Passive smoking is associated with cognitive and emotional impairment in adolescent girls

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Running title: Passive smoking and neuropsychological function

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Abstract

It is well established that smoking is associated with impaired mental health and sleep problems. However, the possible effects of passive smoking on cognitive and emotional characteristics have not previously been evaluated in adolescents. We investigated the association between passive smoking and cognitive and emotional function, and sleep patterns in 940 adolescent girls. The girls were divided into 2 groups [305 exposed subjects and 635 non-exposed subjects (the controls)]. The passive smokers had a significantly lower cognitive function and higher depression, aggression, and insomnia scores compared to the control group (P <0.05). No significant difference was detected with respect to day-time sleepiness and sleep apnea. Logistic regression analyses showed that the passive smokers were more likely than the controls to have cognitive impairments, depressive mood, aggressive behavior and insomnia. Adolescents passive smokers had significant differences in their cognitive abilities and emotional function.

Key words: passive smoking, cognitive abilities, depression, insomnia
**Introduction**

The association between active smoking and disease has been investigated for many decades. The first case-control studies showed a strong relationship between active smoking and lung cancer (Proctor, 1988). It is now an accepted that smoking is responsible for the development of several chronic diseases as well as increased morbidity and mortality (Gruer et al., 2009). The effects of passive smoking (PS) on aspects of human health are a growing area of research. Smoke in the environment consists of particles much smaller than those in mainstream smoke and therefore has a greater ability to penetrate the airways of children and adolescents. These are the most susceptible population group to the harmful effects of environmental tobacco smoke (Cheraghi and Salvi, 2009). The prevalence of PS among youth in their homes have been reported to vary from, 34.3% in Southeast Asia, 27.6% in Africa and up to 77.8% in Europe (Warren et al., 2008). Recent studies have shown that environmental tobacco smoke exposure in teenagers may cause an increased risk of premature coronary artery disease (Moskowitz et al., 1999).

Tobacco smoke exposure is also a risk factor for sleep problems in adolescents and adults (Zhang et al., 2006). Shabanayagam and Shankar reported that exposure to environmental tobacco smoke was associated with lower rest/sleep among non-smokers (Sabanayagam and Shankar, 2011). There is also evidence that mental health is affected by passive smoking. However, it is less clear how passive smoking influences psychiatric disorders, even though smoking itself is a well-researched risk factor. Some studies suggest that passive smoking is related to an increased risk of depression, anxiety and decreased cognitive abilities (Bauman et al., 1991; Nakata et al., 2008; Poole-Di Salvo et al., 2010). Frank et al found that passive smoking is positively associated with depressive symptoms in never-smokers (Bandiera et al., 2010). Bauman et al suggested that there was a relationship between parental smoking and cognitive performance in children (Bauman et al., 1991).
We wished to investigate whether teenagers who live in households with smokers are more likely than those that live with non-smokers to have cognitive impairment, depression, aggression and sleep problems.

Methods

Subjects

This cross-sectional study included 940 adolescents girl, aged between 12 and 17 years, who were recruited from different areas in Mashhad and Sabzevar cities in Iran, as described previously (Khayyatzadeh et al., 2017; Tabatabaeizadeh et al., 2017). Adolescents with a history of malignancy, connective tissue disorders, treatment with immunomodulatory drugs (e.g., corticosteroids), liver or renal disease, leucocytosis (white blood cell count >10,000/L), thrombocytosis (platelet count >450,000 × 109/L) or who consumed anti-seizure drugs were the excluded from the study. The Ethics Committee of Mashhad University of Medical Sciences approved the study (931188), that conformed with the provisions of the Declaration of Helsinki (as revised in Fortaleza 2013). Parents and children were informed about the study through oral and written information and gave their written consent. All individuals in the study were given a questionnaire, which included the question “Does one/or both of your parent currently smoke cigarettes or tobacco and are you exposed to smoke during the day for more than 1 hour?”

Neuropsychological assessment

Cognitive abilities Task: Cognitive performances were assessed using the Persian Cognitive Abilities Questionnaire (CAQ) which comprised 30 items, each item being rated on a 5-point scale (1 to 5) and summed up to provide a total score ranging from 30 to 150 (NEJATI, 2013). Higher scores represent better cognition abilities. The CAQ evaluates memory (30 items), inhibitory control and selective attention (30 items), decision making (30 items),
planning (15 items), sustain attention (15 items), social cognition (15 items) and cognitive flexibility (20 items).

**Tests of emotional function**

*Depressive mood:* The Beck Depression Inventory-II (BDI-II), which is a reliable questionnaire to measure depression, was used in this study (Dozois et al., 1998). This questionnaire contains 21 items and each answer being scored on a scale value of 0 to 3. Higher total scores indicate more severe depressive symptoms. Each item represents a single symptom associated with depression, including crying, feelings of hopelessness, body image, hypochondriasis, and difficulty working, fear and loss of appetite, sadness, feelings of guilt and sleep disturbance over the past 2 weeks (Osman et al., 2004). The interpretation of scores is as follow: 0 – 13 points: no or minimal depression, 14 – 19 points: mild depression, 20 – 28 points: moderate depression, and 29 – 63 points: severe depression (Osman et al., 2004). Ghassemzadeh et al. (2005) have previously validated this questionnaire in the Persian (Farsi) language with an acceptable internal consistency (Cronbach's alpha = 0.87) and test-retest reliability (r = 0.74) (Ghassemzadeh et al., 2005).

*Aggressive behaviour:* The Buss-Perry aggression questionnaire (BPAQ) was used to measure aggression among the adolescent groups (Buss AH, 1992). The BPAQ has 29 items with a 5-point rating system (1 = extremely uncharacteristic of me to 5 = extremely characteristic of me). The BPAQ produces a total score plus scores on four subscales: physical aggression (PA, 9 items), verbal aggression (VA, 5 items), anger (A, 7 items), and hostility (H, 8 items) (Santisteban and Alvarado, 2009).

**Tests of sleep pattern**

*Severity of Insomnia:* Insomnia Severity Index (ISI) was used for assessing severity of insomnia. It is a 7-item scale evaluating the perceived severity of insomnia symptoms (initial, middle, terminal), the degree of satisfaction with sleep, interference with daytime
functioning, noticeability of impairments, and concern caused by the sleep problems (Bastien et al., 2001). The scale is Likert-type with 5 anchor points ranging from 0 to 4. The usual time frame for responding is the last 2 weeks. The ISI was validated in its Persian translation, and with an acceptable internal consistency, with a Cronbach’s alpha of 0.82 and good validity has been demonstrated previously (Yazdi et al., 2012).

Severity of sleepiness: The Epworth Sleepiness Scale (ESS) was used for assessing severity day time sleepiness. The ESS is an 8-item, 4-point Likert scale that measures the habitual likelihood to fall asleep in common situations of daily living. Total scores range from 0 to 24. Good validity has been shown for Iranian populations in patients with sleep apnoea (Haghighi et al., 2013).

Severity of sleep apnea: This Stop-Bang Sleep apnea questionnaire is a scoring model consisting of eight questions and is scored based on Yes/No answers (score: 1/0). Hence, the range of the total score is 0–8. The severity code scoring the degree of sleep apnea is as follows: low risk (0–2), Intermediate risk (3–4), High risk (5–8) (Sadeghniiat-Haghighi et al., 2015).

Statistical analysis
All statistical analyses were performed using SPSS for Windows™, version 17 software package (SPSS Inc., Chicago, IL, USA). Data were assessed for normality using the Kolmogorov-Smirnov test. Two groups were compared with independent sample t-test. Depression, aggression and insomnia scores were divided into two categories (no or minimal state and some degree of disorder) according to scores and participants in the first group (no or minimal state) were considered as a reference group. Binary logistic regression analyses were applied to estimate the risk, as approximated by the odds ratio (OR). All the analyses were two-sided and p-value <0.05 was considered as significant.

Results
The study was conducted in January 2015, when 940 girls were examined. Three hundred and five of the 940 subjects were exposed to household smoke (32.4%) and comprised the passive smoking group; 635 subjects were not exposed to household smoking, and were categorized as non-passive smoker group (67.6%). The general characteristics of participants at the time of study are described in Table 1. Their mean age was 14.6±1.55 years (range, 12 to 17 years). There was no significant difference in age, BMI and age at menses, between passive and non-passive smokers; so, the two groups were well-matched regarding to age and BMI.

The non-passive smokers scored more favorably than the passive smoker group on most of the cognitive ability tasks (p<0.01). In memory, inhibitory control and selective attention, decision making, planning, sustain attention and cognitive flexibility tests, passive smokers had statistically significant lower scores compared to non-passive smokers.

Passive smokers scored significantly worse than non-passive smokers for: depression, aggression and severity of insomnia (p<0.05). However there were no significant differences in severity of daytime sleepiness and sleep apnea between these two groups (p>0.05) (Table 2).

In our logistic regression analyses, the group who were non-passive smoker, served as a reference group. Logistic regression analysis show that passive smokers were more likely than non-passive smokers to have cognitive impairment (OR=1.8, 95% confidence interval [CI] = 1.4-2.4; P <0.001), depressive mood (OR=1.7; CI: 1.3-2.2; P <0.001), aggressive behavior (OR=1.5; CI: 1.1-2.0; P=0.003) and insomnia (OR=1.7, CI: 1.2-2.3; P=0.001) (Table 3).

**Discussion**

To our knowledge this is the first study that has studied psychological functions in adolescent passive smokers. Our results suggest that passive smoking is associated with lower cognitive function and increased scores for depression, aggression, and severity of insomnia, but the
association between day-time sleepiness/sleep apnea and passive smoking was not significant.

Earlier studies have shown a positive association between passive smoking and depression in male and female adolescents (Bandiera et al., 2011; Lee, 2014; Poole-Di Salvo et al., 2010). Wietzmn et al, reported that adolescents (aged 15-17 years), who live with smokers are more likely than those who do not live with smokers, to have emotional or behavioural problems and to explore this association in households with non-smoking mothers. After adjustment for potential confounders and well established independent predictors of such problems, adolescents who live with one or more adult smokers are 1.4 times more likely than those who do not live with smokers to have emotional and behavioural problems (Poole-Di Salvo et al., 2010). Nakata et al, conducted a study on 1839 men and 931 women working in Tokyo to assess the relation of passive and active smoking to depressive symptoms and found that the self-report of second-hand smoke exposure was related to depression among Japanese workers, although the study participants were adults (Nakata et al., 2008).

Bandiera et al, (2011) conducted a study in a large representative US population sample aged 8 to 15 years and measurement of serum cotinine level to assess smoke exposure among non-smokers. Serum cotinine level was positively associated with symptoms of Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition) major depressive disorder, attention-deficit/ hyperactivity disorder and generalized anxiety disorder among 2901 children and adolescents (Bandiera et al., 2011). Possible explanations for these results are that prolonged smoke exposure among never-smokers may lead to lower levels of dopamine and lower levels of γ-aminobutyric acid and have been related to an increased risk for depression (Li et al., 2004). Being exposed to cigarette smoke may also cause stress, and stress is associated with depression (Bandiera, 2011). Pahl and collogeous reported that homes in which there
were no smokers had individuals with a healthy lifestyle of diet and exercise, which in turn was associated with less risk of depression (Pahl et al., 2011).

With regards to sleep disorders, we found that passive smoking was associated with severity of insomnia, as observed in other studies (Sabanayagam and Shankar, 2011; Yolton et al., 2010). Sabanayagam and Shankar reported that passive smoke exposure was associated with insufficient rest/ sleep among non-smokers (Sabanayagam and Shankar, 2011). But in the 2005–2006 National Health and Nutrition Examination Survey on 4000+ adult participants, passive smoking was not significantly associated with sleep disorders (Davila et al., 2010).

Nicotine induces the release of sleep regulating neurotransmitters such as dopamine and serotonin, leading to sleep disturbance. Smoking is related to disturbances in sleep architecture and sleep efficiency. Moreover, cigarette smoking influences sleep by triggering respiratory symptoms or involving in sleep disordered breathing(Zhang et al., 2006).

There are also several studies indicating an association between passive smoking and cognitive ability among children and adolescences (Bauman et al., 1991; Yolton et al., 2005) which are consistent with our findings. Yolton et al. (2005) conducted a study on U.S. children and adolescents 6–16 years of age to investigating the relationship between environmental tobacco smoke exposure and cognitive abilities and found a noteworthy inverse association between environmental tobacco smoke (ETS) exposure and cognitive development among children even at extremely low exposure levels (Yolton et al., 2005).

Milberger and co-workers employed a case control study design and found that prenatal tobacco exposure is associated with attention deficit disorder in childhood (Milberger et al., 1998). Fried and co-researchers demonstrated that children exposed to tobacco smoke experienced a great difficulty in tests of visual discrimination, memory, and spatial relationships. Its plausible reason will need further investigation(Fried et al., 1997).
Strengths of our study include the large sample size, a population-based study, and standardized tools for assessment of neuropsychological function. Several limitations of our analysis should be noted. First, the cross-sectional nature of the study did not allow us to make causal inferences. Second, we did not assess exposure to smoke in other settings (e.g., restaurants, or motor vehicles). Third, we did not males, who may be at higher risk of engaging in risk-taking behavior like smoking or spending time with peers who smoke. The effects of nicotine on mood and cognition might be dependent on different factors such as neurobiological/genetic background of the subjects. These leading to the substantial heterogeneity in the underlying causes of cognitive impairments in passive-smokers (Besson and Forget, 2016; Hall et al., 2015). Also the causal relationships may be due to the genetic relationships to the parents, not due to their smoking. This possibility should be discussed in detail in future studies of this type. Finally, since no information was gathered about the extent to which passive smoking may have occurred in other daily environments (e.g., motor vehicles while driving, restaurants while eating, etc.), it is important to point out that other factors may have influenced the finding of present study.

Conclusion

In conclusion we have found that passive smokers appear to be at a higher risk of impaired cognitive function, depression, aggression and insomnia.

Acknowledgements

We sincerely thank all students participating in this study because this study would not be possible without their cooperation. We also extend our appreciation to those who helped us in every way possible in this study.

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Compliance with Ethical Standards:

Conflicts of interest: The authors have no conflicts of interest to declare.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.
References

Bandiera, F.C., 2011. What are candidate biobehavioral mechanisms underlying the association between secondhand smoke exposure and mental health? Medical hypotheses 77 (6), 1009-1010.


Table 1. Anthropometric parameters among the study participants

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Non-smoker 635(67.6%)</th>
<th>Passive smoker 305(32.4%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>14.6±1.5</td>
<td>14.6±1.5</td>
<td>0.981</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>21.3±4.3</td>
<td>20.9±4.3</td>
<td>0.120</td>
</tr>
<tr>
<td>Age of manses (year)</td>
<td>12.6±1.3</td>
<td>12.6±1.0</td>
<td>0.995</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± standard deviation. Independent samples T test was performed. BMI: body mass index
### Table 2. Score of cognitive abilities task, emotional function, sleep pattern in passive smokers and control

<table>
<thead>
<tr>
<th></th>
<th>Non-Smoker group</th>
<th>Passive smoker</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>635 (67.6%)</td>
<td>305 (32.4%)</td>
<td></td>
</tr>
<tr>
<td><strong>Test of cognitive abilities</strong>*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Memory</td>
<td>26.0±3.6</td>
<td>25.1±3.9</td>
<td>0.001</td>
</tr>
<tr>
<td>Inhibitory control and selective attention</td>
<td>18.9±3.9</td>
<td>18±4.1</td>
<td>0.004</td>
</tr>
<tr>
<td>Decision making</td>
<td>19.1±4.2</td>
<td>18.0±4.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Planning</td>
<td>11.4±2.9</td>
<td>10.7±3.1</td>
<td>0.003</td>
</tr>
<tr>
<td>Sustain attention</td>
<td>10.2±3.1</td>
<td>9.5±3.1</td>
<td>0.002</td>
</tr>
<tr>
<td>Social cognition</td>
<td>8.4±3.3</td>
<td>8.2±3.2</td>
<td>0.313</td>
</tr>
<tr>
<td>Cognitive flexibility</td>
<td>13.7±3.3</td>
<td>13.0±3.5</td>
<td>0.004</td>
</tr>
<tr>
<td>Total cognitive ability task</td>
<td>106.7±16.2</td>
<td>103.4±17.0</td>
<td>0.006</td>
</tr>
<tr>
<td><strong>Tests of emotional function</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depressive mood</td>
<td>10.1±9.4</td>
<td>11.9±9.1</td>
<td>0.010</td>
</tr>
<tr>
<td>Aggressive behavior</td>
<td>76.7±20.2</td>
<td>81.7±20.8</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Tests of sleep pattern</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insomnia(ISI)</td>
<td>3.5±5.4</td>
<td>5.1±6.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Day time sleepiness</td>
<td>6.7±3.9</td>
<td>7.0±4.2</td>
<td>0.266</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td>0.6±0.5</td>
<td>0.7±0.5</td>
<td>0.099</td>
</tr>
</tbody>
</table>

By using independent sample t-test
*Higher scores indicates better status
**Lower scores indicates better status
Table 3. Logistic regression analysis of passive smoking as a predictor of cognitive impairments, depressive mood, aggressive behavior and insomnia

<table>
<thead>
<tr>
<th></th>
<th>Cognitive impairments</th>
<th>Depressive mood</th>
<th>Aggressive behavior</th>
<th>Insomnia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Smoker</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>Passive smoker</td>
<td>1.8(1.4-2.4)**</td>
<td>1.7(1.3-2.2)**</td>
<td>1.5(1.1-2.0)**</td>
<td>1.7(1.2-2.3)**</td>
</tr>
</tbody>
</table>

Odds ratios with 95% confidence intervals (95% CI) obtained from binary logistic regression tests adjusted for potential confounders (age and BMI).
*P < 0.05; **P < 0.01; ***P < 0.001.