject. This process was repeated for both the
 152 occipital (Oz) region and the frontal region, which comprised the average signal from the four frontal
 153 electrodes. This algorithm was written as a MATLAB function; each stimulus frequency is denoted
 154 by its position in a vector, and the function outputs the maximum frequency index, which is a vector
 155 displaying the frequency detected in each epoch. This information was then used to calculate the
 156 detection accuracy of theta, alpha, and beta stimulus frequencies, as the percentage of epochs where
 157 the stimulus frequency was detected correctly, in the SSVEPs.

158 The EEG signals were analyzed using the Fourier Transform (Eq. 1), which was used to generate
 159 Power Spectral Density (Eq.2) plots.

160

$$X(\omega) = \frac{1}{\sqrt{T}} \int_0^T x(t) e^{-i\omega t} dt \quad (1)$$

$$S_{xx}(\omega) = |X(\omega)|^2 \quad (2)$$

162 IV. Statistical analysis

163 After the procedures described above were completed, statistical procedures were applied to
 164 analyze and synthesize the study's data. Polynomial and linear regressions were used to delineate
 165 the relationship between cognitive aging and detection accuracy of stimulus frequencies in SSVEPs,
 166 as well as SSVEP band power. Accuracy of general trends identified in this study were evaluated
 167 using Analyses of Variance (ANOVAs) and measures of spread, such as coefficients of variation and
 168 standard deviations.

169 A neural network was constructed using MATLAB's neural fitting app, in order to predict
 170 cognitive age based on frequency detection accuracy and SSVEP band power. This network consisted
 171 of 10 neurons and the input layer (training data for the model) consisted of 2 variables (Fourier
 172 Amplitude and Frequency Detection Accuracy), and was trained using the features extracted after
 173 epoching the data into intervals of 2, 3, 4, and 5 seconds. In this manner, there was 78 samples per
 174 subject, for 16 subjects in total. 70% of the data (12 samples) were used for training, 15% (2 samples)
 175 for validation, and 15% for testing. The network was then trained using the Bayesian Regularization
 176 Algorithm, which adjusts an initial weight vector, which is used to generate predictions based on
 177 existing data, according to the input data used using training, in order to generate predictions of
 178 optimal accuracy. In this method, back-propagation occurs often to reduce prediction error. This
 179 experiment was repeated 10 times for 10-fold cross-validation and the data was randomly divided
 180 for training, validation, and testing.

181 3. Results

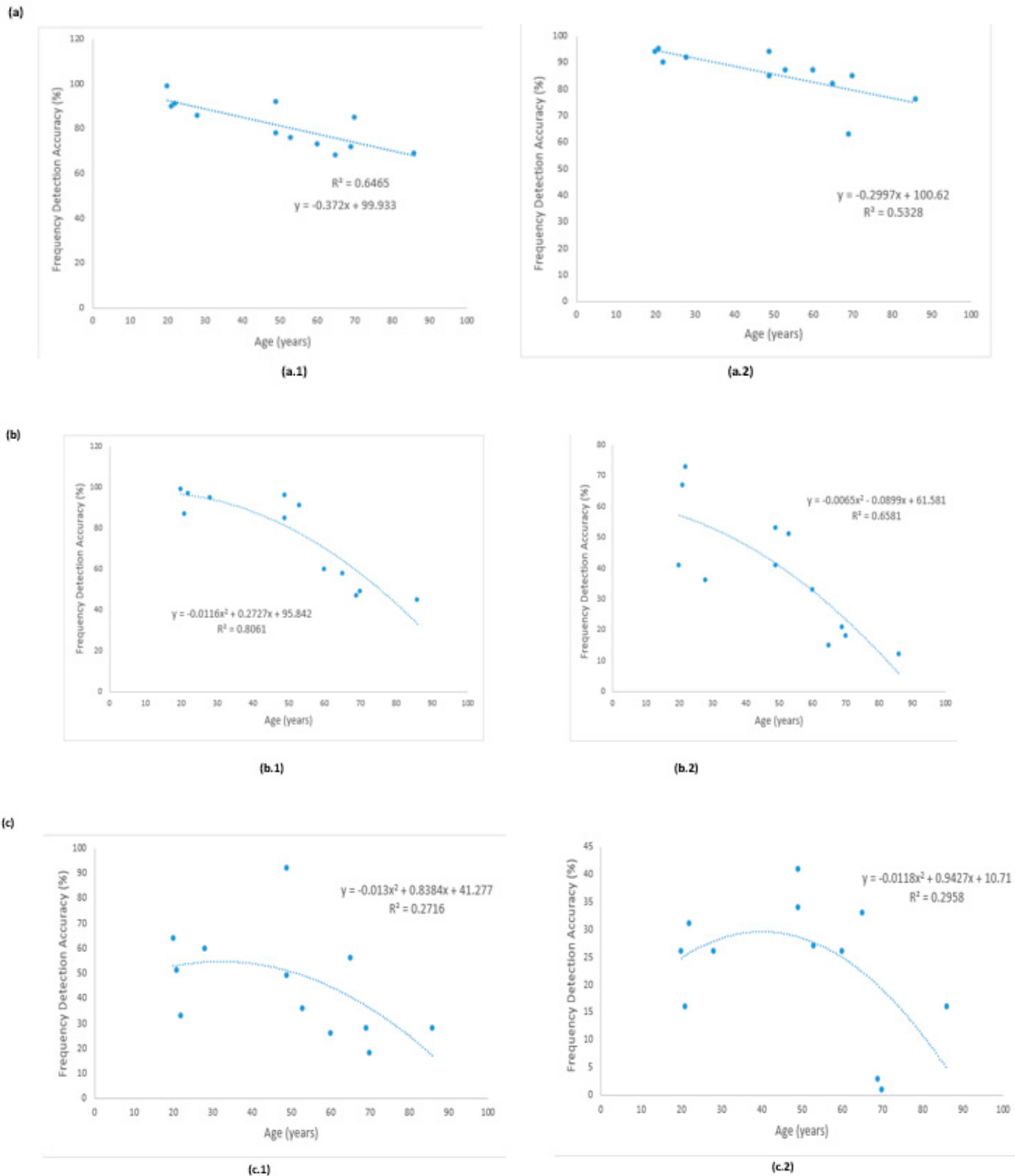
182 Stimulus frequency detection accuracy and SSVEP Fourier amplitude as a function of age are
 183 presented below. The best cerebral regions and stimulus frequencies that were optimal in delineating
 184 cognitive aging are presented.

185 3.1.1. Detection accuracy of stimulus frequencies

186 Detection accuracy of theta, alpha, and beta stimulus frequencies increased between age groups
 187 10-20 and 20-40 and decreased continuously from age groups 20-40 to >60. This trend is shown in
 188 **Figure 2** in further detail. Frequency detection accuracy is thus representative of cognitive decline
 189 only in age range 20-40 and above, because of higher levels of cognitive development. These results
 190 are shown in **Table 1**.

191 **Table 1.** Theta, alpha, and beta frequency detection accuracy in varying age groups and
 192 corresponding statistics.

SSVEP Band (Hz)	Age Group	Mean		Standard Error		Standard Deviation		Coefficient of Variation	
		F	O	F	O	F	O	F	O
Theta (4-8)	10-20	90.25	77.75	2.21	3.57	5.07	6.24	6.70	8.60
	20-40	93	92.75	1.22	3.59	2.22	5.45	2.40	6.00
	40-60	88	78.5	3.37	1.50	3.95	8.42	4.50	10.6
	>60	73.75	76.5	1.89	3.28	9.75	7.85	12.7	10.7
Alpha (8-13)	10-20	18.5	56	3.20	1.55	10.25	7.26	55.4	13.0
	20-40	54.25	94.5	1.50	0.71	18.46	5.26	34.0	5.60
	40-60	44.5	83	1.93	1.25	9.292	16.0	20.9	19.3
	>60	16.5	49.75	8.75	9.08	3.873	5.74	23.5	11.5
Beta (14-30)	10-20	16.49	38.45	0.75	1.58	10.65	24.0	64.6	62.4
	20-40	27.25	52	1.32	7.94	6.292	13.8	25.4	26.5
	40-60	32	50.75	1.08	2.61	6.976	29.1	21.8	57.3
	>60	13.22	32.5	4.82	7.40	14.78	16.4	112	50.3



194

195

196

197

198

199

200

201

202

203

Figure 2. Graphical and mathematical relationship between age and detection accuracy of stimulus frequency bands in SSVEP signals: (a.1) Detection accuracy of theta frequency band in occipital region (a.2) Detection accuracy of theta frequency band in frontal region (b.1) Detection accuracy of alpha frequency band in occipital region (b.2) Detection accuracy of alpha frequency band in frontal region (c.1) Detection accuracy of beta frequency band in occipital region (c.2) Detection accuracy of beta frequency band in frontal region.

204 3.1.2. SSVEP Fourier Amplitude

205 As demonstrated by the results, the relationship between age and SSVEP Fourier amplitude is
 206 inversely proportional, and like frequency detection accuracy, it has a tendency to peak at age group
 207 20-40. SSVEP Fourier amplitude as a function of age is illustrated in **Table 2**. Moreover, according to
 208 the data spread presented in **Table 3**, Fourier Amplitude is the most reliable indicator of cognitive
 209 deterioration in theta and alpha SSVEPs; band power at these frequency bands as a function of age
 210 are shown in **Figure 3**.

211 **Table 2.** Band Power (dB/Hz) of SSVEPs evoked by theta, alpha and beta frequencies.

SSVEP Band	Harmonic	Age Group (years)			
		10-20	20-40	40-60	>60
Theta (4-8 Hz)	1	20.55	25.42	18.01	12.333
	2	19.3	28.717	17.47	14.174
	3	12.39	13.55	9.137	13.04
	4	12.18	16.313	8.369	9.6
	Mean	16.105	21	13.2465	12.28675
Alpha (8-13 Hz)	1	22.5	27.72	15.773	12.583
	2	14.225	26.71	18.367	10.816
	3	13.075	15.538	10.725	6.1018
	4	10.347	13.818	10.786	5.2189
	Mean	15.03675	20.9465	13.91275	8.679925
Beta (14-30 Hz)	1	20.953	23.1	16.835	13.473
	2	18.08	19.4	17.868	14.53
	3	10.505	12.123	9.2393	8.168
	4	9.842	8.386	6.7793	6.2207
	Mean	14.845	15.75225	12.6804	10.597925

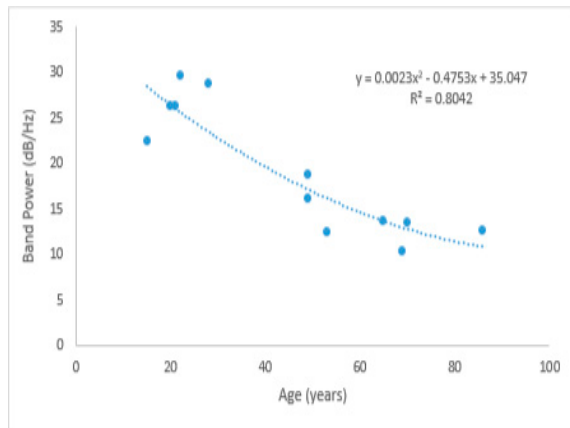
212

213 **Table 3.** Statistics of spread (standard deviation and coefficient of variation) for band power of first 4
 214 SSVEP harmonics evoked by theta, alpha, and beta frequencies.

SSVEP Band	Age Group	Harmonic							
		1st Harmonic		2nd Harmonic		3rd Harmonic		4th Harmonic	
		Std. Dev.	Coeff. Var.	Std. Dev.	Coeff. Var.	Std. Dev.	Coeff. Var.	Std. Dev.	Coeff. Var.
Theta (4-8 Hz)	10-20	1.56978	7.64	0.91099	0.392	1.41	16.12	1.6217	7.38
	20-40	0.6149	2.42	2.215	7.71	4.59	33.86	3.17	19.44
	40-60	3.66	20.33	3.99	22.82	2.57	28.11	3.054	36.49
	>60	2.57	20.81	5.33	37.58	3.7	28.37	N/A	N/A
Alpha (8-13 Hz)	10-20	N/A	N/A	2.14	15.06	1.62	12.39	4.47	43.23
	20-40	1.76	6.37	1.82	6.82	1.92	12.37	3.32	24.02
	40-60	3.24	20.56	5.43	29.54	6.66	62.09	2.08	19.27
	>60	1.54	12.28	4.81	44.5	2.73	44.7	2.52	48.2
Beta (14-30 Hz)	10-20	4.03	19.25	6.58	36.41	3.25	30.95	4.07	41.37
	20-40	8.68	37.57	6.47	33.34	5.62	46.37	6.01	71.66
	40-60	3.96	23.51	3.37	18.85	4.72	51.07	2.54	37.51
	>60	0.6025	4.47	6.12	42.09	1.38	16.83	3.07	49.43

215

216



217

218

(a)

219

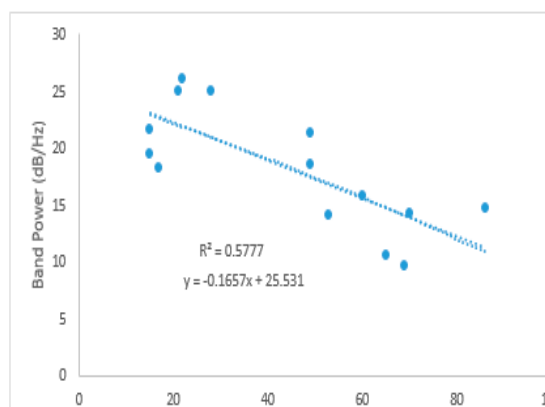
220

221

222

223

224



225

(b)

226

Figure 3. Band Power (dB/Hz) of SSVEPs evoked by (a) theta and (b) alpha frequencies.

227

3.2. Cognitive function, development, and deterioration

228

229

230

231

232

233

As mentioned before, SSVEP frequency detection accuracy and band power/Fourier amplitude peak between ages 20–40 (approximately 30) and decrease thereafter. Furthermore, **Table 4** shows that the Pearson correlation coefficients between age, frequency detection accuracy, and SSVEP band power, which exhibit inverse variation between the two factors, are significantly stronger when excluding age group 10–20 than when including it, suggesting that the method is feasible only for the age groups above 20.

234

235

Table 4. Coefficients of correlation with age for SSVEP band power and stimulus frequency detection accuracy including (light beige) and excluding (light blue) age group 10–20.

SSVEP Feature	Stimulus Frequency Band (Hz)					
	Theta (4-8)		Alpha (9-13)		Beta (14-30)	
	F	O	F	O	F	O
Frequency Detection Accuracy	-0.62	-0.29	-0.27	-0.34	-0.09	-0.21
	-0.73	-0.804	-0.81	-0.87	-0.37	-0.45
Band Power	-0.80		-0.82		-0.54	
	-0.87		-0.91		-0.55	

236

3.3. Optimal Frequency Range and Cerebral Region for Cognitive Assessment

237

238

239

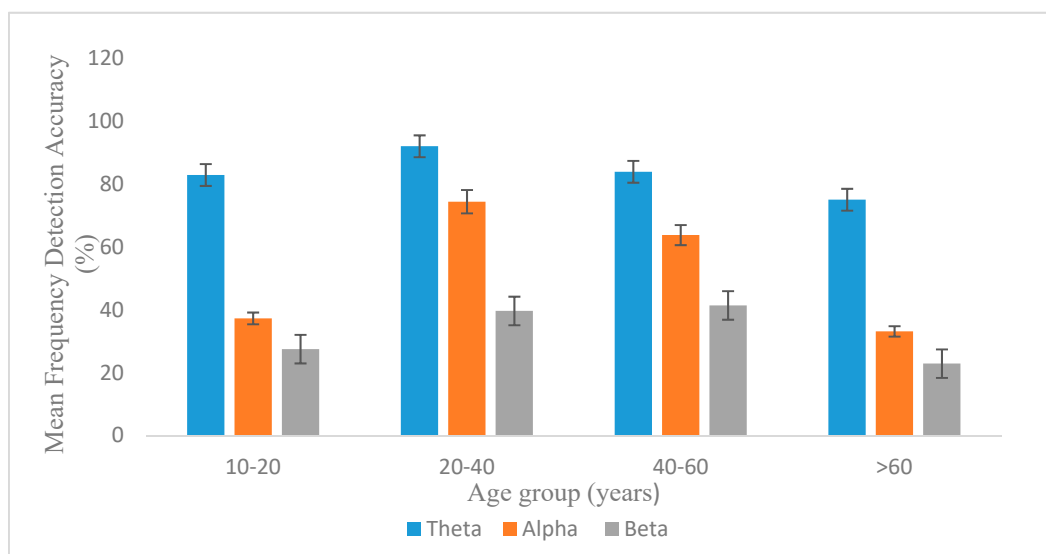
240

Results showed that the alpha frequency band was the best indicator of cognitive decline. **Figure 4** shows a clear correlation between frequency detection accuracy and age; as shown, the alpha stimulus frequencies elicited the greatest change in detection accuracy as function of age. Moreover, as shown in **Table 1**, the variation obtained for theta and alpha frequency stay within an acceptable

241 range (<30%), whereas spread in beta frequency detection accuracy often exceeds standards of
 242 reliability. Furthermore, although frontal responses demonstrated feasibility as indicators of
 243 cognitive aging, trends pertinent to occipital responses were significantly stronger, as demonstrated
 244 by **Figure 5**. Thus, as demonstrated by R^2 values in **Figures 2** and **3**, occipital responses to alpha
 245 frequencies are the best indicators of cognitive deterioration.

246 Analysis of Variance (ANOVA) with $p < 0.05$ showed that age group, frequency band, and
 247 electrode region have substantial effect on frequency detection accuracy and SSVEP band power.
 248 Furthermore, EEG signals elicited by 7.5 Hz ($p = 0.00037$) and 12 Hz ($p = 0.0008$) were most impacted
 249 by age. The alpha stimulus frequencies were, on average, the strongest indicators of cognitive aging.
 250 This finding, however, was not present in the effect of age group on detection accuracy of beta
 251 stimulus frequencies, suggesting that the variation in beta frequency detection accuracies is too high
 252 for the data to be considered reliable.

253
 254

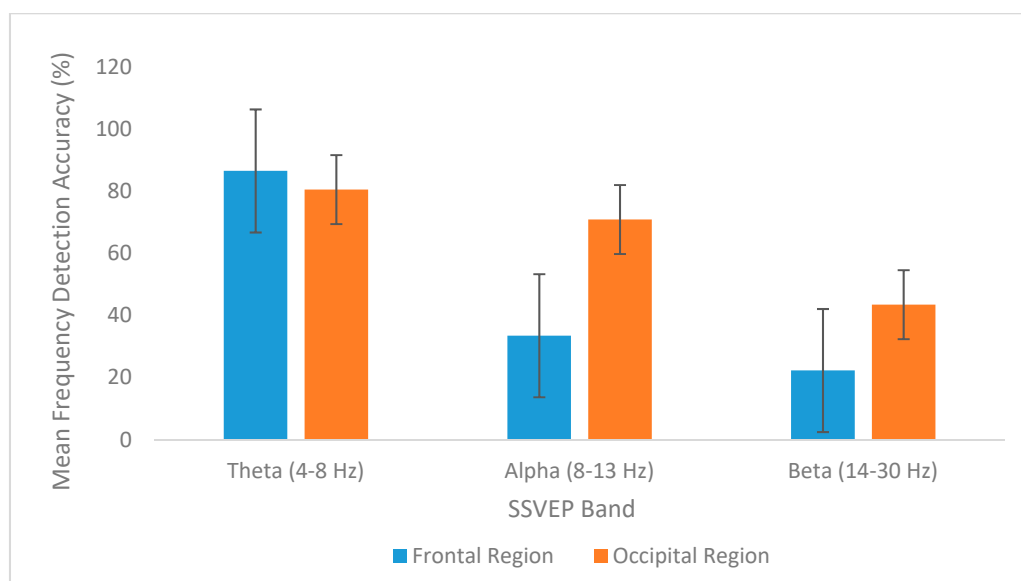


255

256

257

Figure 4. Mean detection accuracy of Theta, Alpha, and Beta stimulus frequencies in SSVEP signals pertaining to varying age groups.



258

259

260

Figure 5. Mean detection accuracy of Theta, Alpha, and Beta stimulus frequencies in frontal and occipital SSVEP signals.

261 3.4. Prediction using Neural Network

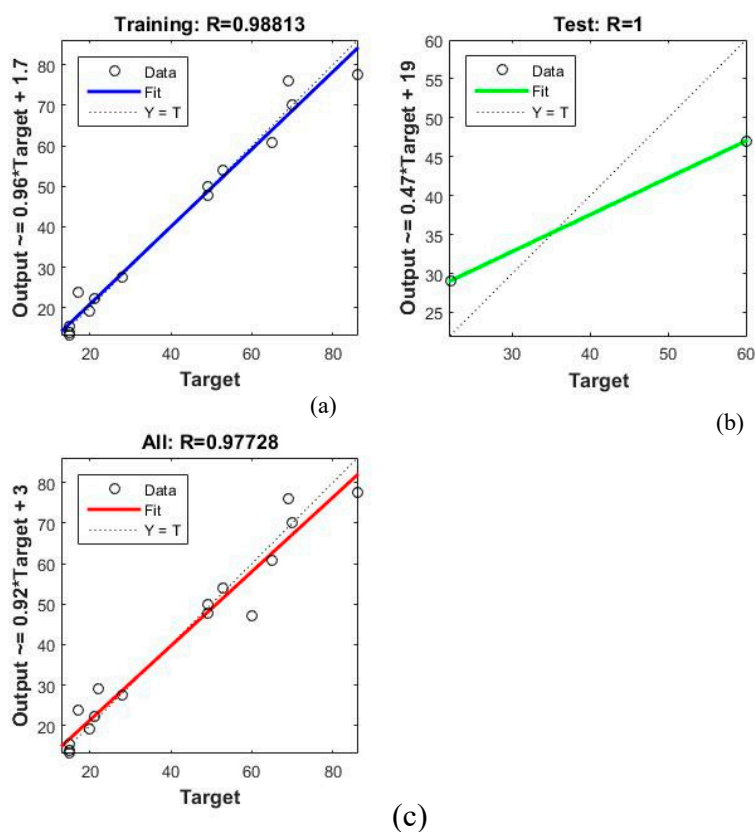
262 A neural network was trained (Bayesian regularization) using stimulus frequency detection
 263 accuracy and band power (dB/Hz) of SSVEPs evoked by alpha stimulus frequencies in age groups
 264 20-40 and above. This neural network displays high predictive power, as the correlation coefficient
 265 between the target values and the output values is a high ~ 0.988 . **Table 5** shows the neural network
 266 outputs when tested with random inputs. The training, testing, and validation results of the neural
 267 network are shown in **Figure 6** and the training performance of the neural network at varying data
 268 segments is shown in **Figure 7**.

269

270 **Table 5.** Neural network predictions of cognitive age when given random frequency detection
 271 accuracies (alpha band, occipital region) and band power values as inputs.

Inputs		
Alpha Frequency Detection Accuracy (%)	Alpha Band power (dB/Hz)	Output (Predicted Cognitive Age)
94.0	28.1	22.7
86.5	25.9	20.2
59.0	15.8	49.0
45.0	16.1	53.7
57.0	12.8	68.6
46.0	10.3	81.3

272



273

274 **Figure 6.** Output of neural network model according to provided targets during training (blue),
 275 validation (green) and testing (red), with corresponding correlation coefficients.

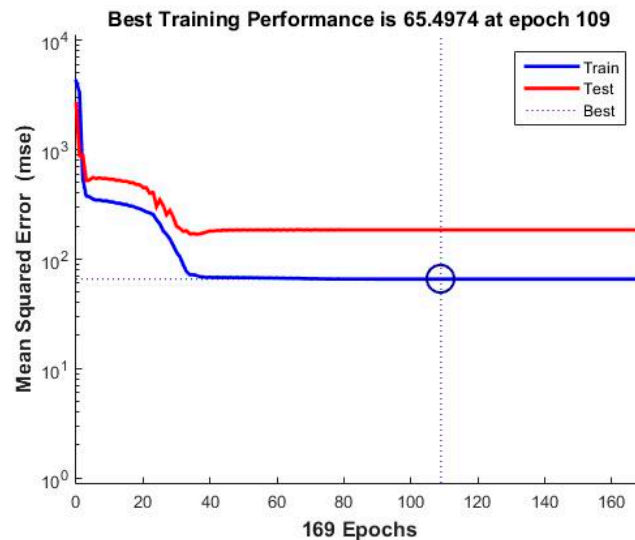


Figure 7. Training performance of the neural network.

276

277

278 4. Discussion, and Conclusions

279 The SSVEP based diagnosis BCI system was used with subjects of varying age to determine its
 280 ability to detect cognitive aging, and if possible, identify the manner in which it is manifested by
 281 features of Steady-State Visually Evoked Potentials (SSVEPs). The results of this study suggest that
 282 SSVEPs elicited by flickering stimuli may be valuable biomarkers of cognitive deterioration because
 283 SSVEP features such as band power and presence of stimulus frequencies in the signal, exhibited a
 284 sharp decline as a function of age, particularly in EEG signals elicited by alpha (8-13 Hz) flicker
 285 frequencies. These results were used to train an artificial neural network that effectively predicts
 286 cognitive age based on SSVEP band power and detection accuracy of stimulus frequencies in the
 287 signal.

288 The results of this study suggest that detection accuracy of stimulus frequencies in SSVEP signals
 289 indicate cognitive decline in age groups 20-40 and above. As demonstrated by **Figure 4**, frequency
 290 detection accuracy within the SSVEP signal reaches a peak for age group 20-40 and declines
 291 continuously afterwards. Similarly, other studies report a recession in accuracy in elderly subjects^[6].
 292 The increase in detection accuracy between age groups 10-20 and 20-40 can be attributed to ongoing
 293 cognitive development, which, according to recent studies may continue up to the mid-twenties;
 294 cognitive deterioration typically begins in the 30's or 40's^[4]. For this reason, it is more practical to
 295 use this application to gauge cognitive function for this age range. This is further corroborated by
 296 **Table 4**, which shows that the Pearson correlation coefficients between age, frequency detection
 297 accuracy, and SSVEP band power, which exhibit inverse variation between the two factors, are
 298 significantly stronger when excluding age group 10-20 than when including it.

299 **Figure 2** demonstrates an inversely proportional relationship between age (20 and above) and
 300 detection accuracy of Theta, Alpha, and Beta stimulus frequencies in the SSVEP signal. However,
 301 while the relationship between Theta frequency detection accuracy and age seems to be linear, as
 302 shown in **Figure 2(a)**, detection accuracy of Alpha and Beta frequencies, shown in **Figures 2(b)** and
 303 **3(c)**, reaches a plateau between ages 20 and 40, and exhibits a precipitous decline afterwards.
 304 Likewise, studies indicate that larger SSVEP responses are associated with more efficient functional
 305 network topology in the human brain, suggesting that this trend could be caused by aging of these
 306 systems^[13]. Additionally, while detection accuracy of theta stimulus frequencies in SSVEPs can be
 307 effectively modeled using linear regression, detection accuracies of alpha and beta frequencies are
 308 better represented by quadratic regression models.

309 Similar trends are manifested by SSVEP band power (or Fourier amplitude) at theta, alpha, and
 310 beta frequencies, as can be seen in **Figure 3** and **Table 2**. SSVEP band power displays an overall
 311 decrease as a function of age, in EEG responses to all three frequency bands. Like in the case of

312 frequency detection accuracy, its relationship with age can be delineated using quadratic regression,
313 and it peaks at age group 20-40. **Table 2** also demonstrates that SSVEP Fourier amplitude is typically
314 highest at the first and second harmonics. Furthermore, **Table 3** shows that the first harmonic of
315 theta-evoked and alpha-evoked SSVEPs are the most reliable indicators of cognitive deterioration.

316 The results demonstrate that although these trends can be discerned in EEG responses to all
317 frequency bands, the alpha band was shown to be the best indicator of cognitive decline. As shown
318 in **Figure 4**, the alpha band displays the most change as a function of age. In addition, as shown in
319 **Figures 2** and **3**, detection accuracy of and SSVEP band power at alpha stimulus frequencies display
320 the highest R^2 -values (0.80-occipital and 0.81, respectively), and thus demonstrate greatest conformity
321 with the previously described trends. The lowest R^2 values (0.3046 for frequency detection accuracy
322 and 0.2923 for SSVEP band power) occurred for EEG responses to beta stimulus frequencies, shown
323 in **Figure 2(c)**, suggesting that these frequencies are least reliable indicators of cognitive decline.
324 Furthermore, in **Fig. 2(c.2)**, various outliers can be noted. These outliers may arise as a result of high
325 levels of variation, which are typical of human systems, within EEG responses to beta stimuli. It is
326 interesting to note that the highest outlier, occurring between ages 40 and 60, belongs to a subject
327 who is a regular yoga practitioner.

328 Another significant trend, presented in **Figure 5**, was established by the results, in which the
329 mean detection accuracy of theta stimulus frequencies was detected with higher accuracy in frontal
330 SSVEPs than in occipital SSVEPs, while alpha and beta frequencies were detected with higher
331 accuracy in occipital SSVEPs. Furthermore, detection accuracies in occipital SSVEPs have lower
332 variation levels, as demonstrated by fairly shorter error bars. This suggests that detection accuracy of
333 stimulus frequencies in SSVEPs elicited in the occipital region have greater reliability. These trends
334 can be attributed to the origin of theta and alpha SSVEP signals: while the primary source of theta
335 waves is the frontal midline, alpha waves predominate in the occipital cortex. Thus, one can infer that
336 the detection accuracy of frequencies pertaining to particular bands, found in specific regions in the
337 human brain, depends on the location of the SSVEP being analyzed.

338 An artificial neural network for predicting cognitive age was trained using detection accuracy
339 of alpha stimulus frequencies in occipital SSVEPs and band power of alpha frequencies in the SSVEP
340 signal, as these were the best indicators of cognitive decline in this study. As shown in **Figure 6** (third
341 graph), the correlation coefficient between the network outputs and the target outputs is relatively
342 high, showing that the model fits the data well.

343 The OpenBCI system which was used to collect the EEG data, had high levels of impedance
344 when placing electrodes on the subject's scalp; thus, conducting gel was used to lower the impedance.
345 Furthermore, the data collected from the frontal region had many artifacts compared to data collected
346 from the occipital region, including eye blinks. These were removed by bandpass filtering, but frontal
347 EEG data displayed significantly more error than occipital EEG data. This study can be improved
348 with a broader subject population and sample size; furthermore, in order to achieve a larger level of
349 specificity with this method, it is aimed to test the method on patients with mild cognitive
350 impairment and explore other SSVEP features that can be used as indicators of cognitive
351 deterioration. This study shows that SSVEP based diagnosis BCI system can be used to verify
352 cognitive deterioration due to aging.

353 **Author Contributions:** conceptualization, V.M. and S.S.; methodology, S.S. and V.M.; software, V.M.;
354 validation, V.M. and S.S. formal analysis, S.S.; investigation, V.M. and S.S.; resources, S.S.; data curation, S.S.;
355 writing—original draft preparation, S.S.; writing—review and editing, S.S.; visualization, V.M. and S.S.;
356 supervision, V.M.; project administration, V.M.

357 **Funding:** This research received no external funding.

358 **Acknowledgments:** We want to thank the following graduate students for their invaluable help during this
359 study: Cesar Aceros (UPRM) and Jennifer Ramirez (UPRM) for their technical assistance during the process of
360 coding and experimentation, and Greg Palmer and Mike Patton (UWisc-Madison), for their feedback and
361 suggestions during data analysis and manuscript preparation. We would also like to thank Mrs. Evelyn
362 Montalvo, for her inspiration, mentorship, feedback, suggestions, and manuscript revisions, which were
363 instrumental to this study.

364 **Conflicts of Interest:** The authors declare no conflict of interest.

365 **References**

- 366 1. Alzheimer's Association. Available online: [https://www.alz.org/alzheimers-dementia/what-is-](https://www.alz.org/alzheimers-dementia/what-is-alzheimers)
 367 [alzheimers](https://www.alz.org/alzheimers-dementia/what-is-alzheimers) (accessed on 8 Sep 2018).
- 368 2. Tailard, J; Sagaspe, P; Berthomier C; Brandewinder M; Amieva H; Dartiques JF; Rainfray M; Harston S;
 369 Micoulaud-Franchi JA; Philip P. Non-REM Sleep Characteristics Predict Early Cognitive Impairment in
 370 an Aging Population. *Front Neurol*, **2019**, Vol 10, pp. 197-208.
- 371 3. McBride J; Zhao X; Munro N; Smith C; Jicha G; Jiang Y. Resting EEG Discrimination of Early Stage
 372 Alzheimer's Disease from Normal Aging Using Inter-Channel Coherence Network Graphs. *Ann Biomed*
 373 *Eng*, **2013**, Vol. 41, pp. 1233-1242.
- 374 4. Ishii R; Canuet L; Aoki Y; Hata M; Iwase M; Ikeda S; Nishida K. Healthy and Pathological Brain Aging:
 375 From the Perspective of Oscillations, Functional Connectivity, and Signal Connectivity.
 376 *Neuropsychobiology*, **2017**, Vol. 75, pp. 151-161.
- 377 5. Miraglia F; Vecchio F, Rossini P. Searching for signs of AD and dementia in EEG through network
 378 analysis. *Behav Brain Res*, **2017**, Vol 317, pp. 292-300.
- 379 6. Jorge M; Spindola L; Katata J; Anghinah F. Alpha Band EEG Coherence in Healthy Nonagerians. *Arq*
 380 *Neuropsiquiatr*, **2017**, Vol 75, 609-613.
- 381 7. Horvath A; Szucs A; Csukly G; Sakovics A; Stefanics G; Kamondi A. EEG and ERP Biomarkers of
 382 Alzheimer's Disease: A Critical Review. *Front Biosci*, **2018**, Vol 23, 180-220.
- 383 8. Pagano S; Fait E; Monti A; Brignani D; Mazza V. Electrophysiological Correlates of Subitizing in
 384 Healthy Aging. *Plos One*, **2015**, Vol 10, 17-30.
- 385 9. Hassanien, A. E. & Azar, A.T. *Brain-Computer Interfaces*, 1st ed; Springer International Publishing: New
 386 York, USA,2015, Vol. 74, pp 4-16.
- 387 10. Zhang, Y.; Guo, D. The graph theoretical analysis of the SSVEP harmonic response networks. *Cogn.*
 388 *Neurodyn* **2015**, Vol. 2015, pp. 305-315.
- 389 11. Zhang, Y.; Xu, P. SSVEP Response is Related to Functional Brain Network Stimulus Entrained by the
 390 Flickering Stimulus. *PLOS ONE*, **2013**, Vol. 8, pp. 1-11.
- 391 12. Mewborn, C.; Renzi, L. M. Critical Flicker Fusion Predicts Executive Cognitive Function in Younger and
 392 Older Adults. *Arch Clin Neuropsychol* **2015**, Volume 70, pp. 605-610
- 393 13. Frost, S; Martins R; Kanagasigam Y. Ocular Biomarkers for Early Detection of Alzheimer's Disease. *J*
 394 *Alzheimers Dis*, **2010**, Vol 22, pp. 1-16.
- 395 14. Kropotov, J.D. *Quantitative EEG, Event-Related Potentials, and Neurotherapy*; Elsevier: London, England,
 396 2009, pp. 29-77.
- 397 15. Chang, N.S.; Choi, I.; Wadson, A.; Whang, M. In *Brain-Computer Interfaces*; Nam, C.S., Nijholt, A., Lotte,
 398 F. Taylor & Francis Group: Boca Raton, FL, 2015, pp. 12-17.
- 399 16. Hassanien, A. E. & Azar, A.T. *Brain-Computer Interfaces*, 1st ed; Springer International Publishing: New
 400 York, USA,2015, Vol. 74, pp 4-16.
- 401 17. Hsu, H.; Lee, I. Evaluate the feasibility of using frontal SSVEP to implement an SSVEP-based BCI in
 402 Young, Elderly, and ALS groups. *IEEE Neural Syst Rehabil Eng* **2016**, Vol 24, 603-15.
- 403