BRAIN RESPONSE TO DIFFERENT MESSAGE CONTENT OF PICTORIAL HEALTH WARNINGS FROM TOBACCO PACKAGES: COMPARISON BETWEEN SMOKERS AND NON-SMOKERS USING fMRI

By

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TINDAK BALAS TERHADAP KANDUNGAN MESEJ DALAM AMARAN KESIHATAN BERGAMBAR YANG BERBEZA DARIPADA PAKET TEMBAKAU: PERBANDINGAN ANTARA PEROKOK DAN BUKAN PEROKOK MENGGUNAKAN fMRI

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LIST OF ABBREVIATIONS

AAL	Automated anatomical labeling
AG	Angular gyrus
BOLD	Blood-oxygenated-level-dependent
COS	Cosmetic Consequences
DD	Disease & Death
EN	Endanger Others
FCTC	Framework Convention on Tobacco Control
FFX	Fixed-effect analysis
fMRI	functional magnetic resonance imaging
FOV	Field of view
FTND	Fagerstrom Test of Nicotine Dependence
GHWLs	Graphical health warnings labels
GLM	General Linear Model
GMV	Gray matter volume
HIP	Human Information Processing
IAPS	International Affective Picture System
IFG	Inferior frontal gyrus
IFGo	Inferior frontal gyrus pars opercularis
IFGt	Inferior frontal gyrus pars triangularis
IOG	Inferior Occipital gyrus
IPG	Inferior parietal gyrus
ITG	Inferior temporal gyrus
LG	Lingual gyrus
Medial FG	Medial frontal gyrus

Medial TG	Medial temporal gyrus
MFG	Middle frontal gyrus
MNI	Montreal Neurological Institute
MOG	Middle occipital gyrus
mPFC	Medial prefrontal cortex
MTG	Middle temporal gyrus
NA	Natural
NE	Negative Lifestyle
PCC	Posterior cingulate cortex
PG	Precentral gyrus
PHWLs	Pictorial health warnings labels
PSAs	Public service announcements
PSC	Percent signal change
ROI	Region of interest
SAM	Self-Assessment Manikin
SEATCA	Southeast Asia Tobacco Control Alliance
SFG	Superior frontal gyrus
SMA	Supplementary motor area
SMG	Supramarginal gyrus
SOG	Superior occipital gyrus
SPG	Superior Parietal gyrus
SPM	Statistical Parametric Mapping Software
STG	Superior temporal gyrus
TE	Echo time
TR	Time repetition

VAC	Visual association cortex
vmPFC	Ventromedial PFC
WHO	World Health Organization

ABSTRAK

Keberkesanan label amaran kesihatan bergambar (PHWLs) daripada paket tembakau dalam mengawal penggunaan tembakau masih menjadi kontroversi. Sehingga ini, masih terdapat kekurangan dalam kajian pengimejan resonans magnet kefungsian (fMRI) pada kandungan mesej label melalui penekanan nilai yang berbeza. Nilai-nilai ini merupakan komponen yang penting dalam membuat keputusan yang berkaitan dengan gejala merokok. Dalam kajian ini, pengaktifan otak untuk perokok dan bukan perokok dalam kalangan kumpulan umur yang muda sebagai tindak balas terhadap tema PHWLs (Akibat Kosmetik "COS", Membahayakan Orang Lain "EN", Gaya Hidup Negatif "NE" serta Penyakit dan Kematian "DD" telah dikaji. Untuk memastikan keberkesanan label dalam membangkitkan keadaan afektif untuk status yang dikehendaki, soal selidik tentang penilaian normatif atas talian telah dilengkapkan oleh 100 orang responden untuk mendapatkan nilai valens dan rangsangan bagi setiap tema PHWLs. Pengukuran berulang ANOVA sehala ($p < 0.05$) membuktikan semua tema PHWLs menunjukkan penilaian yang signifikan dalam memberi gambaran yang tidak menyenang dan merangsang berbanding dengan imej kawalan (Semulajadi "NA"), kecuali imej-imej NE dalam dimensi rangsangan. Berikutnya, 10 perokok dan 10 bukan perokok berbaring dalam mesin MRI untuk melihat satu siri imej yang dikategorikan kepada tema yang berbeza. Tindak balas kebergantungan kepada aras oksigen darah sewaktu tugas fMRI telah direkodkan untuk memeriksa pengaktifan otak terhadap tema PHWLs antara kumpulan-kumpulan dari segi tahap spatial. Seperti yang ditunjukkan daripada kesan-rawak analisis (2 x 5 ANOVA campur) dengan $P_{\text{uncorrected}} < 0.001$, kawasan otak yang berkaitan dengan fungsi kognitif dan afektif telah diaktifkan oleh perokok dan bukan perokok ketika melihat imej-imej PHWLs, dengan atau tanpa mengambil kira status merokok. Girus temporal tengah kiri (berkaitan dengan integrasi maklumat) telah diaktifkan ketika kedua-dua kumpulan sedang melihat imej-imej daripada semua tema. Tanpa mengira status merokok, pengaktifan yang berkaitan dengan penglihatan

(i.e. girus oksipital inferior (IOG), girus temporal inferior) telah dibangkitkan oleh imej-imej tema PHWLs dengan tahap yang agak sama manakala pengaktifan yang berkaitan dengan limbic (i.e. amygdala kanan) telah dibangkitkan oleh imej-imej DD berbanding dengan imej-imej NA. Beberapa penemuan baru telah dicatatkan. Pertama, pengaktifan otak yang lebih besar telah diperhatikan di kawasan-kawasan yang berkaitan dengan pengesanan rangsangan yang penting (i.e. girus parietal inferior kanan, girus frontal tengah (MFG) kiri) terhadap imej-imej COS berbanding dengan imej-imej EN dalam kalangan perokok, persepsi sosial (i.e. girus presentral (PG) kiri, IOG kiri) terhadap imej-imej EN berbanding dengan imej-imej NA dalam kedua-dua kumpulan atau tanpa mengira status merokok, kefahaman metafora (i.e. girus frontal inferior (IFG) kiri) terhadap imej-imej NE berbanding dengan imej-imej EN dalam kalangan perokok dan pemprosesan emosi yang kuat (i.e. amygdala kanan) terhadap imej-imej DD berbanding dengan imej-imej NA tanpa mengira status merokok. Kedua, pengaktifan yang berkaitan dengan peraturan emosi (PG kiri) sebagai tindak balas terhadap imej-imej EN dan DD berbanding dengan imej-imej NA tidak muncul dalam kalangan perokok sahaja. Ketiga, pengaktifan yang berkaitan dengan pengesanan rangsangan yang penting dan pemprosesan penumpuan perhatian sebagai tindak balas terhadap imej-imej COS berbanding dengan imej-imej EN telah diperhatikan dalam kalangan perokok sahaja. Keempat, pengaktifan frontal medial yang berkaitan dengan pemprosesan kendiri telah dipamerkan lebik banyak oleh perokok kepada imej-imej COS dan DD berbanding dengan tema lain, dengan atau tanpa pertimbangan status merokok. Walau bagaimanapun, pengaktifan ini adalah lebih responsif kepada imej-imej COS daripada DD bagi perokok. Kelima, perubahan isyarat (PSC) yang lebih besar dan ketara dalam IFG kanan yang berkaitan dengan pemprosen kawalan yang melarang telah diperhatikan ketika perokok dan bukan perokok sedang melihat imej-imej NE berbanding dengan imej-imej NA dan COS masing-masing seperti yang ditunjukkan daripada bergantung ujian-t dan ujian *Wilcoxon-Signed Rank* ($p < 0.05$) dalam pemeriksaan pengaktifan otak dari

segi kekuatan. Berdasarkan kepada penemuan-penemuan baru ini, beberapa kesimpulan dapat dilakukan. Pertama, ciri-ciri utama setiap tema PHWLs mungkin dapat digambarkan seperti berikut: ciri yang menonjol dalam imej-imej COS, aspek sosial merokok dalam imej-imej EN, sifat simbolik dalam imej-imej NE dan ciri emosi yang menonjol dalam imej-imej DD. Kedua, disensitisasi terhadap risiko merokok yang umum diketahui (isu-isu kesihatan dan perokok pasif) mungkin telah berlaku dalam kalangan perokok sahaja, menekankan keperluan untuk menangani risiko merokok tersebut dengan cara yang baru. Ketiga, perokok muda mungkin mempunyai lebih banyak kerisauan tentang kesan merokok kepada sifat-sifat fizikal daripada kesihatan mereka. Perkaitan kandungan mesej ini disokong dengan lebih banyak perhatian diberikan oleh perokok kepada imej-imej COS berbanding dengan EN. Penemuan-penemuan ini mencadangkan bahawa COS boleh menjadi mesej yang ideal untuk disampaikan kepada perokok muda dengan berkesan. Akhirnya, kekurangan imej-imej NE dalam mencapai komunikasi mesej yang berkesan menekankan keperluan untuk memperbaiki rekaan jenis kandungan mesej ini.

Kata kunci: label amaran kesihatan bergambar, kandungan mesej/tema, fMRI

ABSTRACT

The effectiveness of the Pictorial Health Warnings Labels (PHWLs) from the tobacco packages in tobacco control remains controversial. To date, there is lacking of functional magnetic resonance imaging (fMRI) studies on the message content of the labels with different value emphasis. These values are the crucial components in the cigarette related decision making.

In this study, the brain activation of the smokers and non-smokers from the young age group in response to PHWLs themes (Cosmetic Consequences "COS", Endanger Others "EN", Negative Lifestyle "NE" as well as Disease and Death "DD" were investigated. To ensure the adequacy of the labels in evoking desired affective states, an online normative rating questionnaire was completed by 100 respondents to obtain valence and arousal values for each PHWLs themes. One-way repeated measures ANOVA ($p < 0.05$) revealed that all PHWLs themes were rated significantly more unpleasant and arousing than the control (Natural "NA") images, except NE on the arousal dimension. Followed by that, 10 smokers and 10 non-smokers lied inside an MRI machine to view a series of images that categorized into different themes. Blood-oxygenated-level-dependent responses during the fMRI task were captured to examine the brain activation in response to the PHWLs themes between the groups in terms of spatial extent. As revealed from the random-effects analyses (2 x 5 mixed ANOVA) with $P_{\text{uncorrected}} < 0.001$, a widespread of regions that associated with cognitive and affective functioning were recruited by smokers and non-smokers during the PHWLs viewing task, with or without taking the smoking status into consideration. Left middle temporal gyrus (associated with information integration) was activated when both groups viewing images of all themes. Regardless of the smoking status, visual related activation (i.e. inferior occipital gyrus (IOG), inferior temporal gyrus) were evoked by images of PHWLs themes with relatively similar extent while limbic related activation (i.e. right amygdala) were evoked by DD images in relative to NA images. Several new findings were noted. Firstly, greater brain activation was

observed in regions associated salient stimulus detection (i.e. right inferior parietal gyrus, left middle frontal gyrus (MFG)) to COS images compared to EN images in smokers, social perception (i.e. left precentral gyrus (PG), left IOG) to EN images compared to NA images in both groups or regardless of smoking status, metaphor comprehension (i.e. left inferior frontal gyrus (IFG)) to NE images compared to EN images in smokers and strong emotional processing (i.e. right amygdala) to DD images compared to NA images irrespective of smoking status. Secondly, activation associated with emotional regulation (left PG) in response to EN and DD images compared to NA images was absent in smokers only. Thirdly, activation associated with salient stimulus detection and attentional processing in response to COS images compared to EN images was observed in smokers only. Fourthly, medial frontal activation that associated with self-related processing were exhibited by smokers more to COS and DD images in relative to other themes, with or without the consideration of smoking status. However, such activation was more responsive to COS than DD images for smokers. Fifthly, significant greater percent signal change (PSC) in the right IFG that associated with inhibitory control processing was observed when smokers and non-smokers viewing the NE images in relative to NA and COS images respectively as revealed from the dependent t-test and Wilcoxon-Signed Rank tests ($p < 0.05$) in the examination of brain activation in terms of intensity. Based on these new findings, several conclusions were made. Firstly, the main characteristics of each PHWLs theme might be reflected as the following: the salient feature of the COS images, the social aspect of smoking of the EN images, the symbolic nature of the NE images and the emotionally salient feature of the DD images. Secondly, desensitization towards the commonly known smoking risk (health issues and passive smoker) might have taken place in smokers only, underscoring the needs to address these smoking risk in a novel way. Thirdly, young smokers might have more concern about the smoking effect on their physical attributes than their health. The relevance of this message content type is supported with more attention given

by the smokers only to COS than EN images. These findings suggest that COS could be the ideal messages to reach to the young smokers effectively. Lastly, the inadequacy of the NE images in achieving effective message communication underscores the needs to refine the design of this message content type.

Keywords: pictorial health warning labels, message content/theme, fMRI

CHAPTER 1: INTRODUCTION

1.1 Introduction on Smoking

Tobacco consumption has been one of the long-standing global health issues due to its widespread consequences in the aspects of health, economics and social. According to the WHO (World Health organization) Report on the Global Tobacco Epidemic 2017, more than seven million people were killed due to the tobacco use each year. As reported in the tobacco report under Southeast Asia Tobacco Control Alliance (Tan & Dorotheo, 2016), the smoking prevalence is high in South East Asia region, particularly in the developing countries with low- and middle-income status like Indoneisa, Lao PDR, Vietnam, Thailand and Malaysia compare to the developed countries like Canada and Australia. Such difference could be attributed to the long history of tobacco control in the high-income countries (Anshari, 2017). In term of socio-demographic, high smoking prevalence is often found among the males, young adults and those with lower socioeconomic status (Tan & Dorotheo, 2016). Smoking behavior among females is more stigmatized than among the males due to the social norm (Castaldelli-Maia, Ventriglio & Bhugra, 2015). The development of smoking behaviour is usually initiated before the age of 16 or 18 or perhaps younger due to their curiosity and peer pressure (FCAP, 2008; Tan & Dorotheo, 2016). Once this unhealthy behavior has been developed, it might persist and progress into adulthood (Tan & Dorotheo, 2016). A complete abstinence of smoking is found to be hard. High rate of quit attempt and relapse are the most-often cited issues in the literature (i.e. Janes, Gilman, Radoman, Pachas, Fava & Evins, 2017), reflecting the difficulty in the complete smoking cessation.

There are numerous reasons for the difficulty in quitting smoking, for instance, life stressors (FCAP, 2008). However, the ultimate reason for the smoking maintenance is often traced to the heavy influence of nicotine in human body and brain which in turn affect the behaviour (Castadelli-Maia et al., 2015). Nicotine can be used as an analgesic due to its soothing properties that is very useful for relieving pain and stress (Ditre, Heckman, Zale, Kosiba & Maisto, 2016). Besides, it has been found to increase the cognitive performance such as attention and working memory (Jasinka, Zorick, Brody & Stein, 2014). However, abusive use of nicotine can be dangerous as the high nicotine level in the human body can have the adverse impact on the human functioning. For instance, high nicotine usage has been found to increase the impulsivity and degrade the cognitive performance (Jasinka et al., 2014).

With respective to this global problem, many initiatives have been carried out as evidenced in the establishment of the Framework Convention on Tobacco Control (FCTC) under WHO (Tan & Dorotheo, 2016). Under this framework, a guideline is provided to promote and facilitate the implementation of the pictorial health warnings labels (PHWLs). PHWLs are the labels used to disseminate the smoking associated risks by adopting the aversive graphical content with the strong negative emotional appeal such as fear and disgust (Romer et al., 2013). Consistent with the research evidences, fear appeal is found to be more effective to generate the desired behavioural (i.e. Noar et al., 2016) and cognitive outcomes (i.e. Klein et al., 2017). In addition, graphical use in PHWLs has been found to be more effective than text-only warnings (i.e. Andrew et al., 2016) since images are easier to be comprehended. In spite of these important elements in the PHWLs design, what really determines the efficacy of the labels is suggested to be the content (Hammond & Reid, 2012). The content of the PHWLs must be self-relevant in order to facilitate the internalization of the smoking-related messages.

1.2 Introduction on fMRI

Psychological methods such as self-report measures have been the ubiquitous method to study the impact of PHWLs in the aspect of cognition, affect and behaviour. For instance, perceived effectiveness (Leschner et al., 2011; Farelley et al., 2012; Shen, 2010), which might not capture the mental processes underlie a health-related decision well. This kind of measure does not inform us specifically what are the cognitive and affective processes that have taken place in order to reach to a desired decision when processing the PHWLs, underscoring the needs to explore the underlying the brain mechanism of processing the health information that conveyed by the PHWLs. In addition, such introspection method could challenge the validity of the findings as it allows the possibility of deception. Earlier studies have found that there was an inverse relationship between the activation in the nucleus accumbens (critical in reward circuit) and the reported subjective reaction to the anti-tobacco images (Neuroscience Limited, as cited in Calvert et al., 2010). This observation supported one of the caveats in self-report measure which is deception. Participants can lie about their desire to quit but their brains reveal another story. The deception during experimental task is usually motivated by the social desirability factor to protect their self-image from degradation, especially when the stigmatized behaviour like smoking is involved (Riddle Jr. et al., 2016). Besides, we could be struggling to identify our internal states accurately sometimes. The struggle could be even more prominent among the smoker population (Riddle Jr. et al., 2016) due to the influence of nicotine in their brain.

To overcome these limitations, neuroimaging tools like fMRI can be adopted to reveal the brain mechanism of the studied populations during the task as this imaging tool allows us to reveal the cognitive and affective processes during the message processing as inferred from the brain activity. The measurement of the brain activity during the task is dependent on the fMRI signal generation based on the physiological principle (refer to Figure 1.1). According to Astofli et al. (2004) and Gore (2003), human brain is comprised of many regions which made up of neurons. These neuronal cells need to consume oxygen from the blood vessels for metabolism in order to get sufficient energy to work (A). During the task performance, there will be an increase in the blood flow that carries oxygen with its transporter, hemoglobin (oxygen + hemoglobin → oxyhemoglobin) to the task-associated regions, indicating the presence of the metabolic activity in those regions to generate sufficient energy for processing the information related to task (B). A surplus of blood with oxyhemoglobin will be accumulated around the task-associated regions as a gradient pressure must be produced for the oxygen to be transported into the mitochondria of the neurons in a down gradient concentration for metabolism. Due to the surplus of oxyhemoglobin, an increased ratio between the oxyhemoglobin and deoxyhemoglobin (hemoglobin without oxygen) will take place. By taking advantage of the different magnetic properties of the oxyhemoglobin and deoxyhemoglobin, the fMRI signal or blood-oxygenated-dependent-level (BOLD) signal can be generated and reflected as the activation on the brain map for us to identify the regions activated in response to the task.

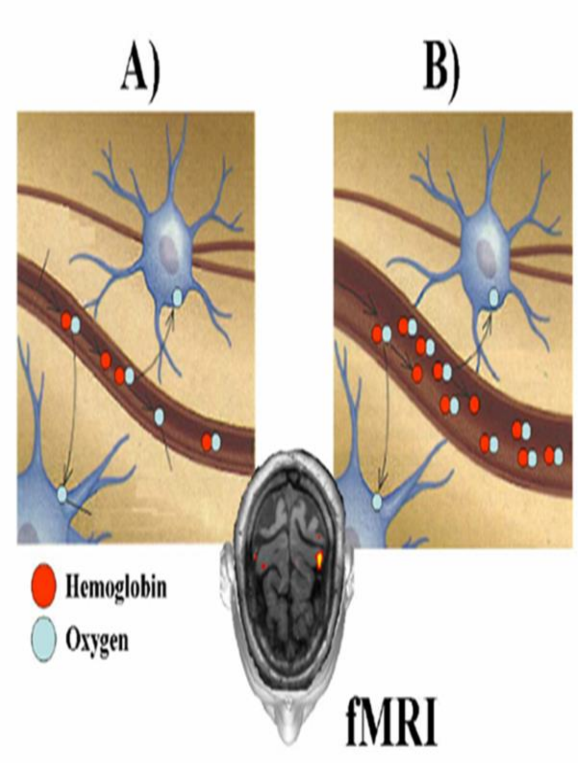

Figure 1.1: Physiological principle in the fMRI signal generation (Astofli et al., 2004).

(A) Oxygen is transported from the blood vessels into the surrounding neurons for metabolism.

(B) Increased oxygen consumption by the surrounding neurons in the task-associated regions for metabolism. This in turn resulting in difference between the amount of oxyhemoglobin and deoxyhemoglobin. Such contrast leads to the generation of the activation in the brain map.

fMRI is receiving more attention in the research investigation on psychological phenomena today due to its non-invasive nature as well as its relatively high spatial and temporal resolution compare to other neuroimaging tools (Gore, 2003). Unlike electroencephalography (EEG) which studies the cortical activity, fMRI allows deeper brain regions to be studied (Gore, 2003). The topic of interest of this study is best studied with the use of fMRI since critical regions like amygdala and hippocampus are embedded deep into the medial temporal lobe.

1.3 Introduction of Pictorial Health Warnings Labels Stimuli

Amongst the measures included in the FCTC guideline, PHWLs is the most cost-effective channel to communicate the health risks of smoking to the public (Tan, 2016) to promote better informed health-related decision making. Previous psychological findings have provided some evidences regarding the effectiveness of the PHWLs on emotional, cognition as well as behavioural outcome variables. For instance, PHWLs were found to be recalled better (i.e. Klein et al., 2017), more emotionally arousing (i.e. Andrew et al., 2016) as well as associated with more phone calls to the smoking quit line (i.e. Noar et al., 2016). On the other hand, corroborating neural evidence from the fMRI studies have observed several brain processes during the PHWLs processing, including the visual processing, emotional processing, learning and memory as well as self-related processing (i.e. Green et al.). These processes are important in concert to achieve effective message communication.

The purpose of the labels is to deliver a message about the danger of smoking in attempt to discourage people from smoking. Therefore, the content of the PHWLs must be self-relevant to facilitate the internalization of the message and henceforth, to encourage smoking quit attempt. The self-relevance of the message in facilitating the persuasiveness of the message has gained support from both the neuroeconomics studies, a discipline that study human decision making using neuroscience tool as well as the findings on anti-smoking related stimuli (activation in the medial prefrontal cortex, mPFC that associated with self-related and value-related processing) (i.e. Cooper, Tompson, O’Donnell & Falk, 2015).

In the present study, PHWLs stimuli were classified into four themes that reflect the human value system:

(a) Cosmetic Consequences (COS): messages that emphasize the unattractive side effects on the physical attributes due to smoking. These messages reflects the aesthetic value on one's physical attributes.

(b) Endanger Others (EN): messages that emphasize the health-illness of family and friends due to secondhand smoke. These messages reflect the valuation in the important loved ones.

(c) Negative Lifestyle (NE): messages that portray the loser lifestyle of smoker, implying smoking can degrade the life quality. These messages reflect the valuation in one's life quality.

(d) Disease and Death (DD): messages that emphasize the adverse health outcomes such as lung cancer and mortality. These messages reflect the value on one's health.

1.4 Hypotheses

In the present study, the PHWLs stimuli were collected from different countries and classified into four themes. These stimuli were validated through the ratings on the (1) valence and arousal to ensure that these labels have enough capability to evoke the desired emotional valence and arousal level. In regards to this, it is hypothesized that

H1: Images of all PHWLs themes should have high ratings of unpleasantness and arousal compare to the control images (Natural (NA) images which comprised of natural sceneries).

H1 is constructed based on the unpleasant and emotionally arousing nature of the PHWLs that framed negatively regardless of the message content or theme they belong to. Generally, the PHWLs were rated as more unpleasant and negatively aroused (i.e. Noar et al., 2015).

The validated labels were used to construct an fMRI viewing task to study the brain activation of the smokers and non-smokers in terms of the (2) spatial extent and (3) intensity when they viewing the PHWLs that comprised of different themes. Several hypotheses were constructed in regards to this fMRI task.

H2a: Images of PHWLs are expected to activate a broad array of regions associated with the processing of visual, emotional and self-related stimuli as well as learning and memory, regardless of the smoking status.

These regions have been consistently reported in numerous fMRI studies in this topic of interest (i.e. Fridriksson, 2013; Green et al., 2016)

H2b: Greater brain activation in the visual cortex should be observed when viewing the COS and DD images. Similarly, greater limbic activation should be found to COS, EN and DD images. On the contrary, least brain activation in these cortices should be expected when viewing the NE images. These predictions were made regardless of the smoking status.

Greater activity in the visual cortex during the COS and DD images is predicted as these themes consist of the images of diseased organ with the following features: gruesome and vivid graphic in nature. Greater brain activation in the regions associated with the emotional processing should be observed during the presentation of the COS, EN and DD images as these images attempt to evoke negative emotional responses such as fear of being susceptible to the potential harms to self and others. On the other hand, NE images are predicted to show least activities in these regions due to the metaphors used that require abstract reasoning.

H2c: Smokers are predicted to show less brain activation than non-smokers in response to the PHWLs images, regardless of the themes.

This is because non-smokers have less or no personal experience and exposure to the PHWLs when comparing to the smokers who always with their cigarette box. The novelty of the images should stimulate more cognitive and stronger emotional responses in the non-smokers.

H3: Greater intensity change in the regions of interest (ROIs) like mPFC should be demonstrated to COS and DD images for both groups respectively. When comparing between two groups, the PSC should be greater in non-smokers in those ROIs to COS and DD images.

mPFC is expected to be defined as the ROI of this study due to its strong predictive power in the smoking-related outcomes investigated. COS and DD images are predicted to show greater intensity change in this ROI in both groups as these images depict the warning content that are more relevant to the viewer themselves in the health context compare to the EN images that pay more focus on the smoking impact on others as well as NE images which might require more reasoning with respect to the self because of its abstractness of the message. The magnitude of the intensity change is predicted to be stronger for non-smokers as justified by the rationale given for H2c.

1.5 Objectives

1.5.1 General Objective

To investigate the brain activation of the smokers and non-smokers in response to the message content/theme of the anti-tobacco PHWLs using fMRI

1.5.2 Specific Objective

(1) To obtain normative ratings of emotion (valence and arousal) for each PHWLs theme

(2) To examine the brain activation of the smokers and non-smokers in response to PHWLs theme (spatial extent)

(3) To examine the percent signal change (PSC) in the regions of interest (ROIs) of the smokers and non-smokers to PHWLs themes (intensity change)

1.6 Rationale of this Study

In the meta-analysis of Kaye, White and Lewis (2017), mPFC has been found as a significant predictor in assessing the health message communication in the context of various health behaviour such as anti-smoking as well as sunscreen use. Although this region has been commonly found to be associated with the self-related processing function, its involvement in the value computation process has been noted in the neuroeconomics studies as well. From the neuroeconomics perspective, the subjective value of the options given has been found to play an important role in the decision making related to health behaviour (Barta, McGuire & Kable, 2013; Berkman, 2017 Brosch & Sander, 2013; Falk, 2018). The importance of the subjective value may be reflected in the temporal discounting studies, a famously adopted experimental paradigm to study value based decision making. Temporal discounting refers to the phenomenon in which people tend to devalue the distant rewards compare to when they can obtain the rewards in shorter time. In these studies, a persistent preference for an option that has a high subjective value to the smokers is observed despite knowing the fact that an alternative option is much better (Mackillop et al., 2012). For instance, in the face of two options (receive less cigarette now or more cigarette later), smokers have been consistently observed to opt for the former option though the latter option is better (Mackillop et al., 2012). Such findings actually underscores the central feature of the nicotine addicts which is the impulsivity (Bickel et al., 2011). Indeed, numerous lines of inhibitory control studies have observed the impulsive tendency in smokers as compared to the non-smokers (Carim-Todd, Mitchell & Oken, 2015). Consequently, the persistent poor decision making in the smokers might be attributed to the hyperactive state of the impulsive system in relative to the hypoactive state of the executive system which could have driven the smokers to act more impulsively, especially when comes to the cigarette related decisions (Bickel et al., 2011). To put it simply, either the impulsivity tendency of the smokers might be the motivator for the smokers to value the instant pleasure that derived from the nicotine use or it could be the subjective value the smokers place on the instant pleasure obtained through nicotine consumption, therefore, motivate them to act more impulsively. Regardless of the causality, it suggests a link between the subjective value and impulsivity in the decision making of the smokers. Based on the neural findings of Kaye et al. (2017) and Mackillop et al., (2012), both the self-relevance of the message and the subjective value of the viewers has for the message could be the critical components in the persuasiveness of the message to motivate the desired health decisions, and thus, desired health behavioural change.

Existing fMRI research on the message content of the PHWLs is still limited. Most of them focused on the imagery type (i.e. graphic health effect, human suffering as well as symbolic representation of the smoking consequences) or these studies just aimed to investigate the overall impact of the PHWLs on the brain response. Across these fMRI studies, the researchers have successfully identified the important cognitive and affective processes an effective label should engage in such as visual and self-related processing. However, the subjective value aspect of the PHWLs has yet to be included in these previous fMRI investigations. Therefore, this present study is interested to find out how the message content of the PHWLs with different value emphasis might engage the cognitive and affective processes differently using fMRI. In addition, we also interested to find out how these labels might recruit the medial frontal activation at different extent level.

Besides, smokers and non-smokers have been found to process the information differently. The persistent impulsive behaviour of the smokers is suggested to be motivated by the dysregulation of activity between the impulsive and executive systems, supported with neural evidence (Bickel et al., 2011). This justifies the importance to compare the brain response between these two subpopulations since their decision might be influenced by the same health information or same theme. Moreover, studying the non-smoker subpopulation could be meaningful as well since the tobacco control initiatives also aims to prevent smoking initiation, especially among the vulnerable group (Tan & Dorotheo, 2016). Meanwhile, it is also useful to understand how this subpopulation able to maintain their non-smoking status despite of the susceptible factors such as life stressors. Nevertheless, previous fMRI studies did not include them in their investigations.

Future findings in this topic of interest on the brain response of smokers and non-smokers have several implications. Firstly, it helps to improve our understanding on how these subpopulations with different brain mechanisms process the PHWLs differently. A health message can result in different decisions due to the different interpretations by the individuals with different characteristics during decision making. These underlying brain processes when processing the health message are mediated and modulated by the interactions among the brain networks. Identifying the regions involved is significant as these regions could be used to further develop the neural pathway model of processing the PHWLs that comprised of different themes. The identified regions and neural pathway can be used as a reference to predict the effectiveness of the PHWLs. Appropriate and effective PHWLs can be tailored according to their respective brain mechanism with the aims to encourage the smokers to engage in smoking cessation while discourage the non-smokers, especially the vulnerable group like those who susceptible to stressors from smoking initiation.

1.7 Organization of Thesis

In the present thesis, different components of the study were detailed out in the following sections. In Chapter 2, cigarette smoking, PHWLs and message content were reviewed together with the past findings. Specifically, the message content of the labels were reviewed with the studies using self-report measures as well as neuroimaging measures. In Chapter 3 (methods and materials), two studies were carried out: PHWLs normative ratings study (valence and arousal) as well as PHWLs viewing task using fMRI. In Chapter 4, a series of statistical analysis were performed on the normative ratings of the labels as well as brain responses of the smoking and non-smoking groups in terms of spatial extent and intensity. The findings of the normative ratings and brain activities were reported in Chapter 4 and discussed in detail in Chapter 5. Last but not least, the findings of the study were concluded in Chapter 6 together with the limitations and recommendations of the future improvement and work.

CHAPTER 2: LITERATURE REVIEW

2.1 Smoking and its Effect

Cigarette smoking is one of the popularly known global health issues that demand for global control due to its association with various health diseases, social impact and economic burden. The smoking-related diseases can range from the commonly known illness such as lung cancer and heart disease to less commonly known illness like blindness, gangrene and throat cancer (Ng, Roxburgh, Sanjay & Au Eong, 2010). In fact, the impact of smoking can affect the whole body functioning (Tan & Dorotheo, 2016) which is less commonly to be known by the public. If the tobacco control measures fail to reduce the smoking consumption effectively, the cost will be getting increasingly high due to the raise in the healthcare cost like insurance as well as the decline in the economic productivity since there will be a great loss of human resources for optimum working performance (Tan & Dorotheo, 2016).

2.2 World Health Organization Framework Convention on Tobacco Control (WHO FCTC)

Since smoking is one of the leading causes of a variety of health issues and economic burden, international collaboration has been done to tackle the tobacco issue. In 2005, WHO FCTC has been established to offer a comprehensive guideline in regulating the tobacco consumption on the basis of evidence-based research for the state members (WHO FCTC, 2018). Such convention represents the first international global health treaty that has been ratified by many countries against the tobacco consumption throughout the world (WHO FCTC, 2018). Today, 180 governments which are the representatives of the 90% world populations have ratified the FCTC (Tan & Dorotheo, 2016), including the nine out of ten countries in ASEAN (Brunei, Cambodia, Lao PDR, Malaysia, Myanmar, Philippines, Singapore, Thailand and Vietnam except Indonesia) which are parties of the Southeast Asia Tobacco Control

Alliance (SEATCA, 2016). Under FCTC guideline, the regulation of tobacco use can be achieved through the interventions in several domains such as price, tax, smoke-free environment, media advertising, tobacco industry interference, and the packaging as well as labelling of the tobacco products (Tan & Dorotheo, 2016).

2.3 Pictorial Health Warning Labels (PHWLs)

Out of all the aforementioned measures, health warning labels printed on the cigarette packaging which under the Article 11 of the FCTC has been widely adopted in many countries (Tan, 2016). It is regarded as the most cost-effective communication channel to raise the awareness and convey the risks of cigarette use to the consumers and potential consumers compare to other measures (Tan, 2016). The efficacy of the health warning labels in achieving the goals has been evidenced in many studies (i.e. Noar et al., 2016).

The history of health warning labels can be traced to the earlier stage when the health warnings on the cigarette packages were restricted to text only such as "Smoking can cause cancer". Over the time, the adoption of the graphical content has become popular with the increasing supporting research evidences since its first implementation in Canada in 2000/2001 (Romer, 2016). Today, graphical use in the design of health warning labels is termed as graphical or pictorial health warnings labels (GHWLs or PHWLs). These warning labels aim to communicate the health risk of smoking via the depiction of the potential detrimental consequences of tobacco use by using the vivid and emotionally arousing graphical content in attempt to induce an aversive response that may deter the public from smoking (Romer et al., 2013).

Generally, many lines of research have demonstrated that GHWLs or PHWLs were more effective than text-only warning labels on the emotional (i.e. greater ability to evoke negatively arousing emotions such as fear, disgust, worry and anger (Andrew et al., 2016; Cho et al., 2017), cognition (i.e. increased attention as measured by number of eye fixation on the labels (Maynard et al., 2014), better recall (Klein et al., 2017; Strasser et al., 2012) and recognition of the warning content (Wang et al., 2018), increase in the comprehension of the content (Borzekowski; 2014), beliefs regarding the conveyed smoking-related risk (Byrne et al., 2017; Reid et al., 2017) and intention to quit (Cantrell et al., 2013; Brewer et al., 2016)), behavioral (i.e. increased quit attempts such as increase in the calling of smoking quit line (Noar et al., 2016) and reduction in the cigarette consumption per day (Shi et al., 2016)), physiological (i.e. reduced cotinine level at follow up – one of the measures of nicotine dependence (Riddle Jr., 2016)) and neuroimaging outcomes (i.e. increased brain activity in (mPFC) that associated with greater predictive ability in the success of anti-tobacco health measures (Kaye et al., 2017)). Such findings can be explained by the theory of dual process in which graphic imagery requires less cognitive resources than text during the processing (Anshari, 2017). This is in line with the heuristic nature of human. In the follow up investigation, the combination of the graphic and text as the core components is seen as the best practice of the PHWLs' implementation compared to graphic or text alone (Evans et al., 2015).

Currently, plain or standardized packaging with the removal of potentially appealing elements such as the brand logo and images, colors and promotional information except the names of the brand and products in the standard color and font size is getting attention due to its ability in undermining the appeal of the product as well as in enhancing the visibility of the PHWLs (Tan, 2016). Australia has implemented it fully in 2012 and it is getting the interest of other countries like Malaysia, Thailand and Singapore (Tan & Dorotheo, 2016).

Investigation on the design characteristics of the PHWLs is highly promoted as they are the crucial components that determine the overall effect of the PHWLs on the cigarette packaging in reducing the cigarette use, encourage smoking cessation for smokers and prevent non-smokers, especially the youth from smoking initiation. Based on the evidences gathered from the years of research, several recommendations have been provided in the FCTC guidelines to develop effective PHWLs:

(a) *Location:* PHWLs should be placed on both the front and back panels rather on the side panels. PHWLs that covered both the front and back of the tobacco packages were attended more than on the sides (Tan, 2016).

(b) Size: The size of the PHWLs should be at least 50% but not less than 30% of the total size of the tobacco package. PHWLs with larger size (i.e. 50%, 75% and 85%) were perceived as more effective than with smaller size (i.e. 30%) (Gravely et al., 2014; Li et al., 2016). In fact, PHWLs from Thailand is regarded as the best practice in this aspect as the country owns the biggest PHWLs among the ASEAN countries (Tan, 2016).

(c) *Color:* Color restriction on the cigarette package has been applied to avoid misleading information that could result in false perception and belief. For instance, blue and green colors are banned from the usage as these colors are perceived with appealing effect such that they can provide the sense of healthiness and harmony which can undermine the efficacy the PHWLs (Tan, 2016). Colors like brown and grey might reduce the attractiveness of the product. In addition, contrasting color should be applied (i.e. white text on black background for the messages and yellow or red text on the black background for the word "Warning") has been found to enhance the noticeability of the warnings (Tan, 2016).

(d) Rotation: The guideline has mandated the PHWLs to be changed in every one to two years in the respective country due to the wear-out effect of the PHWLs (Tan, 2016). This is supported with the reduction in brain response with repeated exposure to the PHWLs (Fridriksson et al., 2018).

(e) Message content: PHWLs with a wide range of message content that address different issues of cigarette consumption is mandated (Tan, 2016). Although there is an increase in the awareness of the existing PHWLs, it is found that many of them still lacking of a good

knowledge and beliefs about the potential smoking-related harms that is not only restricted to lung cancer, stroke and heart problem (Ng et al., 2010). These three physical health effects have been found to have better believability and recall than the rest but not others like blindness and gangrene (Ng et al., 2010). In addition, PHWLs should equip themselves with the great ability to evoke strong negative emotions to be associated with the tobacco use. The effectiveness of strong negative emotion has been addressed earlier. Moreover, smoking cessation assistance should be provided as well. The combination of the smoking cessation related information and PHWLs has been supported with greater efficacy in reducing the smoking behavior as these advices can help to increase the self-efficacy and response efficacy of the individuals to quit when the fear is too overwhelming that might lead to the boomerang effect like defensive or avoidance response (Shi et al., 2016).

(f) Language: The principal language of the country must be used for effective communication. Moreover, additional language beside the principal language of the country can be used as well to reach to the broader segments of the country's population (Tan, 2016). This is particularly important for the multiracial countries that practicing multiple languages.

(g) Source Attribution: PHWLs with the specification of the expert source like Ministry of Health have been found to increase the credibility and believability of the message if the governments were trusted by the audiences (Tan, 2016).

(h) Information on Constituents and Emissions: Harmful ingredients like the tar level can be included as well. Disclosure of such information can enhance the effectiveness of the PHWLs in delivering the message (Swayampakala et al., 2014).

Amongst all of the design features of the PHWLs listed above, message content is the main focus in this study as the ultimate determinant of the PHWLs' effectiveness is depended on the message content (Hammond & Reid, 2012). To understand how message content influences an individual's behavior, it is important to study the underlying affective and cognitive processes during the message processing. In addition, message content of the PHWLs that reflects different human values can be targeted to examine how different message content may shape the smoking-related behavior differently. This is inspired from the studies of behavioral economics and neuroeconomics in which a behavior is translated from a decision in accord to the value a person place on (Monterosso, Piray and Luo, 2012).

The purpose of the present investigation is to study the influence of message content or theme of the PHWLs that reflect different human value system on the cognitive and affective processes from the neuroscience perspective. We think that by identifying the brain processes involved during the message processing, it will be insightful instead of relying on the self-report measures which is more subjective in the measurement compared to the functional magnetic resonance imaging (fMRI) measure. This will be insightful to compare the brain activity between the smokers and non-smokers due to their different decision making systems (Bickel, Jarmolowicz, Mueller and Gatchalian, 2011).

In the following literature review, this thesis will provide a background for message content. Past studies on this topic of interest will be covered from the perspectives of self-report measure as well as neuroimaging measure.

2.3.1 Message Content of Pictorial Health Warning Labels

As addressed earlier, message content is a core element in designing effective PHWLs. A wide range of smoking-related topics are included in the health message design, ranging from the physical health consequences (i.e. stroke, oral cancer and blindness), social consequences (i.e. secondhand smoke) to cessation assistance (i.e. smoking cessation helpline). To date, majority of the content adopted by the governments are framed in term of the adverse impacts regarding the tobacco use which is named as the loss-framed health message (Hammond, 2011). These health warning messages which carry different sensory, emotional and cognition properties can generate varying level of effectiveness in discouraging the smokers and non-smokers from smoking.

Health warning messages of the PHWLs are constructed on the basis of the health behavioral change models such as health belief model and theory of planned behavior (Cooper et al., 2015). According to these models, cognition is assumed as the antecedent of the behavior. Under this framework, it is postulated that a change in cognition should precede the change in the behavior. This assumption highlights the importance of identifying the underlying cognitive processes involved and understanding their interaction patterns in giving rise to a behavioral change. In relation to this, Human Information Processing (HIP) model (Norman, 1969) may offer a good framework to elucidate the underlying processes during the processing of the message content using the computer's way of handling the information as the analogy. In this model, information processing begins from the input store and ends at the output store. Information received from the external environment (design features of the PHWLs such as imagery, text and color) is assumed to be processed by a series of processing systems such as attention, perception, memory and decision. The information will be processed and integrated later to generate an interpretation regarding the information received (the content).

Relating to the model above, the reason why message content is chosen as the main focus of this study is justified with two rationales. Firstly, the characteristics of the sensory, emotional and cognition that embedded in the message content of the PHWLs are proposed to be processed in the computer-like manner. Processing of these features can be inferred from the brain activity. The second rationale is based on the inspiration drawn from the behavioral economics and neuroeconomics studies. The work from these disciplines highlights the role of subjective value in studying human decision making which provides a good direction in examining the message processing as the contents of the PHWLs are designed with an emphasis on different human value system. For example, "Smoking can cause heart problem" reflects the value of an individual place on his or her health. However, decision is not a simple process to be understood as human can have multiple value system. In this context, a smoker places a great importance on his or her health but also on the pleasure derived from smoking. In the question of whether to quit smoking or not, the resultant decision of the smoker is the outcome of the subjective value computation of each value the smoker has, depending the degree of importance the smoker place on each value. To make it simple, if the smoker prioritizes more on health, he might quit smoking or vice versa. Such computation lies in the underlying processes as described in the HIP model during the message processing is worth to be explored.

To summarize, the interplay among the aforementioned components of the PHWLs' message content may provide a better picture on how they motivate a behavioral change. In this section, research works in this topic of interest will be detailed out from the perspectives of psychological sciences using the self-report measures as well as the neuroimaging using fMRI measure.

2.3.1.1 From the Psychological Sciences Viewpoint

The findings from the existing literature have reached to a consensus regarding the effective components in warning message design in which the use of graphical imagery and negative emotional appeal are strongly recommended (Tan & Dorotheo, 2016). In the existing literature, fear appeal is the most commonly adopted strategy in the anti-tobacco health message communication (Leshner, Bolls & Thomas, 2009). It is suggested that the fear induction by the PHWLs content can activate the human aversive system in order to motivate an individual to engage in defensive or avoidance processing to the stimuli of the PHWLs according to the Motivated Processing Framework (Leshner, Bolls & Wise, 2011). Such processing is expected to result in defensive or avoidance smoking behavior (Leshner et al., 2011).

There are a wide range of message topics have been introduced and implemented in the PHWLs, including the tobacco industry manipulation (Shadel, Fryer & Tharp-Taylor, 2009; Shen, 2010), actor appeal (Shadel et al., 2009), secondhand smoke (Netemeyer et al., 2016), detrimental physical health effects, addiction and degradation of life quality (Hammond, 2011). These themes or content are typically implemented and investigated in the anti-tobacco public service announcements (PSAs) and PHWLs. A series of the relevant studies are summarized as below.

The importance of emotion has been consistently underscored across the studies (i.e. Netemeyer et al., 2016). A broad array of emotion can be elicited to the warning messages with different content in order to have a broad reach to the audiences (Netemeyer et al., 2016). In the study of Shen (2010), anti-smoking PSAs which framed in terms of the health consequences, secondhand smoke and manipulation of tobacco industry have demonstrated their ability in eliciting stronger negative emotion such as fear and disgust in the undergraduate students due to the unpleasantness of the topics. However, only health consequences and industry manipulation messages were found as the significant predictors of attitude towards smoking except secondhand smoke messages. It is suggested that the focus of the secondhand smoke message used in the study might have contributed to such findings. The message was framed to give the idea such that smoking is bad to the surrounding people rather the important ones or smoking in the public areas. In addition, anger response was reported as well to the secondhand smoke and industry manipulation message. It is explained that anger could have directed at the tobacco companies due to their unethical practice. The influence of the emotion on the individuals can be further elaborated by another study conducted. In examining the role of emotions on smoking consideration and secondhand smoke beliefs (Netemeyer et al., 2016), both adolescent smokers and non-smokers did not differ on the fear response to the PHWLs. However, significant differences on the guilt and disgust response were observed in which smokers felt guiltier than non-smokers whereas non-smokers were more disgusted by the PHWLs than the smokers. The former observation is said to be the consequence of public judgment regarding the smoking impacts on children.

To summarize, fear and disgust appear to be the more appealing alternatives in conveying the smoking risks as supported by a numerous of studies besides the two studies above. On the other hand, social judgment or social norms appears to play an important role as well to motivate the withdrawal or defensive reactions from the audiences through the guilt induction. The glamorous impression of cigarette smoking in the past has been replaced with a stigmatized perception in the eye of the public today when more adverse consequences of smoking has been revealed with the efforts of governments in tobacco denormalization.

The classification of PHWLs into the message themes or content can vary with different criteria, depending on the objectives of the study design. In 2013, Cameron, Pepper and Brewer examined the response of young adults to PHWLs have observed a greater fear response and smoking discouragement as reported by smokers and non-smokers when exposed to the graphic warnings in relative to text. This effect is particularly strong for non-smokers. Themes like diseased organ, human suffering or deceased people as well as children or babies were reported with the strongest smoking discouragement effect whereas the participants were discouraged to smoke the least by the themes of art graphic, metaphors and unpleasant experience of smoking of the smokers. In a comparison study of the impact of health warning labels among three countries with different health warning labels implementation approach (Thrasher et al., 2010), themes of human suffering and gruesome diseased organ due to smoking which adopted by Brazil have showed greater cognitive and behavioral impacts among the smokers than Uruguay which using the abstract or symbolic representation imagery (i.e. limp cigarette that represents impotence) and text-only warning from Mexico. Similar to the above findings, researcher who investigated the efficacy of the Indonesia’s PHWLs have found that graphical imagery (Anshari, 2017), a representative of highest frightening image type was rated the highest on negative emotional response, perceived credibility and effectiveness than the human suffering, a representative of moderate frightening image type. The ratings of these outcome variables for human suffering were higher than the symbolic images, a representative of least fearful imagery type.

Although the outcome variables examined differed in each study, these studies have provided a consistent supportive evidence for message theme that framed in negative health consequences (diseased organ and human suffering) as well as in social impact (secondhand smoke to children or babies) with the use of real victims to enhance the vividness of the graphic imagery (Hammond, 2011). The vividness of the graphic imagery may enhance the emotional appeal to facilitate the persuasiveness of the message (Hammond, 2011). On the other hand, abstract or symbolic representations are not strongly recommended due to the lesser effectiveness as evidenced in the studies above. The comprehension of the message could be a challenge as the content is ambiguous to be interpreted which could hamper the emotional and cognitive processing performance.

2.3.1.2 From the Neuroimaging Viewpoint

The emergence of neuroimaging techniques has opened a new avenue in complementing the knowledge gained from the research work using self-report measures. A series of fMRI studies (i.e. Falk et al., 2015) has been conducted to study the PHWLs, particularly more in the developed countries with better resources accessibility. The rationale behind of these research works is to infer the underlying emotional and cognitive processes from the brain activity in attempt to capture the relationship between the PHWLs or anti-smoking PSAs and smoking-related behaviors besides measuring the outcome variables in the aspect of cognition, affect and behavior using the introspection method which can impose validity issues if the studies were not controlled well. The usual argument received in the self-report studies often lies on the subjective nature of the measure. This argument can be counteracted with the measuring approach from brain perspective which is seen as a relatively objective measure. Such measure has the advantage in overcoming the social desirability effect as it would be hard for human to control their brain response instantly in the context of stigmatized behavior due to the concern of social judgment (Kaye et al., 2017).

Generally, a wide network of brain regions was recruited when the smokers viewing a series of anti-smoking images or PHWLs as revealed by most of the fMRI studies. In the study of Green et al. (2016), significant greater neural activation was observed in the regions located at medial frontal and temporal cortices, middle occipital gyrus (MOG), orbital gyrus, precuneus and amygdala in response to the graphical health warning images with the themes of health illnesses (lung and heart) as well as death than the control images, reflecting the engagement of processing in the emotional and cognition as well as memory formation. However, only amygdala activation is correlated with motivation to quit when exposed to the graphical health warning images, implying the emotional saliency of the GHWLs might be adequate for the subjects.

In the study of Fridriksson (2013) to compare the neurological response to the PHWLs foreign images and FDA proposed images among a group of young adult smokers, right lateral occipital cortex was observed more for the foreign PHWLs. It might be due to their more explicit emphasis on the negative health consequences of smoking. When comparing the activation between the PHWLs and control images, the former showed greater activation in the bilateral occipital cortex. Activity in this region seems to relate to emotional processing of the PHWLs as occipital cortex can serve as a mediator to other limbic system such as insula and amygdala.

To investigate the facilitation of the emotional reaction of the GHWLs on the brain activity and behavioral outcomes, Wang et al. have conducted a study in 2015. Compare to