北京航空航天大学四年级博士生和五年级直博生
学校奖学金申报表

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<tr><td>姓　名</td><td>张志敏</td><td>学　号</td><td>BY1510118</td><td>指导教师</td><td colspan="2">牛海军</td></tr>
<tr><td>类　别</td><td colspan="3">✔ 三年级博士生 ☐ 四年级直博生</td><td>学科/专业</td><td colspan="2">生物医学工程</td></tr>
<tr><td rowspan="4">承担科研任务情况</td><td colspan="2">项目名称</td><td>课题来源</td><td>课题负责人</td><td colspan="2">本人承担的具体工作</td></tr>
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<tr><td colspan="2">生理信息采集系统的加工与测试</td><td>12 企、事业单位委托项目</td><td>牛海军</td><td colspan="2">1）搭建肌电、心电、脉搏及血样采集平台；2）进行无创连续血压监测方案调研和设计。</td></tr>
<tr><td rowspan="3">已取得研究成果（论文、专利、获奖等）</td><td colspan="2">论文题目</td><td>本人排名</td><td>发表年月</td><td>期刊（会议）名称</td><td>被检索类型</td></tr>
<tr><td colspan="2">Quantitative EEG in Mild Cognitive Impairment and Alzheimer’s Disease by AR-Spectral and Multi-scale Entropy Analysis</td><td>2</td><td>2018.6</td><td>The World Congress on Medical Physics and Biomedical Engineering 2018</td><td>2EI/3ISTP</td></tr>
<tr><td colspan="2">A Hybrid BCI-based Environmental Control System Using SSVEP and EMG Signals</td><td>2</td><td>2018.6</td><td>The World Congress on Medical Physics and Biomedical Engineering 2018</td><td>2EI/3ISTP</td></tr>
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	Study of Steady State Motion Visual Evoked Potential-based Visual Stimulation	2	2018.4	The 12th International Convention on Rehabilitation Engineering and Assistive Technology	2EI/3ISTP
	基于 SSMVEP 的脑-机接口视觉刺激探究	2	2018.3	中国医疗器械杂志	7MEDLINE
	基于 LZ 复杂度的早期认知障碍和阿尔兹海默症脑电分析	2	2017.8	第六届国际康复医学与工程大会	99 其他
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	专利名称	**本人排名**	**发布年月**	**专利号**	**专利类型**
	用于重障碍者的脑肌电结合家居控制系统训练软件	2（1 为导师）	2017.5	2017SR371212	5 软件著作权
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导师意见	同意 / 不同意 该同学申报学校奖学金。 导师签字：______________ 年 月 日				
学院学位评定分委员会意见	同意 / 不同意 该同学获得学校奖学金。 签字：______________ （学院代盖） 年 月 日				

Quantitative EEG in Mild Cognitive Impairment and Alzheimer's Disease by AR-Spectral and Multi-scale Entropy Analysis

Xiaoke Chai[1], Xiaohong Weng[1],Zhimin Zhang[1] ,Yangting Lu[1] ,Guitong Liu[1]and Haijun Niu[1,2*]

[1] School of Biological Science and Medical Engineering, Beihang university, Beijing, China
[2] Beijing Advanced Innovation Center for Biomedical Engineering, Beihang University, Beijing, China
hjniu@buaa.edu.cn

Abstract.
To assist effective and precise diagnosis for mild cognitive impairment(MCI) and Alzheimer's disease(AD),Electroencephalograph(EEG) has been widely used in clinical research of patients with AD at MCI state. To study the linear and non-linear abnormality of EEG in AD and MCI patients, multiple characteristics was applied to distinguish AD and MCI patients from the normal controls(NC). EEG signals was recorded from 28 subjects, including 10 AD patients, 8 MCI subjects and 10 healthy elderly people. EEG signals in all channels was computed by auto-regressive model and multi scale entropy(MSE) to obtain relative power spectral density (PSD) value of each frequency band and entropy value in different time scales. Area under Receiver operating characteristic curve (AUC) was used to compare the classification ability of the two method. The ratio Alpha/theta of MCI group in left frontal area can distinguish MCI from NC subjects. Also the long scale entropy value in left frontal-central area manifests a better accuracy in distinguish AD and MCI from NC group. In addition, the combined feature from alpha/theta and long scale entropy in the left frontal central area can discriminate AD from NC group with higher AUC reaching 0.89. This indicated that combined PSD and MSE can be taken as a potential measure to detect AD in early state.

Keywords: Nonlinear, Multi-scale Entropy, Alzheimer's Disease, Mild cognitive impairment.

1 Introduction

Alzheimer's disease is a degenerative diseases of the central nervous increasingly affects the elderly people, causing loss in cognition, memory, even language function [1].About 10-15% of MCI elderly people each year developed into AD, effective diagnosis and treatment for MCI is very important [2]. The clinical detection of MCI and AD is mainly based on subjective neuropsychological test [3]. The imaging method was used to study the brain structure changes of MCI and AD, but its specificity is not high in the early stage of AD [4]. Also the detection based on biomarkers is invasive

[5]. EEG can reflect the physiological activities of the brain, and because of its low-cost, non-invasive and high time resolution, it has been widely used in clinical research of patients with AD at the MCI stage [6].

Quantitative EEG recordings in rest state provide an ideal methodology of the rapid detection in MCI and AD [7]. Babiloni et al [8] presented the hippocampus volume is related to the loss of alpha rhythms in AD. Moretti et al [9] found the alpha relative power of MCI in the frontal area was decreased, and power in theta band was increased. Compared with traditional spectrum estimation, the parameter estimation based on AR model performs better, it has been used to calculate PSD of EEG in MCI studies [10]. Although linear analysis is important to quantify the abnormal EEG rhythm of patients with MCI or AD, considering the non-stationarity and randomicity of EEG signal, complexity measures such as entropy were widely used to analysis EEG in AD patients. Abasolo et al [11] showed the entropy of AD patients in the parietal area is lower than health elderly. Hogan et al [12] found that the entropy of MCI subjects was reduced. MSE analysis base on entropy can measure the probability of producing new information for sequences under different scales size, it has been used in cognitive neuroscience. Mizuno et al [13] found large scale entropy of AD patients in whole brain areas was higher than healthy elderly. Previous studies suggested the complexity changing of EEG signals related to cognitive impairment may be inconsistent in different time scales.

In this work to further quantify both linear and nonlinear comprehensive abnormality of EEG in MCI and AD patients, the PSD and MSE method was adopted to analysis the MCI, AD and normal elderly. Then we compared the accuracy of PSD value, MSE value and combined index in distinguishing AD and MCI from healthy elderly.

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Age (years)	74.4±9.6	79.1±8.7	80.6±6.7	0.25
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PSD analysis for each segment is estimated using AR Burg method, which is one of the most frequently used parametric method. AR model is based on modeling the data sequence as the output of a causal and discrete filter whose input is white noise. Thus the AR model of order p is expressed by the difference equation. AR parameters was estimated by the Burg algorithm, and the optimal order of AR model was estimated by the final prediction error criterion (FPE). The PSD in each frequency band was normalized to obtain the relative PSD, where the sub-band was selected as delta band in 0.5-4Hz, theta band in 4-8Hz, alpha band in 8-13Hz and beta band in 13-30Hz. And alpha/theta which shows the ratio of PSD in alpha band versus theta band was computed.

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MSE is a method which measure the complexity of a finite length time series to quantify the probability of generating new information on different time scales. MSE method based on sample entropy of different scales was calculated as the following steps[13]: Firstly, for EEG time series X, construct a coarse-grained time series Y according to a scale factor, the length of reconstruction time series is M, in this work set m=2 to get the new time series Y_m. Secondly, quantify the sample entropy of each coarse-grained time series, the distance between each Y_m was computed. Set a threshold, r=0.25, the number of the distance less than r was calculated as B, then obtain the average ratio of this number to the total number of vectors. Lastly, for the next number of dimensions m+1, repeat the above steps to obtain the sample entropy of each scale from 1 to 20.

3.3 Statistical analysis

Comparison between groups (NC and MCI, MCI and AD, NC and AD) was made using the independent samples T-test. ROC curves was used to estimate the discriminating ability of PSD and MSE. Area under curve (AUC) of ROC near the upper left corner indicate diagnostic capabilities. Statistical procedures was performed using SPSS 19.0.

4 Results

4.1 MSE in different scales

The sample entropy value on 1 to 20 scales in each channel of AD, MCI and NC group was shown in "Fig. 1". For each scale we compared the difference between AD and NC group. The red box indicated that within this range of scales, differences was statistically significant between AD and NC group. The long scale entropy of AD group was greater than MCI group, and the value of MCI group was greater than NC group, especially for scales more than 12, there was significant differences in each channel of the left side brain areas.

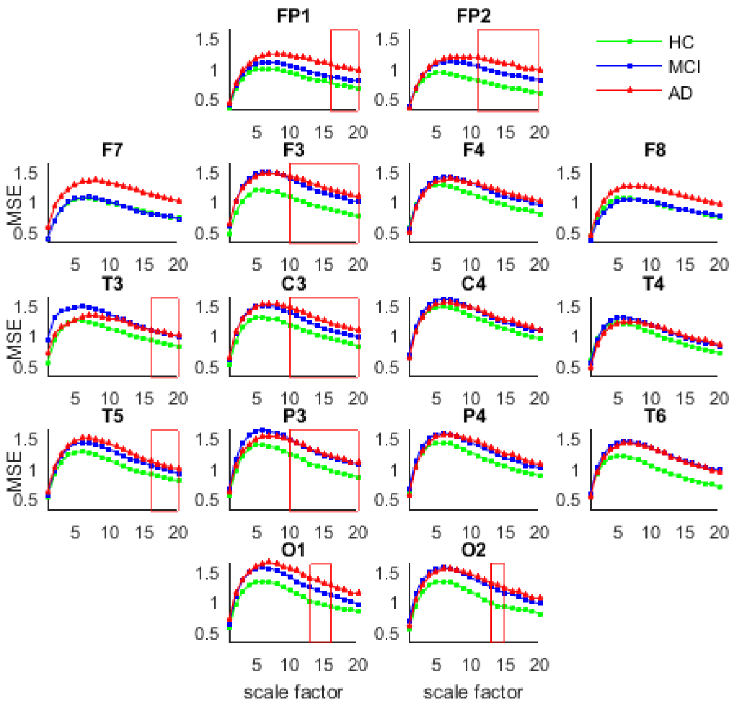

Fig. 1. MSE in different scales of different channel

The average entropy from 13 to 20 were computed as the long scale entropy value. The "Fig. 2" shows the long scale entropy in left frontal, left occipital, left parietal occipital, left temporal, right frontal, right occipital, right occipital area and right temporal areas, differences between AD and NC group were analyzed by t test. The long scale entropy value of AD group was greater than MCI group, and the value of MCI was greater than NC group. Especially the difference between AD and NC group in the left frontal, left frontal-central and left parietal-occipital areas was significant.

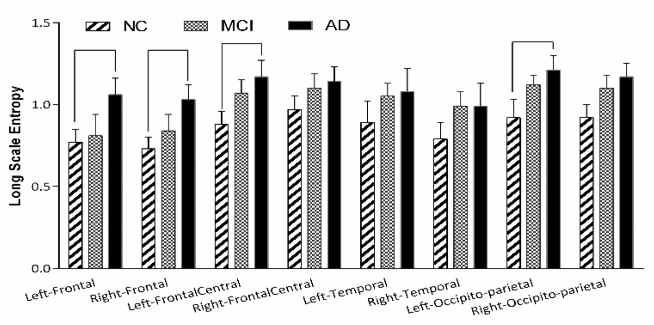

Fig. 2. Alpha/Theta in different areas

4.2 PSD in different band

The average PSD value of different frequency band in each channel of the three group was shown Table 2, '*' means difference between AD and NC group was significant, and '+' means difference between AD and MCI group was significant.

Table 2. PSD index of different frequency band

	β	α	θ	δ	(β+α)/(θ+δ)	α/θ
NC	0.18±0.03	0.41±0.05	0.24±0.02	0.16±0.04	0.72±0.34	2.91±0.33
MCI	0.15±0.02*	0.40±0.06	0.28±0.02*	0.16±0.05	0.60±0.33*	2.13±0.31*
AD	0.12±0.01^{*+}	0.33±0.05^{*+}	0.37±0.02^{*+}	0.19±0.06^{*+}	0.28±0.16^{*+}	0.95±0.12^{*+}

For Alpha/Theta, difference between groups on left and right side of four brain areas were also analyzed by t test. As shown in "Fig.3", the line means $p<0.05$, the difference was significant. There was significant difference of the alpha/theta value in left frontal, left temporal, right temporal and right parietal occipital areas. There was significant difference of the alpha/theta value in left frontal area of MCI and NC group. And there was significant difference of the alpha/theta value in right parietal occipital area of MCI and AD group.

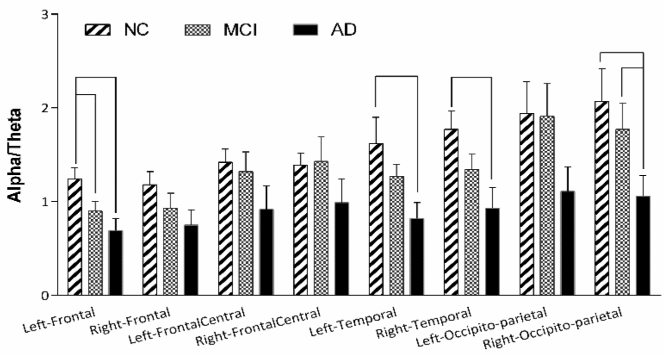

Fig. 3. Long-scale entropy in different areas

4.3 ROC analysis

AUC was used to assess the ability of index in discriminating AD and MCI from NC group, the AUC of alpha/theta and long scale entropy in eight areas was computed, as Table 3 shows, * means AUC is more than 0.7. The results indicated that the two indexes in left frontal-central and occipito-parietal areas has certain accuracy in discriminating AD from NC group. AUC of linear and nonlinear index in the Left Frontal-Central area was all more than 0.7, with 0.75 and 0.81. We further combined those two value in left frontal-central area to distinguish AD from NC group, the AUC of combined index reached 0.89, which is higher than AUC from any single feature.

Table 3. AUC of Alpha/Theta and long scale entropy

	AUC of Alpha/Theta		AUC of Long Scale Entropy	
Brain areas	AD and NC	MCI and NC	AD and NC	MCI and NC
L-Frontal	0.61	0.76*	0.77*	0.55
R-Frontal	0.68	0.56	0.80	0.54
L-FrontalCentral	0.75*	0.48	0.81*	0.73*
R-FrontalCentral	0.59	0.58	0.68	0.61
L-Temporal	0.56	0.69	0.65	0.58
R-Temporal	0.65	0.58	0.63	0.65
LOccipitoparietal	0.86*	0.55	0.74*	0.69
ROccipitoparietal	0.79*	0.74*	0.67	0.69

5 Discussion

In this study, linear and non-linear method, PSD and MSE analysis was employed to distinguish MCI and AD patients from normal elderly. Cognitive impairment is related to the spontaneous EEG activity rhythm, the abnormality of all the PSD index in MCI and AD patient was consistent with the prior studies. The significant declined power of alpha band in AD patients was indicated, and these values of MCI subjects also has a downward trend compared with normal elderly. The alpha/theta ratio in left frontal and right occipito-parietal areas can be a typical feature of cognitive decline, which discriminated MCI from normal elderly significantly.

For MSE analysis, we determined the appropriate range of scale to obtain long scale entropy value, the complexity abnormality of MCI patients was consistent with prior studies. The long scale entropy in left frontal-central and ccipito-parietal areas provided better classification performance between AD patient and normal elderly. And in left frontal-central area it also provided good classification performance between the MCI and NC. This manifests EEG abnormality in dominant side brain areas of AD patients is more notable. The complexity of EEG from MSE analysis can provide more information which may benefit our understanding of cognitive impairment.

Since the brain is a complex system showing both linear and nonlinear features, combining PSD and MSE which can reflect the rhythmicity as well as complexity, to obtain effective multiple quantitative EEG index in rest state, can be taken as a potential measure in early screen of AD.

Acknowledgments

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Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Oulhaj A, Wilcock G K, Smith A D, et al. Predicting the time of conversion to MCI in the elderly: Role of verbal expression and learning [J]. Neurology, 73(73), 1436-42 (2009).
2. Levey A, Lah J: Mild cognitive impairment: An opportunity to identify patients at high risk for progression to Alzheimer's disease. Clin Ther, 28(7), 991-1001 (2006).
3. Serrao V T, Brucki S M D, Campanholo K R, et al. Performance of a sample of patients with Mild Cognitive Impairment (MCI), Alzheimer's Disease (AD) and healthy elderly on a lexical decision test (LDT) as a measure of pre-morbid intelligence[J]. Dementia E Neuropsychologia, 9(3), 265-269 (2015).
4. Hua X, Leow A D, Parikshak N, et al. Tensor-based morphometry as a neuroimaging biomarker for Alzheimer's disease: an MRI study of 676 AD, MCI, and normal subjects [J]. Neuroimage, 43(3), 458-469 (2011)Cabral C, Morgado P M, Campos C D, et al.
5. Predicting conversion from MCI to AD with FDG-PET brain images at different prodromal stages [J]. Computers in Biology & Medicine, 58,101-109 (2015).
6. Poil SS, De HW, Wm V D F, et al. Integrative EEG biomarkers predict progression to Alzheimer's disease at the MCI stage [J]. Frontiers in Aging Neuroscience, 5(2), 99-103(2013).
7. Jeong J: EEG dynamics in patients with Alzheimer's disease. Clinical neurophysiology, 115(7), 1490-1505 (2004).
8. Babiloni C, Frisoni GB, Pievani M, et al: Hippocampal volume and cortical sources of EEG alpha rhythms in mild cognitive impairment and Alzheimer disease.[J].NeuroImage, 44(1), 123-135 (2009).
9. Moretti D V, Miniussi C, Frisoni G B, et al. Hippocampal atrophy and EEG markers in subjects with mild cognitive impairment.[J]. Clinical Neurophysiology, 118(12), 2716-29 (2007).
10. Liu X, Zhang C, Ji Z, et al. Multiple characteristics analysis of Alzheimer's electroencephalogram by power spectral density and Lempel-Ziv complexity [J]. Cognitive Neurodynamics, 10(2), 1-13 (2016).
11. Abasolo D, Hornero R, Espino P, et al.: Analysis of regularity in the EEG background activity of Alzheimer's disease patients with Approximate Entropy. Clinical Neurophysiology, 116(8):1826-1834 (2005).
12. Hogan MJ, Kilmartin L, Keane M, et al.: Electrophysiological entropy in younger adults, older controls and older cognitively declined adults. Brain research, 1445, 1-10 (2012).
13. Mizuno T, Takahashi T, Cho RY, et al.: Assessment of EEG dynamical complexity in Alzheimer's disease using multiscale entropy. Clinical Neurophysiology, 121(9), 1438-1446 (2010).

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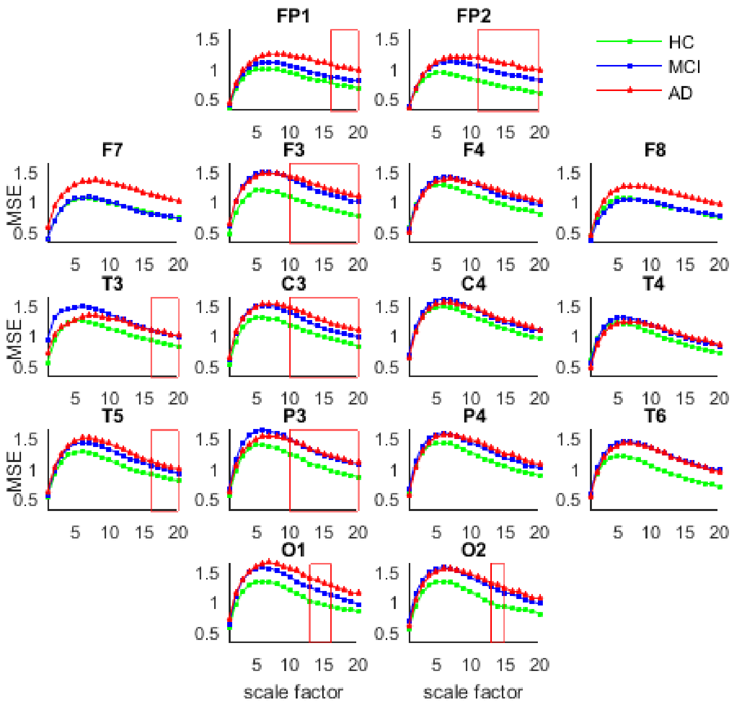

Fig. 1. MSE in different scales of different channel

The average entropy from 13 to 20 were computed as the long scale entropy value. The "Fig. 2" shows the long scale entropy in left frontal, left occipital, left parietal occipital, left temporal, right frontal, right occipital, right occipital area and right temporal areas, differences between AD and NC group were analyzed by t test. The long scale entropy value of AD group was greater than MCI group, and the value of MCI was greater than NC group. Especially the difference between AD and NC group in the left frontal, left frontal-central and left parietal-occipital areas was significant.

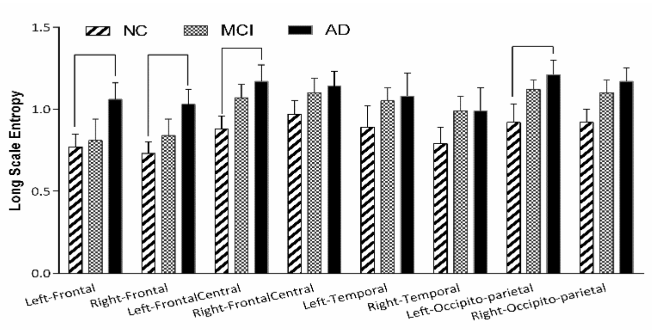

Fig. 2. Alpha/Theta in different areas

4.2 PSD in different band

The average PSD value of different frequency band in each channel of the three group was shown Table 2, '*' means difference between AD and NC group was significant, and '+' means difference between AD and MCI group was significant.

Table 2. PSD index of different frequency band

	β	α	θ	δ	(β+α)/(θ+δ)	α/θ
NC	0.18±0.03	0.41±0.05	0.24±0.02	0.16±0.04	0.72±0.34	2.91±0.33
MCI	0.15±0.02*	0.40±0.06	0.28±0.02*	0.16±0.05	0.60±0.33*	2.13±0.31*
AD	0.12±0.01*+	0.33±0.05*+	0.37±0.02*+	0.19±0.06*+	0.28±0.16*+	0.95±0.12*+

For Alpha/Theta, difference between groups on left and right side of four brain areas were also analyzed by t test. As shown in "Fig.3", the line means $p<0.05$, the difference was significant. There was significant difference of the alpha/theta value in left frontal, left temporal, right temporal and right parietal occipital areas. There was significant difference of the alpha/theta value in left frontal area of MCI and NC group. And there was significant difference of the alpha/theta value in right parietal occipital area of MCI and AD group.

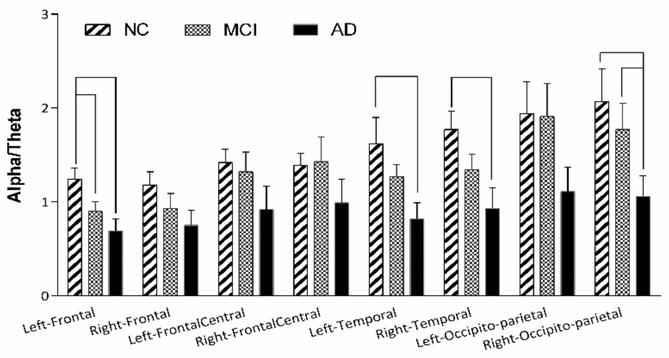

Fig. 3. Long-scale entropy in different areas

4.3 ROC analysis

AUC was used to assess the ability of index in discriminating AD and MCI from NC group, the AUC of alpha/theta and long scale entropy in eight areas was computed, as Table 3 shows, * means AUC is more than 0.7. The results indicated that the two indexes in left frontal-central and occipito-parietal areas has certain accuracy in discriminating AD from NC group. AUC of linear and nonlinear index in the Left Frontal-Central area was all more than 0.7, with 0.75 and 0.81. We further combined those two value in left frontal-central area to distinguish AD from NC group, the AUC of combined index reached 0.89, which is higher than AUC from any single feature.

Table 3. AUC of Alpha/Theta and long scale entropy

	AUC of Alpha/Theta		AUC of Long Scale Entropy	
Brain areas	AD and NC	MCI and NC	AD and NC	MCI and NC
L-Frontal	0.61	0.76*	0.77*	0.55
R-Frontal	0.68	0.56	0.80	0.54
L-FrontalCentral	0.75*	0.48	0.81*	0.73*
R-FrontalCentral	0.59	0.58	0.68	0.61
L-Temporal	0.56	0.69	0.65	0.58
R-Temporal	0.65	0.58	0.63	0.65
LOccipitoparietal	0.86*	0.55	0.74*	0.69
ROccipitoparietal	0.79*	0.74*	0.67	0.69

5 Discussion

In this study, linear and non-linear method, PSD and MSE analysis was employed to distinguish MCI and AD patients from normal elderly. Cognitive impairment is related to the spontaneous EEG activity rhythm, the abnormality of all the PSD index in MCI and AD patient was consistent with the prior studies. The significant declined power of alpha band in AD patients was indicated, and these values of MCI subjects also has a downward trend compared with normal elderly. The alpha/theta ratio in left frontal and right occipito-parietal areas can be a typical feature of cognitive decline, which discriminated MCI from normal elderly significantly.

For MSE analysis, we determined the appropriate range of scale to obtain long scale entropy value, the complexity abnormality of MCI patients was consistent with prior studies. The long scale entropy in left frontal-central and ccipito-parietal areas provided better classification performance between AD patient and normal elderly. And in left frontal-central area it also provided good classification performance between the MCI and NC. This manifests EEG abnormality in dominant side brain areas of AD patients is more notable. The complexity of EEG from MSE analysis can provide more information which may benefit our understanding of cognitive impairment.

Since the brain is a complex system showing both linear and nonlinear features, combining PSD and MSE which can reflect the rhythmicity as well as complexity, to obtain effective multiple quantitative EEG index in rest state, can be taken as a potential measure in early screen of AD.

Acknowledgments

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Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Oulhaj A, Wilcock G K, Smith A D, et al. Predicting the time of conversion to MCI in the elderly: Role of verbal expression and learning [J]. Neurology, 73(73), 1436-42 (2009).
2. Levey A, Lah J: Mild cognitive impairment: An opportunity to identify patients at high risk for progression to Alzheimer's disease. Clin Ther, 28(7), 991-1001 (2006).
3. Serrao V T, Brucki S M D, Campanholo K R, et al. Performance of a sample of patients with Mild Cognitive Impairment (MCI), Alzheimer's Disease (AD) and healthy elderly on a lexical decision test (LDT) as a measure of pre-morbid intelligence[J]. Dementia E Neuropsychologia, 9(3), 265-269 (2015).
4. Hua X, Leow A D, Parikshak N, et al. Tensor-based morphometry as a neuroimaging biomarker for Alzheimer's disease: an MRI study of 676 AD, MCI, and normal subjects [J]. Neuroimage, 43(3), 458-469 (2011)Cabral C, Morgado P M, Campos C D, et al.
5. Predicting conversion from MCI to AD with FDG-PET brain images at different prodromal stages [J]. Computers in Biology & Medicine, 58,101-109 (2015).
6. Poil SS, De HW, Wm V D F, et al. Integrative EEG biomarkers predict progression to Alzheimer's disease at the MCI stage [J]. Frontiers in Aging Neuroscience, 5(2), 99-103(2013).
7. Jeong J: EEG dynamics in patients with Alzheimer's disease. Clinical neurophysiology, 115(7), 1490-1505 (2004).
8. Babiloni C, Frisoni GB, Pievani M, et al: Hippocampal volume and cortical sources of EEG alpha rhythms in mild cognitive impairment and Alzheimer disease.[J].NeuroImage, 44(1), 123-135 (2009).
9. Moretti D V, Miniussi C, Frisoni G B, et al. Hippocampal atrophy and EEG markers in subjects with mild cognitive impairment.[J]. Clinical Neurophysiology, 118(12), 2716-29 (2007).
10. Liu X, Zhang C, Ji Z, et al. Multiple characteristics analysis of Alzheimer's electroencephalogram by power spectral density and Lempel-Ziv complexity [J]. Cognitive Neurodynamics, 10(2), 1-13 (2016).
11. Abasolo D, Hornero R, Espino P, et al.: Analysis of regularity in the EEG background activity of Alzheimer's disease patients with Approximate Entropy. Clinical Neurophysiology, 116(8):1826-1834 (2005).
12. Hogan MJ, Kilmartin L, Keane M, et al.: Electrophysiological entropy in younger adults, older controls and older cognitively declined adults. Brain research, 1445, 1-10 (2012).
13. Mizuno T, Takahashi T, Cho RY, et al.: Assessment of EEG dynamical complexity in Alzheimer's disease using multiscale entropy. Clinical Neurophysiology, 121(9), 1438-1446 (2010).

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Study of Steady State Motion Visual Evoked Potential-based Visual Stimulation Paradigm

Liu Guitong[1], Zhang Zhimin[1], Chai Xiaoke[1], Lu Yangting[1], Zhang Tengyu[1,2],

Niu Haijun[1*], Fan Yubo[1,2]

1. Beijing Advanced Innovation Center for Biomedical Engineering, School of Biological Science and Medical Engineering, Beihang University, Beijing, China

2. National Research Center for Rehabilitation Technical Aids, Beijing, China

[*] Correspondence: hjniu@buaa.edu.cn

ABSTRACT

In this study, a steady-state motion visual evoked potential (SSMVEP) stimulation-the square's ring motion was proposed, and compared with the visual stimulation which are commonly used in BCI system (oscillatory Newton's ring, square flicker and circular flicker) both in objective and subjective aspects. Eight healthy subjects were asked to gaze at those four simulations. For each stimulation, eight targets varying at different frequencies were presented on a LCD screen. Canonical Correlation Analysis (CCA) was used to identify SSVEPs, and subjective questionnaire was used to measure the comfort of the stimulations. The experimental results showed that the accuracy of the square's ring motion was 85±13.2% which has no significant difference with the oscillatory Newton's ring (85.9±9.1%). Meanwhile the accuracy of the square flicker was 98.1±4.38%, and the accuracy of the circular flicker was 99.1±1.9%. The subjective questionnaire reported that the square's ring motion was the most comfortable, followed by the Newton's ring motion, the circular flicker and the square flicker. Taken together, these results suggest that the square's ring motion equaling to the newton's ring can elicit SSVEP accurately and reduce the discomfort caused by flickering of targets. Though there is no obvious improvement in the accuracy of the square's ring motion compared with oscillatory Newton's ring, subjective score of the square's ring is a bit higher than the oscillatory Newton's ring. Under the premise of controlling the incorrect operation, the square's ring motion can be used as a visual stimulation in long-term SSMVEP-based BCI system.

Categories and Subject Descriptors

H.5.2 **[Information interfaces and presentation**]: User Interfaces – e*valuation/methodology, Screen design*

General Terms

Performance, Design, Experimentation,

Keywords

Steady state motion visual evoked potential; Accuracy; Comfort.

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1. INTRODUCTION

Brain computer interface (BCI) is an alternative device which facilitates human–machine interaction without dependence on any muscle or peripheral nervous system actions [1], using human neurophysiological signals to communicate with external device such as computers, wheelchairs [2] and robots [3]. BCI systems are most frequently based on recordings of electroencephalogram (EEG), because of the relatively low price and portability. BCI system based on the Steady State Visual Evoked Potentials (SSVEP) is widely used, due to its stable waveform, obvious spectral characteristics, and less susceptibility to blinking and motion artifact 错误!未找到引用源。[5][6]. SSVEP-based BCI system generally provide higher classification accuracy and information transfer rates (ITR) [7] 错误!未找到引用源。.

For SSVEP-based BCI system, a suitable stimulation paradigm is very crucial. There are three kinds of visual stimulation in previous studies. First, typical SSVEP is frequency coded, visual targets flashing at different frequencies, where a user's choice is determined from the SSVEPs elicited by gazing at a specific target, which is limited by a variety of factors, including user comfort and safety with light stimuli flashing at specific frequencies [9].The second is phase coded SSVEP, the targets were flickering at the same frequency but with different phases. Phase coding can increase the number of available targets and compensate the reduction of limited frequencies [10]-[12]. If a comfortable frequency of stimulation is selected, visual fatigue can be reduced to a certain extent. Thirdly, based on extremely high consistency of frequency and phase observed between visual flickering, the classification accuracy was up to 91.04% and the information transmission rate was 267bits /min [13].

Even though SSVEP-based BCIs have high recognition accuracy, most stimulation is based on flicker which usually causes eyestrain and directly affect the BCI system long time performance 错误!未找到引用源。. In order to overcome the problem of visual fatigue caused by uncomfortable light twinkling and contrast changes, Xie et al. utilized a special visual stimulation of non-direction-specific motion reversals, adopting the Newton's ring as the template, to elicit the SSMVEPs for BCI applications 错误!未找到引用源。. However, SSMVEP-based BCI cannot achieve high accuracy as SSVEP-based BCI. How to improve the accuracy under the condition of reducing visual fatigue has become the goal of researchers.

Due to the different shapes of receptive fields in successive stages of information processing in the visual system, one can hypothesize that square stimuli would evoke better response than circular ones

错误!未找到引用源。. We suspected that changing the motion pattern from Newton’s ring to square ring with sharper edge might increase the classification accuracy. In this paper, we proposed a new stimulation-the square’s ring motion for SSMVEP-based BCI system. In addition, the new stimulation was compared with the visual stimulation commonly used in BCI system (oscillatory Newton's ring, square flicker and circular flicker) both in objective and subjective aspects.

2. EXPERIMENTS AND METHODS

2.1 Stimulation

The square’s ring stimulation is a development of Newton’s ring which can provide a comparable performance with low-adaptation characteristic and less visual discomfort for BCI applications 错误!未找到引用源。. A square’s ring stimulator is made up of a series of concentric black and white squares. The formula is:

$$\mathrm{E} = I_{max}[\,（\mathrm{sign}(\cos(2 * \pi * \frac{\mathrm{d}}{\lambda} + \emptyset(\mathrm{i}) * \frac{\pi}{2})^2 - 0.5)] \quad (1)$$

In the formula, λ is a constant, this article takes 0.05; d is a square matrix of 360 * 360. The ring oscillation motion is formed by $\emptyset(i)$:

$$\emptyset(\mathrm{i}) = \mathrm{abs}(\sin\left(pi * \frac{\mathrm{f}}{2} * (\frac{i}{R})\right)) \qquad (\mathrm{i}=1, 2\ldots60) \quad (2)$$

Where, f is the stimulus frequency; i is the current frame number; R = 60 for the screen refresh rate. When $\emptyset(i)$ increases with i, its phase shift from 0 to π, and then expansion motion was achieved with phase shift from π back to 0[15]. Fig.1 shows a square’s ring motion reversal procedure in one stimulus period. It is illustrated with a 12 Hz motion reversal frequency and each reversal contained 10 frames.

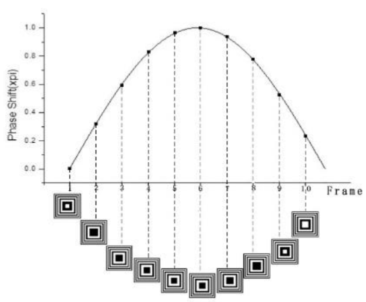

Figure 1. Square’s ring motion reversal stimulation

What’s more, the Newton's ring motion, the square flickering and circular flickering were selected as control.

Presentation of the stimulators and their reversals were coded by the Psychtoolbox 3.0. Acer's 24-inch LCD monitor (60Hz-screen refresh rate, 1920 × 1080 pixels) displayed the stimulation. For the each visual stimulation, there were eight targets flickering at 8, 9, 10, 11, 12, 13, 14 and 15Hz on a black background. There were four kinds of visual stimulation, there were four kinds of targets, square’s ring motion (5.5cm in side length), Newton’s Rings motion (6.2cm in diameter), the square flick (5.5cm in side length) and the circular flick (6.2cm in diameter).

2.2 Experimental procedure

Eight healthy right-handed adults (3 females and 5 males), aged from 20 to 26, participated in this experiment. All subjects gave informed consent. EEG signals were sampled at 1000 Hz (Neuroscan, USA). Those were attached to the head locations PO3, PO_4, PO_7, PO_8, PO_Z, O_1, O_Z, O_2, and C_Z. All electrode impedances were reduced to 10kΩ before data recording. Trigger events were acquired simultaneously. Data were collected continuously and analyzed off-line. The experiment was performed in a quiet room, with the subjects sitting comfortably and gazing at the LCD screen with a distance of about 70 cm.

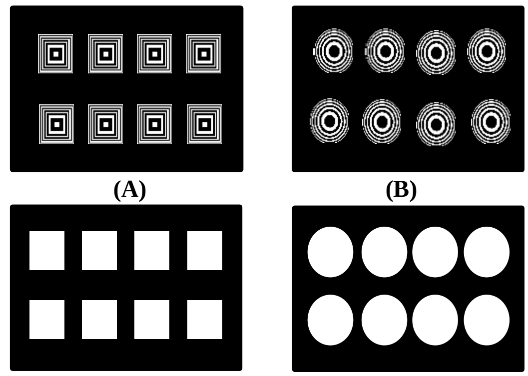

Figure 2.Stimulation interfaces (A) The square’s rings based interface. (B) The Newton’s rings interface. (C) The square based interface (D) The circle based interface.

For each subject, four experimental tasks with different stimulations were carried out. Each task contained 40 trails. Before the start of each trails, a red "+" symbol appears randomly at the location of the stimulus target for a duration of 0.5 s. Then the eight stimulators were simultaneously presented for 4 s as a single trial. Two adjacent trials were isolated by black screen and the interval time was fixed to 0.5 s. After 40 trails, a single task was over (see Figure 3).

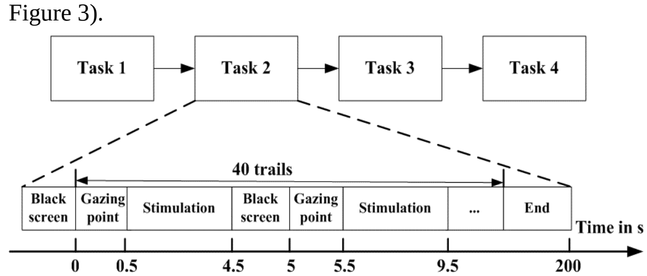

Figure 3. The timing of the experimental sequence

2.3 EEG data processing

Band-passed filter between 3 and 40 Hz and digital notch filter from 48Hz to 52Hz were used to remove artifacts and power line interface when acquiring EEG signals. Then the segmented EEG signals were superposition averaged and spectral analyzed. After determining four visual modes can effectively induce SSVEP, Canonical correlation coefficients (CCA) was implanted for off-line target classification [19]错误!未找到引用源。.

CCA is a statistical method for measuring the linear relationship between two sets of multivariate data. In the CCA-based SSVEP analysis, X=($x_1, x_2, \ldots x_n$) is assigned as the set of the multi-channel EEG signals, and Y_f refers to the set of reference signals which have the same length as X. The reference signals Y_f is set as

$$Y_{f_i} = \begin{Bmatrix} sin(2\pi \cdot f_i \cdot t) \\ cos(2\pi \cdot f_i \cdot t) \\ \cdot \\ \cdot \\ sin(2\pi \cdot kf_i \cdot t) \\ cos(2\pi \cdot kf \cdot t) \end{Bmatrix}, \ t = \frac{1}{f_s}, \dots, \frac{m}{f_s} \tag{3}$$

Where k is the number of harmonics, which is dependent on how many frequency harmonics existed in SSVEP. The f_s is the sampling rate, and m is sample points. By calculating:

$$\rho_i = \frac{E(W_x^T X Y_i^T W_{y_i})}{\sqrt{E(W_x^T X X^T W_x) \cdot E(W_{y_i}^T Y_i Y_i^T W_{y_i})}} \tag{4}$$

By calculating correlation coefficient ρ_i can be obtained, and i corresponding to the maximum is the focused target 错误!未找到引用源。. The accuracy of classification of the four stimulation was calculated from eight subjects.

2.4 Subjective Evaluation

At the end of each task, subject was asked to fill out a questionnaire in order to find out how comfortable they were. They had to give a score between 1 (not) and 7 (very) for each of the following four questions after gazing at each of the stimulation in turn 错误!未找到引用源。:

- How much do you like this stimulation?
- How much will this stimulation increase your tiredness?
- How long could you look at this stimulation?
- How annoying is this stimulation?

3. RESULT

3.1 Different visual modes SSVEP spectrum analysis

As for spectrum analysis of EEG signals results, one or two peaks were found in eliciting fundamental frequency or harmonic frequency. The amplitude of the spectrum peak of the square's ring motion and Newton's ring motion were smaller than that of the square flicker and the circular flicker. Fig. 4 showed the spectrum amplitude of channel PO4 while S7 gazing at visual stimulations flickering at 14Hz.

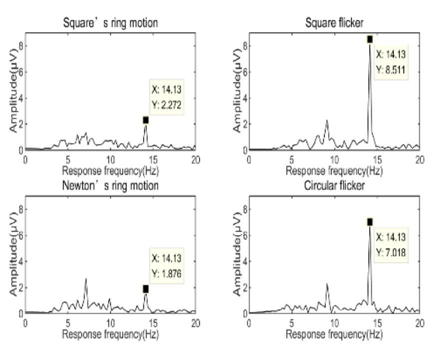

Figure 4.SSVEP spectrum amplitude of S7 elicited by 14 Hz

3.2 Accuracy of different visual stimulations

Fig.5 showed the CCA classification accuracy of four kinds of stimulations. The result indicated that the accuracy of the square's ring motion and Newton's ring were similar to each other, and were lower than that of the square flicker and the circular flicker. Double factor variance analyzed that there was a significant difference (p = 0.0000 ＜0.05) between motion mode and flicker mode, but no significant difference between square and circular mode (p=0.947 ＞0.05). In addition, there was no interaction between the two elements (mode and shape).

3.3 Subjective evaluation of different visual stimulations

As shown in Fig.6, the eight subjects' comfort scores of four visual stimulations. The order of the score from high to the end was the square's ring motion, the newton's ring motion, the circular flicker and the square flicker. The Square's ring seemed to have less negative effect on subjects' comfort than other three stimulations.

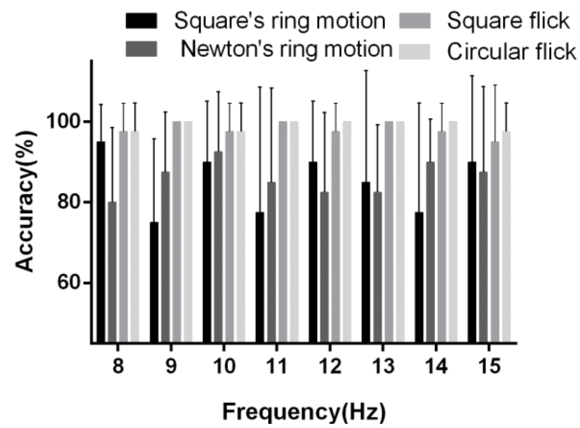

Figure 5. SSVEP recognition accuracy of different stimulations

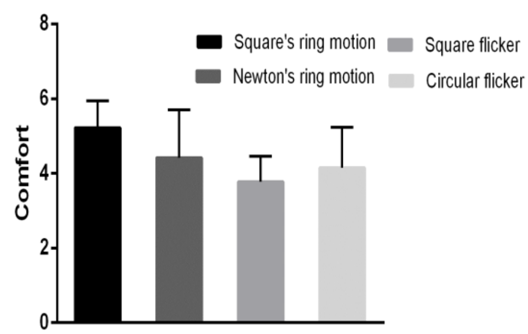

Figure 6. Subjective comfort evaluation of different stimulations.

4. DISCUSSION

In this paper, a steady-state motion visual evoked potential (SSMVEP) stimulation-the square's ring motion was proposed, and compared with the visual stimulation which are commonly used in BCI system (oscillatory Newton's ring, square flicker and circular flicker) both in objective and subjective aspects. From the frequency spectrum of electroencephalogram, the square's ring motion can effectively induce SSVEP as same as other three stimulations. Similar to Newton's ring, the amplitude of square's ring motion spectrum amplitude was smaller than that of the square flicker and the circular flicker.

According to result of CCA, the accuracy of SSVEP elicited by motion mode is lower than that of flicker mode. Although the average brightness of motion mode and flicker mode was the same, but the change of the former was more obvious than the latter. There is a positive correlation between the SSVEP response and the change of brightness[24].Therefore, the classification algorithm had lower recognition correct rate in the motion mode, compared with the flicker mode. In the meantime, the accuracy shows that equally with flicker mode, shape did not significantly affect motion mode accuracy[25]-[26]. What's more, we selected eight frequencies to compare effects of stimulation frequency on the efficiency of stimulation paradigms. The results demonstrated that the square's ring had higher accuracy at some frequencies (8, 12, 13, 15Hz) than the Newton's ring. The subjective comfort indicated that motion mode has higher comfort scores than the flicker mode

As a SSVEP-BCI stimulation paradigm, motion mode can effectively reduce the discomfort of the subjects because of its low contrast stimulus, but it also causes a certain loss of accuracy. If we can effectively control the erroneous operation of the BCI system, motion mode can be used as a visual stimulation for a long term. Admitting that the accuracy is not significantly improved by the square' ring motion in comparison with the Newton's ring, the comfort is slightly improved. Further studies will focus on the enhancing accuracy of the square's ring motion and improving its applicability in BCI system.

5. ACKNOWLEDGMENTS

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6. REFERENCES

[1] Wolpaw, J., Wolpaw, E.W. (eds.): Brain-Computer Interfaces: Principles and Practice. Oxford University Press (2012).

[2] Rebsamen, Brice, et al. "A Brain Controlled Wheelchair to Navigate in Familiar Environments." IEEE Transactions on Neural Systems & Rehabilitation Engineering 18.6(2010):590-598.

[3] Bell, C. J., et al. "Control of a humanoid robot by a noninvasive brain-computer interface in humans." Journal of Neural Engineering 5.2(2008):214.

[4] Cheng, M., et al. "Design and implementation of a brain-computer interface with high transfer rates." IEEE transactions on bio-medical engineering 49.10(2002):1181.

[5] Vialatte, F. B., et al. "Steady-state visually evoked potentials: focus on essential paradigms and future perspectives." Progress in Neurobiology 90.4(2010):418-438.

[6] Chalfie M. "The Journal of neuroscience: the official journal of the Society for Neuroscience." Society for Neuroscience (1985).

[7] Ng, Kian B., R. Cunnington, and A. P. Bradley. "Enhancing the classification accuracy of Steady-State Visual Evoked Potential-based Brain-Computer Interface using Component Synchrony Measure." International Joint Conference on Neural Networks IEEE, 2012:1-6.

[8] Sengelmann, Malte, A. K. Engel, and A. Maye. "Maximizing information transfer in SSVEP-based brain computer interfaces." IEEE Transactions on Biomedical Engineering PP.99 (2017):1-1.

[9] Cao, T., et al. "Flashing color on the performance of SSVEP-based brain-computer interfaces." International Conference of the IEEE Engineering in Medicine and Biology Society IEEE, 2012:1819-1822.

[10] Burkitt, G. R., et al. "Steady-state visual evoked potentials and travelling waves." Clinical Neurophysiology 111.2(2000):246-258.

[11] Li, Yun, et al. "Analysis of phase coding SSVEP based on canonical correlation analysis (CCA)." International Ieee/embs Conference on Neural Engineering IEEE, 2011:368-371.

[12] Owen, Falzon, C. Kenneth, and M. Joseph. "Complex-valued spatial filters for SSVEP-based BCIs with phase coding." IEEE Transactions on Biomedical Engineering 59.9(2012):2486-95.

[13] Chen, X., et al. "High-speed spelling with a noninvasive brain-computer interface." Proceedings of the National Academy of Sciences of the United States of America 112.44(2015):E6058.

[14] Punsawad, Yunyong, and Y. Wongsawat. "Motion visual stimulus for SSVEP-based BCI system." 2012(2012):3837-40.

[15] Xie, Jun, et al. "Steady-State Motion Visual Evoked Potentials Produced by Oscillating Newton's Rings: Implications for Brain-Computer Interfaces." Plos One 7.6(2012):e39707.

[16] Regan, David. "Human Perception of Objects." Optometry & Vision Science 78.11(2000):2324-2324.

[17] Manyakov, N. V., et al. "Sampled sinusoidal stimulation profile and multichannel fuzzy logic classification for monitor-based phase-coded SSVEP brain-computer interfacing." Journal of Neural Engineering 10.3(2013):747-754.

[18] Brainard, David H. "The Psychophysics Toolbox." Spatial Vision 10.4(1997):433.

[19] Bin, G, et al. "An online multi-channel SSVEP-based brain-computer interface using a canonical correlation analysis method." Journal of Neural Engineering 6.4(2009):046002.

[20] Xie, Jun, et al. "Recognition of SSMVEP signals based on multi-channel integrated GT2circ statistic method." International Conference on Ubiquitous Robots and Ambient Intelligence IEEE, (2017):169-173.

[21] Spüler, Martin, et al. "Spatial Filtering Based on Canonical Correlation Analysis for Classification of Evoked or Event-Related Potentials in EEG Data." IEEE Transactions on Neural Systems & Rehabilitation Engineering 22.6(2014):1097-1103.

[22] Bieger, J., and G. G. Molina. "Light Stimulation Properties to Influence Brain Activity: A Brain-Computer Interface Application." Philips Research (2010).

[23] Wu, Z., et al. "Stimulator selection in SSVEP-based BCI." Medical Engineering & Physics 30.8(2008):1079-1088.

[24] Zhang, X., et al. "Brain response to luminance-based and motion-based stimulation using inter-modulation frequencies." Plos One12.11 (2017):e0188073.

[25] Embrandiri, S. S, et al. "Effect of stimulation shapes on the Steady-State Visual-Evoked response." Biomedical Engineering Conference IEEE, (2015):1-2.

[26] Duszyk, A, et al. "Towards an optimization of stimulus parameters for brain-computer interfaces based on steady state visual evoked potentials." Plos One 9.11(2014):e112099.