

IMPACT OF E-CIGARETTE USAGE ON COGNITIVE PERFORMANCE LEVEL AMONG UNIVERSITY STUDENTS IN MALAYSIA: A CASE-CONTROL STUDY

Siti Norsyafika Kamarudin¹, Natiara Mohamad Hashim², Ahmad Zamir Che Daud³,
Fatimah Ahmedy⁴, Mazatulfazura Sf Salim⁵ and Salmah Anim Abu Hassan⁶

¹Department of Pharmacology, ²Department of Rehabilitation Medicine, Faculty of Medicine, ³Centre for Occupational Therapy Studies, Faculty of Health Sciences, Universiti Teknologi MARA; ⁴Rehabilitation Medicine Unit, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah; ⁵Department of Rehabilitation Medicine, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia; ⁶Department of Orthopaedics, Traumatology and Rehabilitation, Faculty of Medicine, International Islamic University Malaysia

Abstract. The electronic cigarette, or “e-cigarette”, is a device with a cartridge containing liquid nicotine and other ingredients that creates inhalable smoke. Malaysia is considered to be one of the world’s major markets for e-cigarettes since it has the greatest reported proportion of teenage consumers. E-cigarettes can cause multiple pulmonary complications or direct injury as a result of the device explosion. Little is known about its effects on cognitive performance and its potential hazard to the brain. It is crucial to look at any potential impacts on cognitive function because Malaysia’s young population differs from those of other countries in terms of different sociodemographic background and e-cigarette use. The cognitive performance of e-cigarette users and non-users among Malaysian university students are compared in this case-control study. We recruited 70 non-e-cigarette users and an equal number of e-cigarette users among university students in Malaysia and performed a face-to-face cognitive evaluation using WHO Auditory Verbal Learning Test (WHO-AVLT), Trail Making Test (TMT) and Digit Span Test (DST) for both groups. Using a self-reported questionnaire, we looked into the relationships between e-cigarette awareness, attitude and behavior. DST demonstrated a significant difference with a p-value of 0.05, with e-cigarette users outperforming non-users with 21.75 and 20.17 points respectively. According to WHO-AVLT and TMT, there are no significant differences between e-cigarette users and non-users. E-cigarette users’ attitude and lower level of awareness can help explain their behavior. This study provides preliminary evidence of a lack of e-cigarette effect

on cognitive function among the local university student population. The finding may serve as a baseline for a more robust study in the future.

Keywords: e-cigarettes, cognition, students, Malaysia

Correspondence: Natiara Mohamad Hashim, Department of Rehabilitation Medicine, Faculty of Medicine, Sungai Buloh Campus, Jalan Hospital, 47000, Sungai Buloh, Selangor, Malaysia

Tel: +60 193803105 E-mail: natiara@uitm.edu.my

INTRODUCTION

Cigarette smoking is the single most important cause of avoidable premature mortality worldwide, and quitting is known to rapidly reduce the risk of serious diseases, such as lung cancer, cardiovascular disease, stroke, chronic lung disease, and other cancers (Jha *et al*, 2020; WHO, 2021). The electronic cigarette (e-cigarette) is an electronic device, also known as a vape, containing a cartridge filled with liquid nicotine and/or other chemicals, producing inhalable smoke (Gravely *et al*, 2014). Since its introduction in the early 2000s, e-cigarette use has quickly gained popularity worldwide (Gravely *et al*, 2014), especially among current and former smokers (Gravely *et al*, 2014; Farsalinos *et al*, 2015; Weaver *et al*, 2018). E-cigarette manufacturers promote it as a safer, cheaper and alternative product for smoking cessation (Farsalinos *et al*,

2015; Weaver *et al*, 2018).

It has become a public health concern as its usage has garnered popularity (WHO, 2009). In 2009, Australia, Brazil, China, Uruguay, Brunei, Cambodia, Indonesia, Singapore, Thailand and Vietnam banned the sale and marketing of e-cigarettes (WHO, 2009; Schmid, 2016). Southeast Asia has the highest number of countries (6 of 11) that banned the use of e-cigarettes (Schmid, 2016). In countries without strict regulations, such as Bangladesh, China and Zambia, awareness and usage of e-cigarettes is not as high. On the other hand, in countries with restrictive policies, such as Australia, Brazil and Uruguay, where it is not legal to sell or market them, ever- and current-use rates are relatively lower (ever-use = 7.1-48.9%; current use = 0.3-3.5%). Countries with less restrictive policies, such as

Netherlands, Republic of Korea, United Kingdom and United States, where e-cigarettes can be sold and marketed under regulations, have higher ever- and current-use rates (ever-use = 38.9-66.6 ; current use = 5.5-17.2%). Meanwhile, in countries with restrictive policies that do not approve sale or marketing but with weak enforcement, such as Canada, Malaysia, Mexico, and New Zealand, ever- and current-use rates are somewhere in between countries with and without strict regulations (ever-use = 10.0-62.4%; current use = 1.4-15.5%) (Gravely *et al*, 2019).

The prevalence of e-cigarette users among the young age population in Malaysia was recorded to be the one of the highest in Southeast Asia, as reported by the 2015 Global Adult Tobacco Survey: Indonesia at 0.3%, Malaysia at 0.8%, Philippines at 1.7%, and Vietnam at 0.2% (WHO, 2009). About 39.9% of young students from higher institutions, followed by 36% of young professionals from two highly populated states in Malaysia (Kuala Lumpur and Selangor) were reported to consume e-cigarettes (Wong *et al*, 2016).

It is widely believed that e-cigarettes have a much lower health risks than tobacco smoking. Hence, e-cigarettes have become

a popular alternative option to tobacco smoking or to wean off the withdrawal symptoms upon quitting tobacco smoking (Bhatnagar *et al*, 2014). There is an increasing trend of health hazards secondary to e-cigarettes that have been frequently reported. These health hazards are related to respiratory system complications, such as lipoid pneumonia, acute eosinophilic pneumonia, hypersensitivity pneumonia, organizing pneumonia, diffuse alveolar hemorrhage, multiple reactive pulmonary nodules, and subacute bronchiolitis (Gülşen and Uslu, 2020). There are also direct injuries from e-cigarette explosions, which cause mouth, tongue and dental injuries, complex facial fractures, thermal injuries, nickel contact allergy, C1 and C2 fractures, and fatal intoxication from ingesting the liquid content (Gülşen and Uslu, 2020).

Young and middle-aged adults who consume tobacco smoking have long been shown to have a higher risk for cognitive decline upon neurocognitive assessment, including memory, attention and executive function deficits (Chamberlain *et al*, 2012; Sabia *et al*, 2012). Morphologically, development of the prefrontal cortex and its activities can be stunted by nicotine exposure during

adolescence and early adulthood, which lead to long-lasting cognitive impairment (Counotte *et al*, 2011). Recently, in addition to the respiratory complications that have been frequently reported, e-cigarettes have also been reported to adversely impact cognitive performance (Dawkins *et al*, 2012; Caponnetto *et al*, 2017; Xie *et al*, 2020a). Caponnetto *et al* (2017) have utilized the Wisconsin card sorting test (WCST), Working memory test (N-BACK) and Continuous Performance Test - AX version (CPT-AX) to objectively measure cognitive performance.

To the best of our knowledge, there is limited study utilizing WHO Auditory Verbal Learning Tests (WHO-AVLT), Trail Making Test (TMT) and Digit Span Test (DST) in objective assessment of cognitive performance in e-cigarette users. WHO-AVLT[NBMH(1)], TMT and DST have proven to be valuable tools in assessing cognitive performance or dysfunction in several population-based studies (Schaffner *et al*, 2018; Zaytseva *et al*, 2018, Jia *et al*, 2023). These tests have also been used to identify cognitive impairment in individuals with schizophrenia (Zaytseva *et al*, 2018), explore the link between a healthy lifestyle and memory decline in older adults in China (Jia *et al*, 2023) and examine the effects of daylight saving on cognitive

performance in residents of New South Wales (Schaffner *et al*, 2018).

Xie *et al* (2020a) utilized self-reported questionnaire to survey the presence of any subjective cognitive complaints. The questionnaire asked if the participants had significant difficulty concentrating, remembering or making decisions due to physical, mental or emotional conditions. These results demonstrated that individuals who smoke cigarettes or use e-cigarette devices have a 2.07-fold higher likelihood of experiencing subjective cognitive complaints. Similarly, people who are currently using e-cigarettes but used to smoke or have never smoked in the past have a 1.94- and 1.96-fold higher chance respectively of experiencing subjective cognitive complaints. These findings suggest that using both cigarettes and e-cigarette devices, as well as using e-cigarettes alone, may contribute to cognitive complaints (Xie *et al*, 2020a). This phenomenon can be explained by the fact that the amount of nicotine delivered by e-cigarettes is comparable to that delivered by traditional cigarettes (Jackler and Ramamurthi, 2019). This scenario also was supported by a recent animal laboratory study, which found that exposing male Wistar rats to e-cigarette aerosol for 4 and 12 weeks resulted in impaired short- and long-term memory (Alzoubi

et al, 2021). There is a reduction in the hippocampus brain-derived neurotrophic factor (BDNF) and oxidative stress biomarkers. These findings suggest that exposure to e-cigarette aerosol may have detrimental effects on cognitive function and overall brain activity (Alzoubi *et al*, 2021).

Several aspects of e-cigarette use in Malaysia were reported in various studies, but there is a limited number of studies on cognitive performance among Malaysian university students (Wong *et al*, 2016; Goh *et al*, 2017; Robert Lourdes *et al*, 2019). Cognitive deficits are described as impairments in information processing, which can lead to difficulty in paying attention, rapid processing and responding to information, recalling information, initiating speech, reasoning, and making judgments (Trivedi, 2006). This cognitive ability is crucial for university (and other) students to excel in their education. Thus, it is essential to conduct a study on the effect of e-cigarette smoking among young adults in Malaysia. The study may give rise to different results compared to other published reports, considering the differences in the test populations, the types of e-cigarette consumed, which depend on their availability, and the consumption pattern. The findings will provide an initial baseline evidence of the

effects of e-cigarette consumption, particularly on cognitive performance, which is currently lacking in Malaysia.

MATERIALS AND METHODS

Study design and setting

A case-control design study was conducted from September 2021 to January 2022. University students from higher institutions in Malaysia located in Klang Valley, state of Selangor, were recruited. All students were studying in the same degree course but from different universities, greater than 18 years of age, actively using e-cigarettes and in good general health, with no history of hospitalization and outpatient follow-up for any chronic disease, disability or mental illness. The control group was composed of university students who were non-smokers or non-users of e-cigarettes and complied with the health status required for the test group. Students who were either on regular psychotropic medication, had a current or past history of alcohol or drug abuse, or used smokeless tobacco or nicotine replacement therapy were excluded from the study.

The sample size was calculated using G Power software version 3.1 (Kang *et al*, 2021). We used a t-test design to evaluate the effect of e-cigarettes on cognitive performance.

We set the significance level (α) at 0.05, indicating a 5% chance of obtaining a significant result due to random chance alone with a medium effect size (Cohen's $d = 0.5$). For statistical NBMH(1) power ($1-\beta$), we selected a desired value of 0.80 (80%) to ensure an adequate likelihood of detecting difference in cognitive performance [scores from WHO Auditory Verbal Learning Tests (WHO-AVLT), Trail Making Test (TMT) and Digit Span Test (DST)] between e-cigarette users and non-users. A two-tailed test was employed to account for an effect in both directions. Based on these inputs, a total sample size of 102 participants with 51 participants in each group were determined to achieve the desired statistical power. To address potential attrition or incomplete data, we aimed to recruit 140 participants recruited by a snowballing non-probability sampling via phone calls.

Data collection procedure

Data were collected using a structured questionnaire on sociodemographic characteristics (*eg*, age, gender and level of education) and e-cigarette consumption profile (duration of usage, type of e-cigarette used and frequency of usage). For cognitive performance evaluation, three trained occupational therapists evaluated cognitive performance

via face-to-face assessment with the participants using WHO-AVLT, TMT and DST. The three occupational therapists were highly trained and held degrees in health science. Each had over three years of clinical experience and were very familiar with the measures which were also used in their daily practice. The time taken to perform the assessments was about 20-30 minutes. Awareness and attitude on e-cigarette usage were obtained from the participants' self-reported questionnaire.

Instruments

a) WHO-AVLT

WHO-AVLT is used to assess the memory performance of the participants ≥ 16 years of age. The test evaluates different aspects of learning and memory, and is sensitive in detecting cognitive decline in the general population and individuals with neurological conditions (Creighton *et al*, 2011). The immediate recall trial provides information on acquisition and learning rate, and the delayed and recognition trial explores aspects of information retention. The test is designed as a list-learning paradigm in which the individual hears a list of 15 nouns and is asked to recall as many words from the list as possible. The higher the score, the greater the memory function of the individual.

The validated Malay version of ALVT demonstrates good validity (factor analysis of 0.66-0.98) and test-retest reliability (Pearson correlation range of 0.24-0.84) (Jamaluddin *et al*, 2009).

b) TMT

TMT is used to evaluate the attention and executive function of the individual. TMT is one of the most widely used instruments in neuropsychological assessment as an indicator of the speed of cognitive processing and executive functioning (Salthouse, 2011). Several other cognitive domains, such as visual search, perceptual/motor speed, speed of processing, working memory, and general intelligence, are among the most frequently described to contribute to TMT performance. The test consists of two parts (A and B). Part A (TMT-A) involves the participant using a pencil to draw lines connecting numbered circles in sequence from 1 to 25; while Part B (TMT-B) requires the participant to connect numbered and lettered circles in alternating alphanumeric sequencing (*ie*, 1-A-2-B-3-C, and so-on through to L-13). The direct score of each part is represented by the time of completion of the tasks. The shorter the time taken to complete the task, the better is the attention and executive function of

the individual. This test is validated and reliable to be administered to the general population and individuals with cognitive deficits.

c) DST

DST is an instrument to measure an individual's verbal working memory, overall intelligence, attention, and cognitive functioning. It is administered by asking the participants to count digits both in ascending order and descending order. The higher the score, the better is the executive function and learning potential of the individual. The test is validated and reliable to be used with the general population and individuals with cognitive deficits.

d) Awareness of e-cigarette users

This is a self-reported questionnaire that measures the awareness of e-cigarette users. These items are adopted from a cross-sectional study measuring awareness and practice among adolescents on the usage of e-cigarettes (Gorukanti *et al*, 2016). The items used in the questionnaire are derived from a qualitative interview that delves into the perceptions of teenagers regarding the benefits and risks of smoking conventional cigarettes, e-cigarettes and marijuana (Roditis *et al*, 2015). It consists of 10 items that explore their perceptions of e-cigarette's benefits,

safety and consumption risks. It is scored using a 4-point Likert scale, with 1 for strongly disagree to 4 for strongly agree. The higher the score, the poorer is the awareness and attitude toward e-cigarettes.

Data analysis

Normality testing was conducted to determine the distribution of the data. Descriptive analysis was conducted on the socio-demographic characteristics. To compare the level of cognitive performance, awareness and attitude between case and control, a t-test was used to determine whether the difference in data between the two groups is normally distributed, and if not, the Mann-Whitney U test was used. To identify the predictive ability of awareness and attitude towards the use of the e-cigarette, a binary logistic regression analysis was employed. Statistical analyses were calculated using Statistical Package for Social Sciences (SPSS) software version 22 (IBM, Armonk, NY).

Ethical consideration

The study was approved by the Medical Research Ethics Committee of Universiti Teknologi MARA (Approval no. IREC 2021-213). Each participant read the study information sheet and prior written consent was obtained from each participant.

RESULTS

A total 140 participants was successfully recruited in the study. The participants consisted of 70 non-e-cigarette users and 70 e-cigarette users, with 70% of the e-cigarette users having a mean duration of e-cigarette consumption of 29.7 months and 52% consuming e-cigarettes more than once daily (Table 1).

DST score (mean \pm SD) of e-cigarette users was 21.7 ± 4.6 , significantly higher than that of non-e-cigarette users (20.0 ± 4.83) (p -value = 0.048; 95% confidence interval (CI): 0.01-3.16, using a t-test) (Table 2). The higher the mean score, the higher level of cognitive performance is.

WHOAVLT score was the same for e-cigarette and non-e-cigarette users (median = 29.00, $U = 2317$, $z = -0.57$, p -value = 0.57; using Mann-Whitney U test) (Table 3).

TMT-A revealed that the time taken to complete the test was higher but not significantly different for the e-cigarette users' group (median score = 36.05) than the non-e-cigarette users' group (median score = 34.50) (Table 4). Similarly, the TMT-B score is not significantly different between the two groups (median score of 59.50 and 57.30 for e-cigarette and non-e-cigarette users' group respectively) (Table 4).

Table 1

Demographic characteristics of e-cigarette users and properties of e-cigarettes (N = 140)

Demographic characteristics	Frequency <i>n</i> (%)
Age	
18-25 years	135 (96)
26-35 years	5 (4)
Gender	
Male	105 (75)
Female	35 (25)
Level of education	
Diploma	21 (15)
Bachelor of Engineering	118 (84)
Master	1 (1)
E-cigarette users	70 (50)
Non-e-cigarette users	70 (50)
Duration of e-cigarettes usage (months), mean \pm SD	29.7 \pm 24.0
Type of e-cigarette juice	
Without nicotine (with flavors)	11 (8)
≤ 6 mg nicotine to ≤ 9 mg nicotine	14 (10)
≤ 12 mg nicotine	10 (7)
≥ 16 mg nicotine	27 (19)
Unsure	8 (6)
None	70 (50)
Frequency of usage	
More than once daily	52 (38)
Once daily	7 (5)
More than once weekly	2 (1)
Once weekly	3 (2)
More than once monthly	6 (4)
Non-user	70 (50)

e-cigarette: electronic cigarette; mg: milligram; SD: standard deviation

Table 2

Comparing Digit Span score between e-cigarette and non-e-cigarette users

Variable	E-cigarette user (<i>n</i> = 70) Mean ± SD	Non-e-cigarette user (<i>n</i> = 70) Mean ± SD	95% CI	<i>t</i> (df)	<i>p</i> -value
Digit Span score	21.7 ± 4.6	20.2 ± 4.8	0.01-3.16	1.99 (138)	0.048

CI: confidence interval; df: degrees of freedom; e-cigarette: electronic cigarette; *t*: *t*-test value

Table 3

WHOAVLT score between e-cigarette and non-e-cigarette users

WHOAVLT score	Mean rank	Sum rank	Median	Z-score	<i>p</i> -value
E-cigarette users (<i>n</i> = 70)	68.60	4802	29.00	0.57	0.571
Non-e-cigarette users (<i>n</i> = 70)	72.40	5068	29.00		

e-cigarette: electronic cigarette; WHOAVLT: World Health Organization Auditory Verbal Learning Tests

Only 101 of 140 participants completed the self-reported questionnaire, 58 and 43 from the e-cigarette and non-e-cigarette users' group respectively. We used a Mann-Whitney U Test for data that are not normal distributed and an independent t-test for data that are normal distributed in determining the difference in awareness and attitude between e-cigarette and non-e-cigarette users. There is a significant difference with *p*-value of

0.001) in awareness and attitude level related to e-cigarette usage between the users and non-users, with a total score of 27.60 and 21.42 respectively (Table 5). A higher score indicates a lower level of awareness and attitude.

Binary logistic regression analysis was performed to identify the predictive ability of awareness and attitude towards e-cigarettes on the use of e-cigarettes. Based on the model analysis, 45% of e-cigarette use among university students can

Table 4

Trail Making Test A and B scores between e-cigarette and non-e-cigarette users

Trail Making Test	Mean rank	Sum rank	Median	Z-score	<i>p</i> -value
Trail Making Test, Part A					
E-cigarette users (<i>n</i> = 70)	73.67	5157	36.05	0.93	0.362
Non-e-cigarette users (<i>n</i> = 70)	67.33	4713	34.50		
Trail Making Test, Part B					
E-cigarette users (<i>n</i> = 70)	71.86	5030	59.50	0.39	0.690
Non-e-cigarette users (<i>n</i> = 70)	69.14	4839	57.30		

Part A: Time taken for the participant to draw lines connecting numbered circles in sequence from 1 to 25

Part B: Time taken for the participant to connect numbered and lettered circles in alternating alphanumeric sequence (*ie*, 1-A-2-B-3-C, and so-on through to L-13)

e-cigarette: electronic cigarette

be explained by their awareness and attitude toward e-cigarettes (Table 6). This model showed a good fit with a significance value of 0.747 using the Hosmer-Lemeshow Test. Furthermore, the analysis revealed that the higher the score of awareness and attitude towards e-cigarettes, the more likely (1.423 folds) is a university student to use e-cigarette. There is a significant difference in awareness and attitude levels between e-cigarette users and non-users, with the latter demonstrating a lower level of awareness and attitude. This lack of awareness and attitude increases the likelihood of

the students' consuming e-cigarettes as they believe e-cigarettes serve as a safer alternative to tobacco smoking.

DISCUSSION

The study explored the effect of e-cigarettes on cognitive performance among university students in Malaysia. Compared to other similar studies (Dawkins *et al*, 2012; Xie *et al*, 2020a), our study eliminated the bias of pre-existing differences in education and intellectual level that may influence the results. These factors can be controlled by ensuring the test populations have the same

Table 5
Students' awareness and attitude score related to e-cigarette among university students (n = 101)

Item statement	Awareness and attitude score		p-value
	Vape users	Non-users	
1. Smoke from e-cigarette is just water, median (IQR)	2 (2)	1 (1)	0.023 ^a
2. E-cigarette doesn't contain tar, median (IQR)	3 (1)	2 (2)	0.001 ^a
3. E-cigarette isn't addictive, median (IQR)	2 (1)	1 (1)	0.011 ^a
4. E-cigarette isn't a tobacco product, mean ± SD	2.9 ± 0.9	2.2 ± 0.9	0.001 ^b
5. E-cigarette doesn't produce smoke, median (IQR)	2 (2)	1 (1)	0.001 ^a
6. Using E-cigarette feels cleaner than smoking, median (IQR)	4 (1)	2 (2)	0.001 ^a
7. E-cigarette is safer than smoking, median (IQR)	3 (1)	2 (2)	0.001 ^a
8. Teens use E-cigarette to get the same buzz they get from tobacco cigarettes, mean ± SD	2.8 ± 0.8	2.6 ± 1.0	0.281 ^b
9. E-cigarette helps people quit using cigarettes, mean (IQR)	3 (1)	2 (1)	0.001 ^a
10. E-cigarette vapor is dangerous to babies and kids, median (IQR)	3 (1)	4 (1)	0.523 ^a
Total awareness and attitude score, median (IQR)	27 (3)	21 (5)	0.001 ^b

^aMann-Whitney U Test; ^bIndependent t-test
e-cigarette: electronic cigarette; IQR: interquartile range; SD: standard deviation

Table 6

Predicting use of e-cigarette based on awareness and attitude towards e-cigarette using a binary logistic regression analysis

Predictor	B	SE	Wald	df	<i>p</i> -value	Exp (B)	95% CI
Awareness and attitude	0.353	0.075	21.955	1	0.001	1.423	1.228-1.649

B: β ; CI: confidence interval; df: degree of freedom; e-cigarette: electronic cigarette; Exp (B): exponentiated coefficient (β); SE: standard error; Wald: Wald Chi-Square

educational background and are studying a similar course, which in this case is the Bachelor Degree of Engineering. The results of our study demonstrated that consuming e-cigarettes has no significant effect in reducing cognitive performance of the participating students.

Several factors might contribute to this finding. Firstly, the duration of e-cigarette consumption may need to be longer to produce an adverse effect on cognitive functions; the mean duration of e-cigarette exposure in our study was only 29 months. It is unclear how long it takes for e-cigarette consumption to produce cognitive decline. An observational study demonstrated a high incidence of cognitive complaints among middle and high school youths, consisting of students in 6th to 12th grade (Xie *et al*, 2020b). In the aforementioned study, consumption of e-cigarettes beginning in middle

school or earlier has a significant 1.7-fold higher likelihood of experiencing severe cognitive complaints compared to starting the use of e-cigarettes in high school. Tobacco users of more than ten years do not show any difference in cognitive performance (Xie *et al*, 2020b).

In addition, the population of our study consists of young, healthy individuals with no comorbidities that may enhance the risk of having potential complications. This is supported by a study which demonstrated that individuals aged 35 to 49 show a stronger association with subjective cognitive complaints among e-cigarette users. (Xie *et al*, 2020b).

Another factor that might contribute to differences in the findings is the type of e-cigarette consumed, which might be different among countries in terms of the

type of liquid chemical contents or the amount of nicotine, due to the different production processes or compliance to regulatory policies (WHO, 2009). There is difficulty in quantifying the level of nicotine concentration in the e-liquid sold in Malaysia due to discrepancies in labelling, which can be 23-73% of the actual concentration (Zulkifli *et al*, 2018). A laboratory study that examined the nicotine concentrations in e-liquid sold in Malaysia reported an average of 2.07-5.15 mg/ml nicotine, with a mean value of 3.38 ± 1.24 mg/ml. However, this study only randomly tested 17 types of e-liquids among various brands and flavors sold in retailers around Klang Valley, state of Selangor (Zulkifli *et al*, 2018).

Interestingly, contrary to what was hypothesized, we found that e-cigarette users have a higher WHO AVLT score. This finding is similar to a randomized cross-over control trial, in which the researchers studied the effect of different e-cigarettes containing 0 and 24 mg of nicotine and found that there is no significant difference in cognitive performance between the two groups (Caponnetto *et al*, 2017). It has also been shown that while low doses of nicotine exposure might improve cognitive functions, higher doses could impair cognitive functions; this might be

due the interaction of nicotinic receptor systems with neural systems underlying cognitive functions that are dependent on the concentration of nicotine, which acts as a stimulant at a lower dose (Kwan *et al*, 2020). In addition, a randomized controlled trial has shown that a group of users of e-cigarettes containing 18 mg of nicotine has an improvement in working memory performance compared to a placebo group (Dawkins *et al*, 2012).

Nonetheless, smoking e-cigarettes has been shown to be a significant risk of declining cognitive performance. A recent study investigating the prevalence of subjective cognitive complaints, such as difficulty concentrating, remembering or making decisions among smokers, ex-smokers and active e-cigarette users reported that individuals who smoke cigarettes and also use e-cigarette devices have a 2.07-fold higher likelihood of experiencing subjective cognitive complaints (Xie *et al*, 2020a). The same study described that people who currently consume e-cigarettes but used to smoke or have never smoked in the past have a 1.94- and 1.96-fold higher chance respectively of cognitive complaints. These findings suggest that using both cigarettes and e-cigarette devices, as well as using e-cigarettes alone, may

contribute to cognitive complaints. Additionally, the study noted that current cigarette smokers have a 1.49-fold higher chance of experiencing subjective cognitive complaints compared to those who have never smoked, and individuals who used to smoke also have a 1.25-fold higher likelihood. These findings indicate that cigarette smoking, whether currently or in the past, is associated with an increased risk of cognitive complaints.

Our study noted that a low level of awareness and attitude towards e-cigarettes was one of the influencing factors for students to become involved in e-cigarette smoking. The students perceived that e-cigarette provides an alternative option to conventional cigarette smoking that is believed to be more toxic. Interestingly, even individuals with a tertiary level of education still have a misperception of the risk associated with using e-cigarettes. Our study is similar to a survey revealing that the most popular reason for e-cigarette consumption is the belief in the lower toxicity effect of e-cigarettes and this conviction leads to the quitting of conventional smoking for e-cigarette (Puteh *et al*, 2018).

Despite a lack of significant demonstrable reduction of cognitive

performance level associated with e-cigarette consumption, our study, nevertheless, has provided population-based evidence in the young age group of the effect of cognitive performance among e-cigarette users. The data provide a baseline for future research conducted in other age groups. In addition, the findings can counter the claims that e-cigarettes enhance or cause a decline in cognitive performance during consumption or upon cessation (Grana *et al*, 2014).

However, prolonged exposure to e-cigarettes could result in a higher risk of affecting cognitive performance. A similar study should be carried out on different age groups, with focus on prolonged usage. The young adolescent age group with developing pre-frontal cortex and the older age group with long-standing exposure and multiple comorbidities might give rise to different results. A more challenging cognitive assessment should also be performed to give more robust results, such as the Wechsler Adult Intelligence Scale (WAIS-IV), which matches the population accordingly. A limitation of our study is the small sample size, which do not allow sub-analysis to provide more meaningful results and the inability to generalize the results to a whole Malaysian youth population.

In conclusion, our study provides an initial negative evidence of e-cigarette consumption on impairing cognitive function among college students in the country, with the caveat of the small number of participants and the limited region of the survey. The findings may serve as a baseline reference for more robust future studies, which should include the aforementioned recommendations, with focus on the impact of e-cigarettes on the cognitive abilities of young adults.

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CONFLICT OF INTEREST DISCLOSURE

All authors declare no conflict of interest.

REFERENCES

- Alzoubi KH, Batran RM, Al-Samaha NA, *et al.* The effect of electronic cigarettes exposure on learning and memory functions: behavioral and molecular analysis. *Inhal Toxicol* 2021; 33: 234-43.
- Bhatnagar A, Whitsel LP, Ribisl KM, *et al.* Electronic cigarettes: a policy statement from the American Heart Association. *Circulation* 2014; 130: 1418-36.
- Caponnetto P, Maglia M, Cannella MC, *et al.* Impact of different e-cigarette generation and models on cognitive performances, craving and gesture: a randomized cross-over trial (CogEcig). *Front Psychol* 2017; 8: 127.
- Chamberlain SR, Odlaug BL, Schreiber LR, Grant JE. Association between tobacco smoking and cognitive functioning in young adults. *Am J Addict* 2012; 21: S14-9.
- Counotte DS, Goriounova NA, Li KW, *et al.* Lasting synaptic changes underlie attention deficits caused by nicotine exposure during adolescence. *Nat Neurosci* 2011; 14: 417-9.
- Creighton J, Bender HA, Assuras S, Woehr J, Borod JC, Foldi NS. Auditory verbal learning. In: Kreutzer JS, DeLuca J, Caplan B, editors. *Encyclopedia of clinical neuropsychology*. New York, NY: Springer New York; 2011. p. 306-9.
- Dawkins L, Turner J, Hasna S, Soar K. The electronic-cigarette: effects on desire to smoke, withdrawal symptoms and cognition. *Addict Behav* 2012; 37: 970-3.
- Farsalinos KE, Spyrou A, Stefopoulos C, *et al.* Nicotine absorption from

- electronic cigarette use: comparison between experienced consumers (vapers) and naïve users (smokers). *Sci Rep* 2015; 5: 11269.
- Goh YH, Dujaili JA, Blebil AQ, Ahmed SI. Awareness and use of electronic cigarettes: perceptions of health science programme students in Malaysia. *Health Educ J* 2017; 76: 1000-8.
- Gorukanti A, Delucchi K, Ling P, Fisher-Travis R, Halpern-Felsher B. Adolescents' attitudes towards e-cigarette ingredients, safety, addictive properties, social norms, and regulation. *Prev Med* 2017; 94: 65-71.
- Grana R, Benowitz N, Glantz SA. E-cigarettes: a scientific review. *Circulation* 2014; 129: 1972-86.
- Gravely S, Driezen P, Ouimet J, *et al.* Prevalence of awareness, ever-use and current use of nicotine vaping products (NVPs) among adult current smokers and ex-smokers in 14 countries with differing regulations on sales and marketing of NVPs: cross-sectional findings from the ITC Project. *Addiction* 2019; 114: 1060-73.
- Gravely S, Fong GT, Cummings KM, *et al.* Awareness, trial, and current use of electronic cigarettes in 10 countries: findings from the ITC project. *Int J Environ Res Public Health* 2014; 11: 11691-704.
- Gülşen A, Uslu B. Health hazards and complications associated with electronic cigarettes: a review. *Turk Thorac J* 2020; 21: 201-8.
- Jackler RK, Ramamurthi D. Nicotine arms race: JUUL and the high-nicotine product market. *Tob Control* 2019; 28: 623-8.
- Jamaluddin R, Othman Z, Musa KI, Alwi MN. Validation of the Malay version of auditory verbal learning test (MVAVLT) among schizophrenia patients in hospital Universiti Sains Malaysia (HUSM), Malaysia. *ASEAN J Psychiatry* 2009; 10: 54-74.
- Jha P. The hazards of smoking and the benefits of cessation: a critical summation of the epidemiological evidence in high-income countries. *Elife* 2020; 9: e49979.
- Jia J, Zhao T, Liu Z, *et al.* Association between healthy lifestyle and memory decline in older adults: 10 year, population based, prospective cohort study. *BMJ* 2023; 380: e072691.
- Kang H. Sample size determination and power analysis using the G* Power software. *J Educ Eval Health Prof* 2021; 18: 17.
- Kwan LY, Eaton DL, Andersen SL, *et al.* This is your teen brain on drugs: in search of biological factors unique to dependence toxicity in adolescence. *Neurotoxicol Teratol* 2020; 81: 106916.

- Puteh SEW, Manap RA, Hassan TM, *et al.* The use of e-cigarettes among university students in Malaysia. *Tob Induc Dis* 2018; 16: 57.
- Robert Lourdes TG, Abd Hamid HA, Mohd Yusoff MF, *et al.* Factors associated with e-cigarette usage and the reasons for initiation among Malaysian adolescents. *Asia Pac J Public Health* 2019; 31 (Suppl 7): 44S-52S.
- Roditis ML, Halpern-Felsher B. Adolescents' perceptions of risks and benefits of conventional cigarettes, e-cigarettes, and marijuana: a qualitative analysis. *J Adolesc Health* 2015; 57: 179-85.
- Sabia S, Elbaz A, Dugravot A, *et al.* Impact of smoking on cognitive decline in early old age: the Whitehall II cohort study. *Arc Gen Psychiatry* 2012; 69: 627-35.
- Salthouse TA. What cognitive abilities are involved in trail-making performance? *Intelligence* 2011; 39: 222-32.
- Schaffner M, Sarkar J, Torgler B, Dulleck U. The implications of daylight saving time: a quasi-natural experiment on cognitive performance and risk taking behaviour. *Econ Modelling* 2018; 70: 390-400.
- Schimd T. Asia's E-Cig Regulations: Confusion & Uncertainty, 2016 [cited 2023 Mar 20]. Available from: URL: <https://www.tobaccoasia.com/features/asia-e-cig-regulations-confusion-uncertainty>
- Trivedi JK. Cognitive deficits in psychiatric disorders: current status. *Indian J Psychiatry* 2006; 48: 10-20.
- Weaver SR, Huang J, Pechacek TF, Heath JW, Ashley DL, Eriksen MP. Are electronic nicotine delivery systems helping cigarette smokers quit? Evidence from a prospective cohort study of US adult smokers, 2015-2016. *PloS One* 2018; 13: e0198047.
- Wong LP, Mohamad Shakir SM, Alias H, Aghamohammadi N, Hoe VC. Reasons for using electronic cigarettes and intentions to quit among electronic cigarette users in Malaysia. *J Community Health* 2016; 41:1101-9.
- World Health Organization (WHO). WHO study group on tobacco product regulation: report on the scientific basis of tobacco product regulation: third report of a WHO study group, 2009 [cited 2023 Mar 20]. Available from: URL: https://apps.who.int/iris/bitstream/handle/10665/44213/9789241209557_eng.pdf?sequence=1&isAllowed=y
- World Health Organization (WHO). WHO study group on tobacco product regulation: report on the scientific basis of tobacco product regulation: third report of a WHO study group,

- 2021 [cited 2023 Jun 10]. Available from: URL: <https://apps.who.int/iris/rest/bitstreams/1344663/retrieve>
- Xie C, Xie Z, Li D. Association of electronic cigarette use with self-reported difficulty concentrating, remembering, or making decisions in US youth. *Tob Induc Dis* 2020a; 18: 106.
- Xie Z, Ossip DJ, Rahman I, O'Connor RJ, Li D. Electronic cigarette use and subjective cognitive complaints in adults. *PloS One* 2020b; 15: e0241599.
- Zaytseva Y, Fajnerová I, Dvořáček B, *et al.* Theoretical modeling of cognitive dysfunction in schizophrenia by means of errors and corresponding brain networks. *Front Psychol* 2018; 9: 1027.
- Zulkifli A, Abidin EZ, Abidin NZ, *et al.* Nicotine, propylene glycol and tobacco-specific nitrosamines content in selected E-liquids in Malaysia: the case support for initiation of standards or guidelines, 2018 [cited 2023 Jun 09]. Available from: URL: https://medic.upm.edu.my/upload/dokumen/2018120409020113_MJMHS_SP_Nov_2018.pdf