

Is prefrontal cortex susceptible to odd visual stimuli?

by

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Abstract

We investigated the prefrontal cortex (PFC) on the following two issues by utilizing Near InfraRed HemoEncephaloGraphy (NIR HEG) measuring hemodynamic response.

First we examined the susceptibility of PFC to the odd visual stimuli. The subject observed the Motion Induced Blindness (MIB), which was odd enough to attract one's attention. We searched the locus where the hemodynamic response was detectable. We studied issues such that the response was transient or sustained and that the neurovascular coupling was oxygenated or deoxygenated. Preliminarily, different length of time sessions were examined. The attentional response was transient. The stimulus condition therefore was that the target figure disappeared by MIB effects for 500ms. The next 500ms had no MIB. The episode repeated 5 times. For the control condition, the similar stimulus was presented without MIB. The subject observed 5 second control, i.e. without MIB, episode then observed 5 second MIB episode. The 10 second episode composed a single session. A short break was taken at the disposal of the subject. He repeated the session. By trial and error, we searched the measurement site where HEG ratio difference was detectable. We obtained a couple of reliable data by the intensive search. At Brodmann 10, where the light source was on the sinus and the light detector was 3cm horizontally apart in the direction to the right hemisphere, the HEG ratio was high for MIB and low for the control conditions.

The second issue was olfaction. The investigation was rather preliminary stage, though, we succeeded salient response to citral aroma oil stimuli. Subjects conducted the maze game on computer screen using the computer mouse holding upside down. Following the narrow maze path with untrained motion response of the mouse was remarkably irritating. The subject tried two-minutes maze following game. At one minute passed, the aroma stimulus was administered in several seconds. We scanned the two-minutes session with NIRS (Near InfraRed Spectrography). We obtained the salient increase of hemodynamics.

Keywords: *Prefrontal cortex, Odd visual stimuli, Olfaction, NIRS*

1. Introduction

Purpose

We investigate the prefrontal cortex (PFC) on the following two issues utilizing Near InfraRed HemoEncephaloGraphy (NIR HEG) measuring hemodynamic response.

First, we investigate the susceptibility of PFC to the odd visual stimuli measuring hemodynamic response. The subject observed the Motion Induced Blindness (MIB), which was odd enough to attract one's attention. We searched the locus where the hemodynamic response was detectable. We thought much of issues such that whether the response was transient or sustained, and that whether the neurovascular coupling was oxygenated or deoxygenated.

Second, we investigate olfaction response of PFC with NIRS response. The olfactory stimulus might be less relevant to cognitive intelligence task. The relationship

to PFC is not well known. While subjects conducted the maze game on computer screen using the computer mouse holding upside down, the aroma stimulus was administered.

Hemodynamic response

We utilized the single channel Near InfraRed HemoEncephaloGraphy (NIR HEG). HEG Sensor was the apparatus with the Red (600nm) light and the InfraRed (850nm) light (Med/TECH). Software was Procomp5 (ThoughtTechnology Ltd.). HEG ratio was recorded. Functional NIRS (fNIRS) measures cerebral oxygenated and deoxygenated hemoglobin that monitor various types of brain activities. The detailed physical and theoretical principles of NIRS are given in [1]. A more specific physical characteristics such as the tissue absorption, the scattering, Lambert Law for light reflection, and the measurement techniques are explained in [2].

Difficulties on NIRS

Some of the major difficulties of NIRS are (1) Spatial resolutions: A single channel spectrography scans brain tissue which is about 3 cubic cm volume. The measurements are highly dependent on whether the tissue,

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especially just beneath the light source or the detector, includes much arterial, or vein. A couple of millimeters displacement of the apparatus gives quite different results. These difficulties are improved by the recent multi channel overlapping sensors techniques if low spatial resolutions are acceptable. (2) The HEG ratio is not necessarily equivalent to the quantities of blood flow. If needed, not the ratio but the absolute flow levels should be measured. (3) The blood flow itself changes spontaneously depending on the head tilt, due to gravity, or the respiratory conditions independent of the cognitive tasks. (4) The dark hair of the head impairs the measurement. Therefore generally the measurements are conducted on forehead. (5) Similar to fMRI spectroscopy NIRS responds almost real time. However the apparatus responds in milli seconds, the cerebral blood flow changes more slowly on some cognitive tasks typically in 20-40 seconds time period [3].

Conventional researches

Exercise bike: Naturally NIRS responds the blood flow change at active muscle. The maximal bike cycling gives decreasing oxy-haemoglobin [HbO_2], increasing deoxy-haemoglobin [HHb], and increasing the total haemoglobin [Hbtot]. Interestingly, during the exercise the brain blood flow also changes similarly at prefrontal cortex [4]. [4]

Brain Exercise Therapy: Intentional enhancement of cerebral blood is possible. A musical note or visual graphics are effective. These brain exercises improve some kind of mental patients [5].

Recent advances

Since Phineas Gage's traumatic accident [6], the prefrontal cortex (PFC) has been the main targets of cognitive task researches which include consciousness, personality, free will, planning, decision making, emotion controls, etc.. PFC is responsible for the executive control and works as a site of the working memory also. Recent researches on PFC with NIRS are summarised in [7]. An advancement on working memory issues is the development of executive function in children [8]. There are different issues including music [9], story-telling [11], problem solving [12], gambling [12]. The emotional visual stimuli are investigated [13]. The recent works [14][15] are particularly interesting in that they conducted the experiments on infants. Infants have usually less hair or their hair is so transparent. The [14] succeeded in scanning such as the occipitotemporal cortex including the superior temporal sulcus for facial movement perception. The [15] scanned the right temporal sulcus for the response of biological motions.

Olfaction

Among different literature, [16] contended that the right forehead responded the olfactory stimulation, but neither the temporal nor the occipital regions did. The

recent study gave rigorous investigation on "orbitofrontal cortex" (OFC) to odorant stimulation [17]. The sensor position was on the forehead of the subject (Figure 1 in the [17]) which was rather on the top of Brodmann 10, though, the response of OFC might be possible. They found the difference between the right and the left hemisphere. The detailed relationship between the hedonic stimuli and the cognitive activity at the prefrontal cortex (PFC) is not well known. The OFC is identified generally as the emotional control, the strategy reevaluation, etc.. The recent review on PFC issues is given in [18]. They critically examined the validity of the conventional claims. The olfaction stimuli might be related to some reward systems.

Attention Control at Prefrontal Cortex

Motion Induced Blindness (MIB) gives sudden unexpected disappearance of salient large visual component. MIB is generally surprising and naturally draw subject's attention. Conventionally visual attention has been investigated on the visual search task in which among many distractors the subject tries to locate the specified target. The task is relevant to the attention control. The classical review was given in [19]. The attention on MIB, in which the subject readily anticipate what figure element disappears and he/she well predict where it happens, differs from the conventional attention, in which some cues such as flash, color, or motion lead subjects to the locus of interests. Another literature [20] reviews the control of attention from the two networks of brain; the goal-directed (top-down) selection for stimuli, and the stimulus-driven (bottom-up) selection.

Odd visual stimuli

The "oddball" stimuli are the infrequent and irregular stimuli in the standard sequence. The stimuli evokes transient activity in prefrontal cortex. The PFC responses were explained in [21]. In a sense, Motion Induced Blindness (MIB) in our study was regular and frequent, and was well predicted by the subjects, though MIB is still odd enough and might activate PFC.

Protection of Human Subjects

The experiments were approved by the Institutional Review Board (Committee for the Protection of Human Subjects) of the author's University ([Approve No. 16057, 2016](#)).

2. Preliminary investigations

Before conducting MIB and olfaction NIRS scanning experiments, we have copied and reexamined the basic NIRS experiments to check the level of reliability of our technical environments.

Exercise bike

In [4] during high load exercise, muscle and brain

were scanned. It is interesting that even the brain hemodynamics changed. The author of [22] witnessed that her brain state was similar to that of [4] during the last 100m of 3000m run. She was an excellent athlete of long-distance running. Her training was to try to endure the cerebral anaemia, being close to lose consciousness, with strong mental will power and keep running faster along the last 100m. She tested the exercise bike. We failed to get the clear results. The load of exercise was not enough for her. Some of the results are presented in the appendix A1.

Mental training

NIRS can be used for mental training to improve brain blood flow. The bio-feedback technique is one thing, and the other is just to try to control the level of brain activities. The author of [23] conducted 10 minutes session of voluntary mental activation training, where the first 1 minute was to be kept empty minded and the next 1 minute, he tried to activate mental state as much as possible. After 2 month training, he succeeded in controlling the mental state. The main results were shown in the appendix A2.

Meditation

Generally, it is rather difficult for laypersons to keep oneself completely blank minded. The technique of the meditation would help control the blank mind. The author of [24] was good at Zen meditation. He tried the 10 minutes session where in the first 1 minute he meditated and the next 1 minute he read a book, then he repeated these scans 5 times. He obtained clear ups and downs of HEG ratio. The main result is shown in the appendix A3.

Arm wrestling

Good athletes can control his/her mental state, from resting state to intensive physical battle condition. The author of [25] was a strong arm wrestling athlete. He was confident to control his mind just synchronizing the start of the match. He made arm wrestling matches against his rival 5 times in 10 minutes. He obtained the sharp increase of HEG ratio at the starting moment of the matches. The result is shown in the appendix A4.

Evaluation of our preliminary investigations.

As explained above, our preliminary investigations were clear, natural, and fairly successful. We are well confident the conventional results and NIRS techniques. Therefore we set out the novel issues on cognitive tasks.

3. HEG response to MIB [26]

MIB stimulus

The Motion Induced Blindness (MIB) stimulus is shown in Fig.1, where colored rings are target figures which disappear and are invisible while MIB. The

surrounding outer and inner white rings are inducing figures, which expand or shrink for 500ms. Subjects experienced MIB while the inducers were moving. The next 500ms only the target figures were shown for adaptation to the next MIB. The one second episode of the adaptation and the MIB repeated 5 times.

In the last page of the article we prepared the flash player motion stimulus video. If the computer has “Flash Player” plug-in, the readers could appreciate the MIB. The demo site is also available [27].

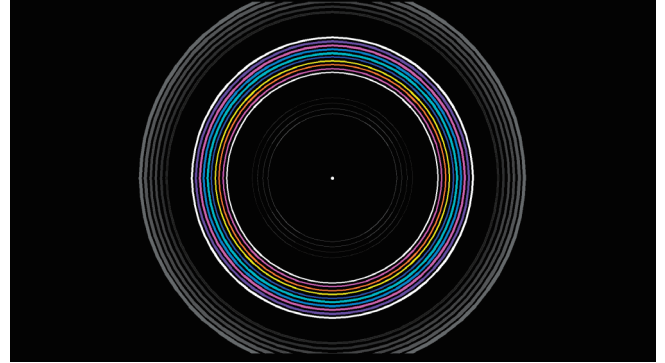


Fig. 1 MIB stimulus

In Fig. 2, the control condition stimulus is shown. At the onset moment of MIB the target rings were thickened in width which destroyed the adaptation and made MIB failed. The one second episode repeated 5 times. The 10 second episode composed a single session which was repeated indefinitely. Two visual stimuli which were with MIB and without MIB were almost equivalent. This equivalence was extremely important, where the difference between the two was the only cognitive difference. The difference on the visual stimuli does not activate anything in prefrontal cortex. It is also important for the subject to operate nothing during the sessions. The somatosensory signal or computer operation, such as key strokes or mouse operations, would activate an extra irrelevant change in prefrontal cortex, especially the noise were synchronized to the MIB and the control sessions.

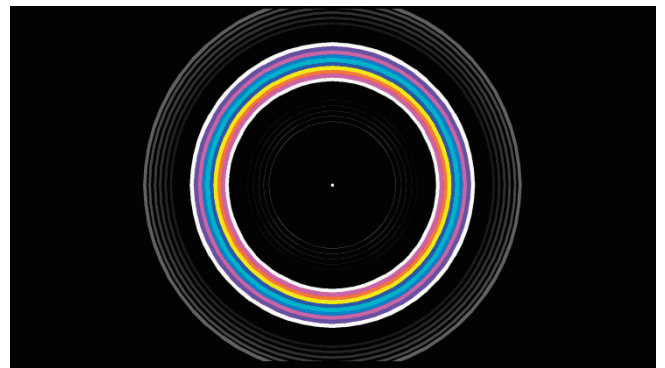


Fig.2 Control Non-MIB stimulus

Method

Apparatus: The stimulus was presented on the Iiyama ProLiteE2773HS 26 inch liquid crystal screen or Sony VAIO note VPCF238FJ/B with 16.4 inch screen in the dimly lit lab. Each experiment was conducted with a neighbouring computer controlling the NIRS. The experimental setting is shown in Fig.3.



Fig. 3 HEG response measurement setting.

Search for time sequence condition: Preliminarily, different length of time periods for measuring sessions were examined. We tried even 10 minute or more long sessions and found that the attentional response was rather transient and could not be sustained for a minute. For reliable HEG response, we needed one second or more time period. We therefore fixed the stimulus condition explained above.

Search for the locus: By trial and error, we searched the measurement site where HEG ratio difference depending on MIB was reliably detectable. The search was not easy. Typically, the response was a wave of ripples with 2 or 3 cycle/s, spontaneously drifting up and down. The gradual drifts might be the conventional hemodynamics but did not likely reflect MIB. Occasionally we found the large 1 cycle/second sinusoidal response which might be arterial pulsation but not to be MIB response either. The several intensive search tries over a month gave a couple of reliable data for the author SN. Once the good spot was found, the response was fairly stable where MIB on or off gave different HEG ratios. We could repeat the measurements at the spot and the statistically significant results were obtained.

Measurement session: After HEG sensor was stabilized, the subject observed 5 second control, i.e. without MIB, episode then observed 5 second MIB episode. The session was 10 second. A short break was taken at the disposal of the subject. The subject repeated the session.

Results

At upper center site of forehead roughly corresponding to Brodmann 10, where the light source was on the superior sagittal sinus and the light detector was 3cm horizontally apart to the right hemisphere, the significant HEG ratio difference was confirmed between the 5 seconds MIB period and the 5 seconds control condition. In Fig. 4, 10 sessions of raw data by the author SN are shown. It has large drift among the sessions comparing with the expected response to MIB in each session.

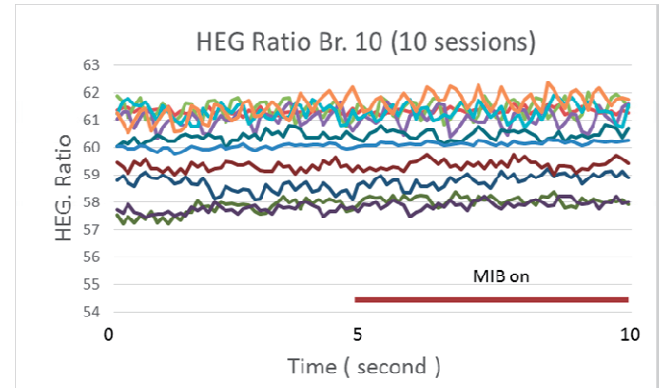


Fig. 4 HEG response of SN 10 sessions

In Fig. 5, the averaged data of Fig. 4 is shown. The first 5 second the stimulus was control and the last 5 second the stimulus was MIB. The last half has a higher HEG ratio.

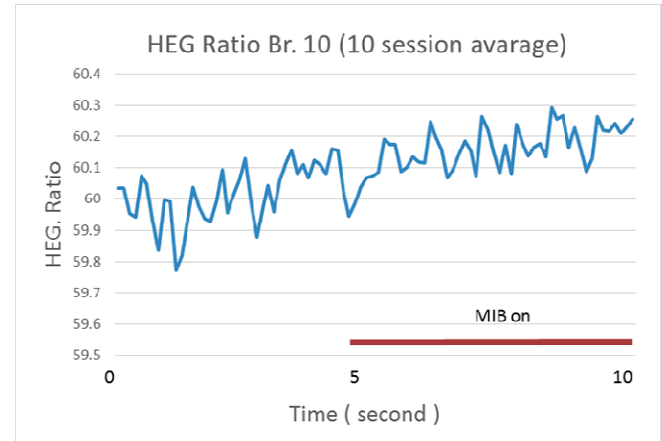


Fig. 5 SN 10 sessions average

In Fig. 6, the averages and the STDVs are shown. It was significant ($n=45$, $t=10.2$, $p<0.1\%$), where n is the number of data and t is the t value of the t -distributions. The statistics and the t -test need some explanatory notes. The average is obtained for the first 5 seconds and the last 5 seconds of the data shown in Fig. 5. They are naturally valid. The STDVs were obtained in the same way from the data in Fig.5, however, the data was already averaged from the 10 times data in Fig. 4. The true deviations might be 10 times larger. Moreover, if the

enormous drift among different sessions shown in Fig. 4 are taken into consideration, the true STDV would be much larger. If we could turn back to the cognitive task itself, however, the drift was simply the unnecessary noise which should be separated out. The STDV in each 5 second sessions might be the true deviation and be justifiable. The similar issue was raised for the $n=45$. In the same way, the number of data might be appreciated. The more critical issue was that the raw data of NIRS was the continuous data where sampling rate was 256/s. The data above was resampled into 8/s.

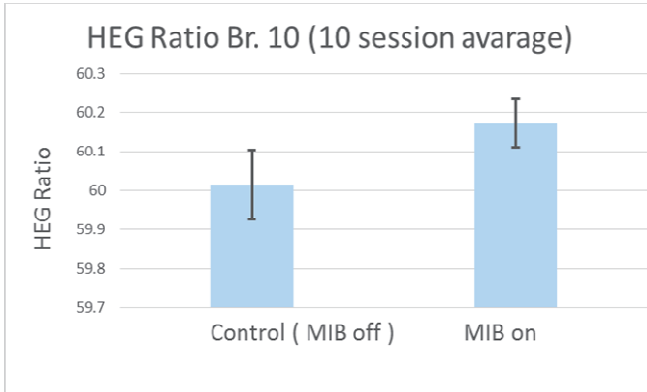


Fig. 6 SN 10 sessions statistics

In Fig. 7 and 8, the similar results obtained by the author EA are shown which are composed of 6 sessions. The difference of the two conditions is more salient than SNs.

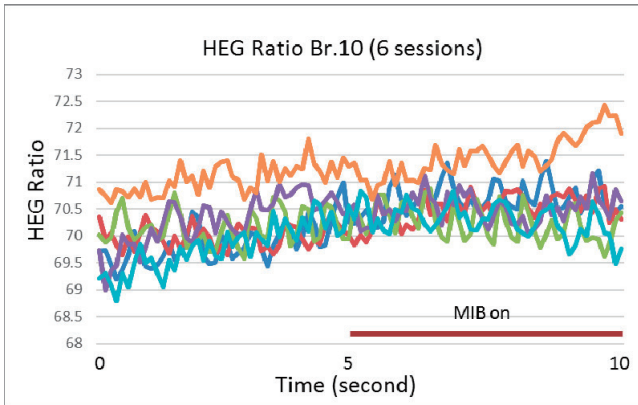


Fig. 7 EA 6 sessions

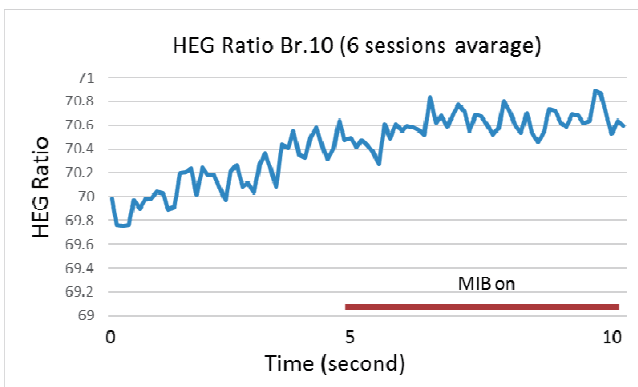


Fig. 8 EA 6 sessions average

In Fig. 9 and 10, the similar results of 5 sessions by the naïve subject HU who was graduate student of engineering department are shown. It was impossible for us to conduct an intensive search for the good locus of measurement. The data are obtained from an accidentally fixed at the center of HU's forehead. The MIB effect was not salient enough.

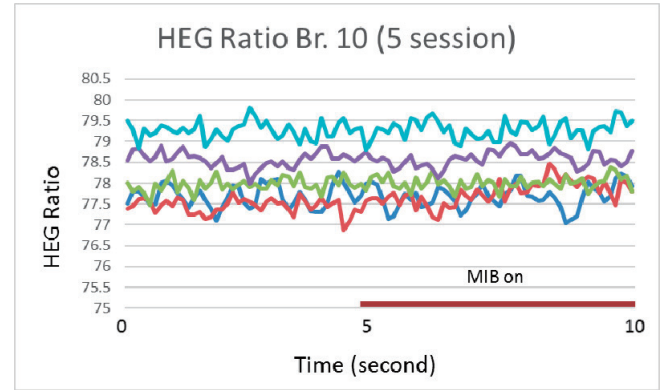


Fig. 9 HU (Naïve) 5 sessions

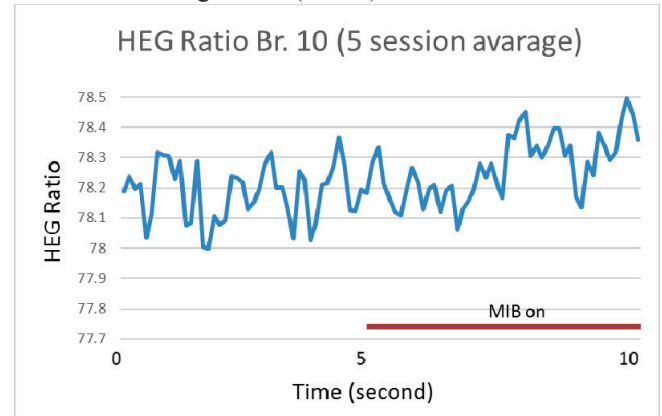


Fig. 10 HU (Naïve) 5 sessions average

Discussion

In Fig. 11, another result also by SN at right Brodmann 46 is presented, where the last half period had lower HEG ratio. If we accept neurovascular coupling hypothesis, the accidental condition that the light detector happened to be close to artery or either close to vein will determine HEG ratio increase or decrease.

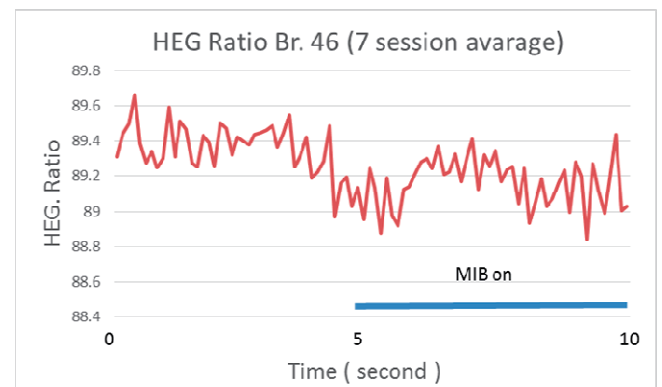


Fig. 11 SN 10 sessions average at Br. 46

Another one session data of EA is investigated the relationship of HEG Red, HEG InfraRed, and HEG Ratio, as shown in Fig. 12. We found that HEG Red increased, HEG infraRed decreased and therefore HEG Ratio increased. They were well reasonable.

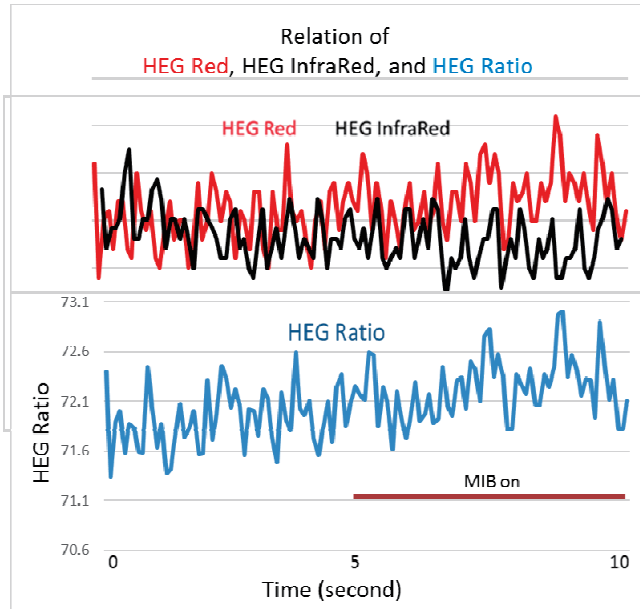


Fig. 12 EA one session
HEG Red, HEG InfraRed, and HEG Ratio

Conclusions

We found a few seconds transient hemodynamics responding to the odd visual stimuli. HEG ratio was either increase or decrease. The sensor position was highly sensitive. In the preliminary study we found that a slight displacement gave quite different responses.

4. HEG response to Aroma

One of the challenging issues was the prefrontal cortex response to olfaction stimuli which we knew less. The olfaction is primitive sense and might have close relationship to the reward system. A brain as higher social functions was reviewed in [28], in which the reward system was located at the Ventromedial Prefrontal Cortex (VMPFC), overlapping to the orbitofrontal cortex (OFC), and the ventral striatum (VS), which is deep inside the brain, close to amygdala. The reward functions, however, are the social rewards, which is quite different from hedonic odor sensory stimuli. Even as “Fork Science,” we could believe in “Aromatherapy,” which claims reduction of pain, anxiety, or energy enhancement. Is it even possible to improve the cognitive tasks in the prefrontal cortex?

Methods

Subjects conducted the maze game on computer screen

using the computer mouse holding upside down or in 90 degree rotated orientation. An example of the maze path figure is shown in Fig. 13. Different maze examples were utilized each time, to avoid the training effects.

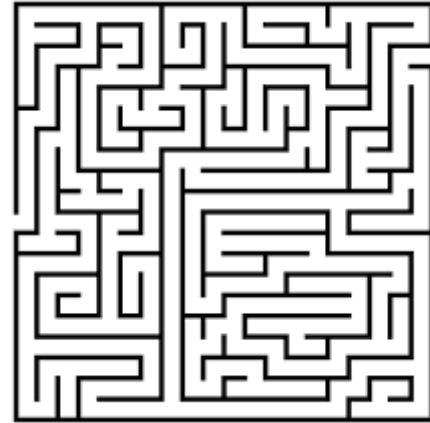


Fig. 13 Example of Maze
(<http://www.shivacharity.com/mazes.html>)

Following the narrow maze path with untrained motion response of the mouse was remarkably irritating. The maze task was nice for the subjects to keep one’s prefrontal cortex activity constant during the scan. After HEG sensor was stabilized, the subject conducted 1-minute maze game, then the citral flavor (*Lavandula angustifolia*) was administered for several seconds. The subject continued the maze game for another 1 minute. The session was 2 minutes. A short break was taken at the disposal of the subject. The subject repeated the session.

Results

The author EA conducted the several scans. One of the clear data is shown in Fig. 14. After the aroma administration, HEG ratio was increased. The increase continued for about 30 seconds and decreased the next 30 seconds. She obtained several similar data, however, they were less salient responses.

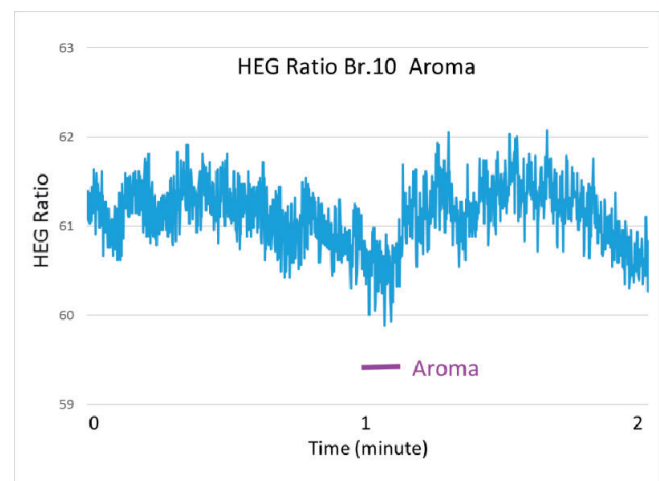


Fig. 14 HEG response to Aroma (EA)

We recruited the naïve subject TY (male faculty of physics department 24-year-old). He knew NIRS well, but perfectly naïve to psychology and cognitive tasks. Two scan episodes are shown in Fig. 15 where the computer mouse was kept upside down. The salient responses were obtained to aroma administration.

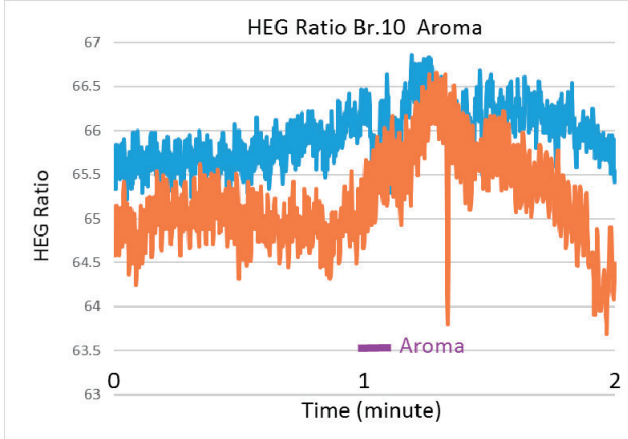


Fig. 15 HEG response to Aroma (TY Mouse upside down)

TY conducted the similar scan with the computer mouse was kept 90 degree rotated. The scan result is shown in Fig. 16. The HEG response was similar to Fig. 15. The mouse orientation conditions might be irrelevant to HEG response.

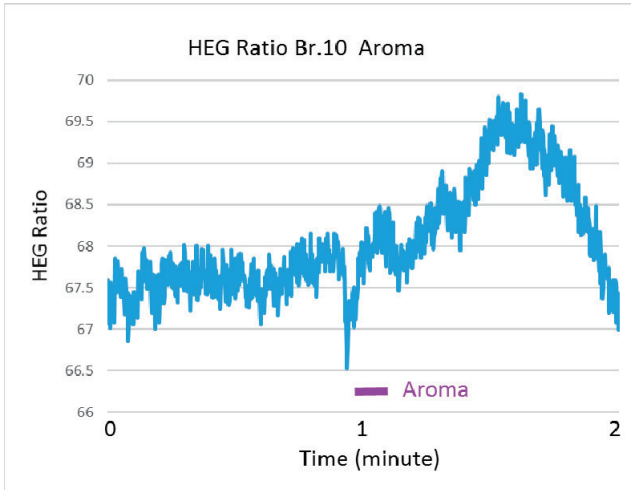


Fig. 16 HEG response to Aroma (TY Mouse 90 degree rotation)

Discussion

The gustation stimuli are also primitive and similar to olfaction. We tried “chocolate” stimuli instead of the aroma. The subject TY was administered a piece of chocolate at 1-minute moment. Two scan results are shown in Fig. 17. In the first scan (blue line), TY chewed the chocolate. The transient dip of HEG might be due to

the mastication. In the second scan, shown in orange color, we asked him just to lick his chocolate. We found that “chocolate” stimulus did not change the HEG response. If we believe in the reward system activation by sweet aroma stimuli, then the sweet gustatory stimuli should work in the same way, since chocolate was TY’s favorite sweet. We realized still again the complexity of the reward system at prefrontal cortex.

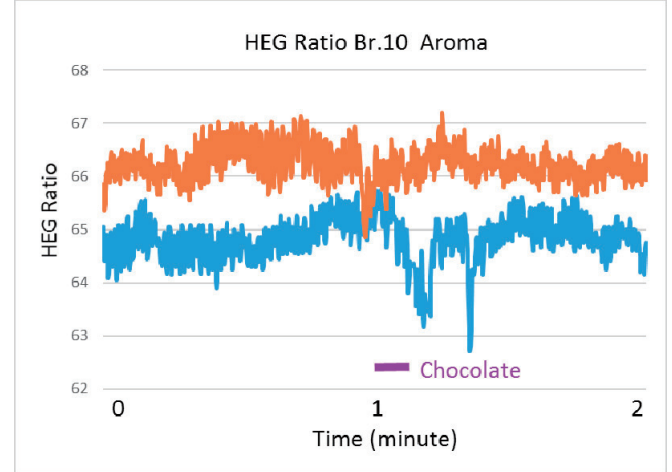


Fig. 17 HEG responses to chocolate

The maze game per se was a cognitive task. We liked to confirm the difference between HEG responses during the game and the rest. TY was scanned for the session in which only the first 1-minute was to be playing the game. The last 1-minute he took a rest. The result is shown in Fig. 18. We had a little higher response at rest, though, the response might not differ much.

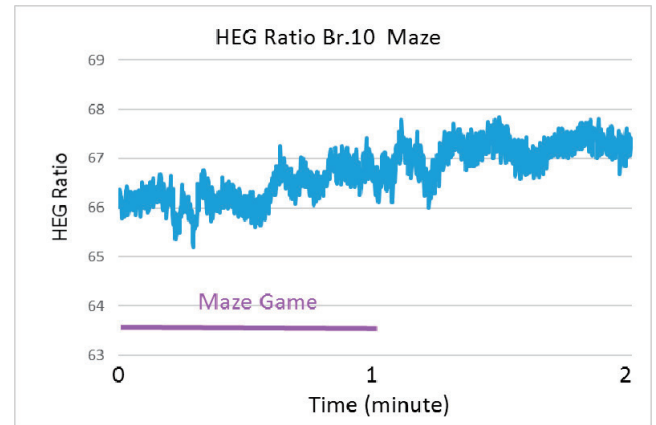


Fig. 18 HEG response to maze game and to rest (TY)

Conclusions

The investigation was at rather preliminary stage, though, we succeeded in obtaining the salient response to citral aroma oil stimuli. One of our findings was that while the aroma stimuli was transient in several seconds, the prefrontal cortex activity was raised for the next 30 seconds and declined in the following 30 seconds. The

time course change had sharp contrast to the results of [17] where the response time was a fraction of second. HEG responses of ours might be higher cognitive task's responses.

Appendix

A1. Exercise bike

The author AW (Female 22-year-old) of [22] tried the exercise bike as shown in Fig. A1-1.



Fig. A1-1 Exercise bike

AW conducted 3-minutes exercise bike and 2-minutes rest. HEG Ratio scan is presented in Fig. A1-2. The spikes are errors due to sensor displacements. It is likely that after rest period the HEG ratio increased.

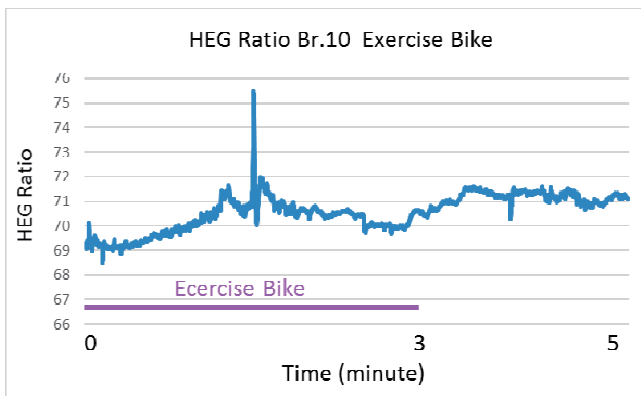


Fig. A1-2 HEG Ratio during exercise bike

A2. Mental training

The author MM (Male 22 year old) of [23] conducted 10 minutes session of voluntary mental activation training, where the first 1 minute was to keep empty minded and the next 1 minute, he tried to activate mental state as high as possible, then he repeated the session. In Fig. A2-1, the early try (1 month) result was shown. No clear

relationship was detectable to 2 minutes repetition of high and lows. After 2 month training, he succeeded in controlling the mental state. The results are shown in Fig. A2-2.

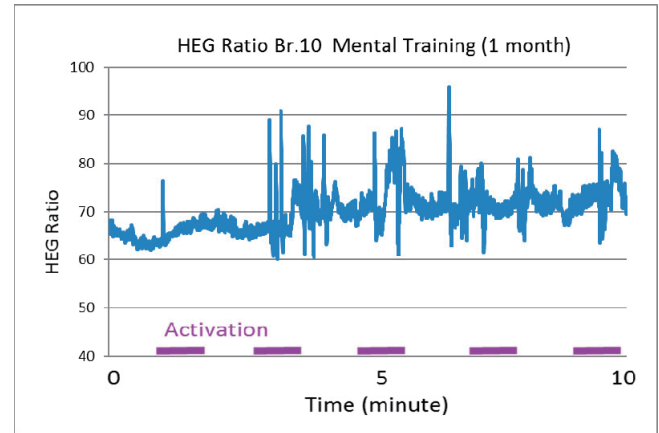


Fig. A2-1 First voluntary mental training.

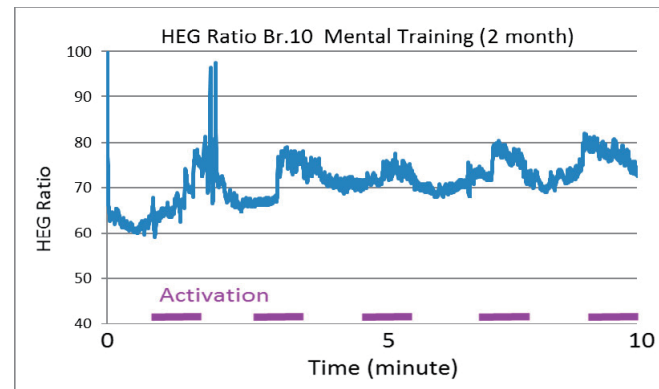


Fig. A2-2 Two month later mental control available.

A3. Meditation

The author KM (Male 23-year-old) of [24] tried the 10-minutes session where in the first 1 minute he meditated and the next 1 minute he read a book, then he repeated these 5 times. He obtained clear ups and downs of HEG ratio. The main result is shown in Fig A3-1.

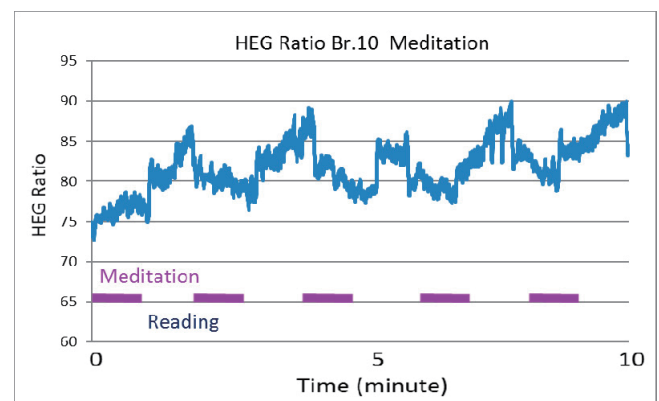


Fig. A3-1 Meditation and Book reading

A4. Arm wrestling

The author TM (Male 22 year old) of [25] made arm wrestling matches against his rival. The arm wrestling match is shown in Fig. A4-1.



Fig. A4-1 Arm wrestling by the author TM.

The battle started and continued 1 minute. The following 1 minute was resting period. The session was repeated 5 times. He obtained the sharp increase of HEG ratio at the starting moment of the matches. The result is shown in Fig. A4-2.

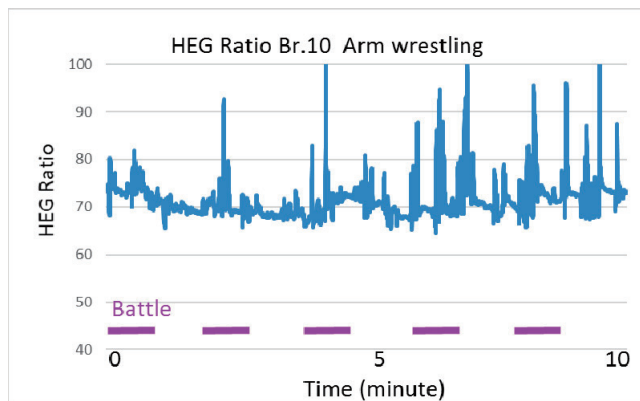


Fig. A4-2 Five matches in 10 minutes

Acknowledgements

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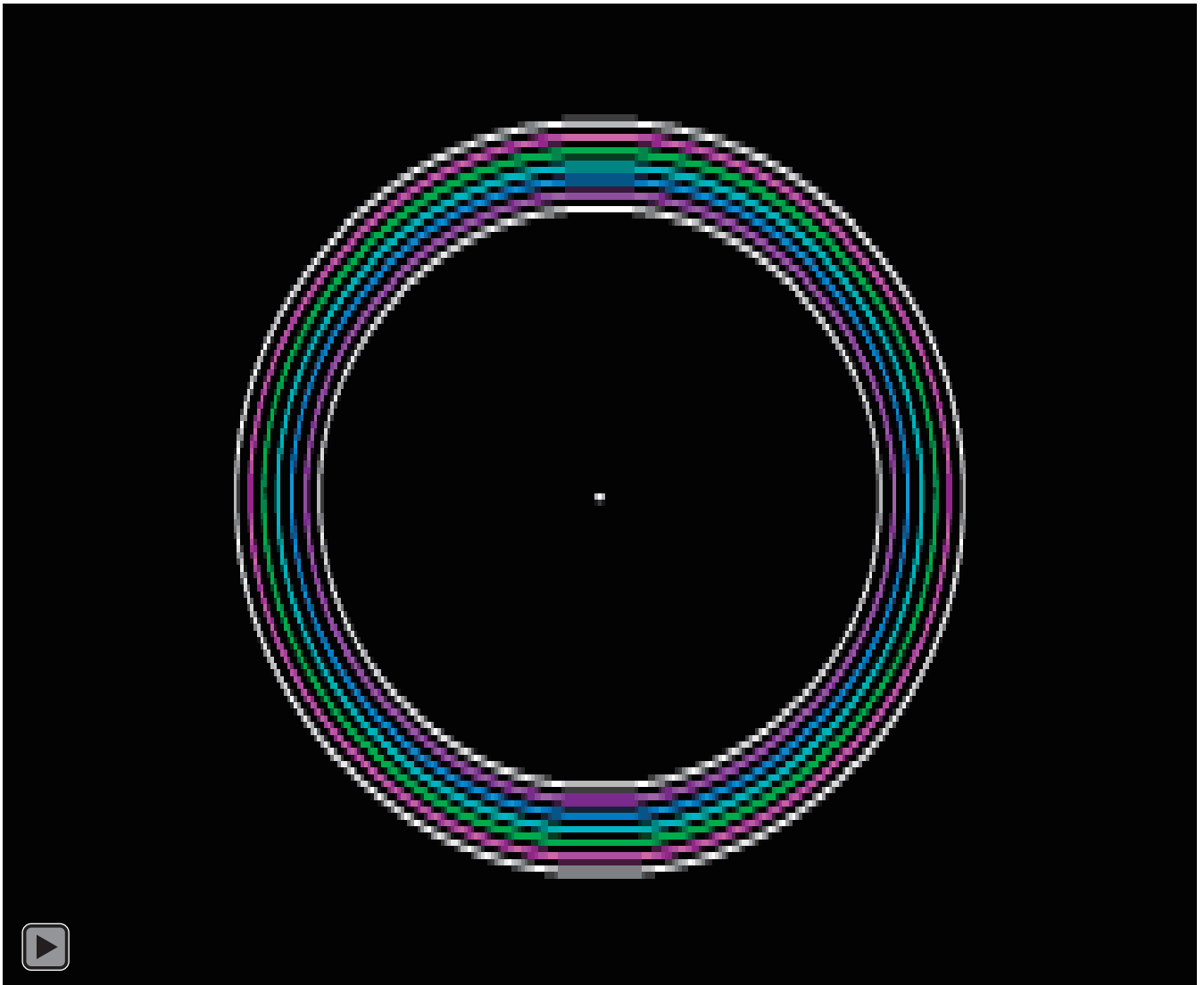
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Appendix MIB Demo

Click the image and fixate the center.

Enlarge the page and observe MIB in a large screen; 17 inch or more is appreciated. Small screen display does not work well.



How to install Flash Player; (Authors will not be responsible for any problem about the installation.)

For Windows 64-bit, <https://get.adobe.com/flashplayer/?loc=jp> or [Install .exe](#)

“install_flash_player_ax.exe” is ActiveX for Microsoft IE. “install_flash_player.exe” is Plug-in for others, or pdf.

The operation has been tested on;

Windows Server 2008 R2 Standard Service Pack1, Updated Nov 5, 2016, Intel® Core™ i7 870.

Windows 10Pro 1607, Updated Nov 5, 2016, Intel® Core™ i7 860.

Microsoft Office Professional 2016, Adobe Acrobat Reader DC, Adobe Flash Player 23.