



**The relationship between olfactory function and executive functioning in
aneurysmal subarachnoid hemorrhage patients**

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Abstract

This study investigates the relationship between different aspects of olfactory function and executive functioning in healthy adults between 20-30 and 50-60 years old. Olfactory function was measured using the Burghart Sniffin' Sticks test, and executive functioning was measured using the D-KEFS Color Word Interference Test (inhibition & cognitive flexibility) and the D-KEFS Tower Test (planning). Multivariate analyses of (co)variance were conducted with and without gender and educational level as covariates. Also, Pearson's correlations were computed without taking age into account, but also for the younger- and older adult group. Results showed that no group differences were found between the younger and older adults on olfactory function or executive functioning. Moreover, without taking age group into account, a positive relationship was found between odor discrimination and planning, which could be mostly accounted for by the older adults. Positive relationships between odor discrimination/TDI score and planning and negative relationships between odor discrimination/-identification and inhibition have been found in the older adult group, whereas no relationship was found in the younger adult group. No relationships between odor threshold and executive functioning have been found. These results support the notion that odor discrimination and -identification rely on the prefrontal cortex and thus encompass overlapping brain regions with executive functioning. For that reason, olfactory function might be cautiously used as a predictor of executive functioning. However, additional research is necessary in both healthy participants as in aSAH patients with various age groups for better understanding about the relationship between olfactory function and executive functioning.

Keywords: Aneurysmal subarachnoid hemorrhage, olfactory function, executive functioning, odor threshold, odor discrimination, odor identification, planning, cognitive flexibility, inhibition

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The relationship between olfactory function and executive functioning in aneurysmal subarachnoid hemorrhage patients

Aneurysmal subarachnoid hemorrhage (aSAH) is known to have a high mortality and morbidity rate. Overall, it leads to fatality in approximately 35-51% of the cases with an early mortality rate between 25 to 35 percent (Al-Khindi, Macdonald, & Schweizer, 2010; Reijmer et al., 2018; Suarez, Tarr, & Selman, 2006). Furthermore, among the survivors aSAH often results in long term consequences leading to a reduced quality of life, social life and not being able to return to work (Al-Khindi et al., 2010; Reijmer et al., 2018). Also, aSAH is a condition that might occur at a variety of ages both young and old but is most common between the age of 40 and 60 years old with a mean age of 55, and with the majority affecting women.

Considering this, most of the patients were still occupied with work and family around the time of aSAH occurrence (Al-Khindi et al., 2010; Jordan, Johnston, Wu, Sidney, & Fullerton, 2009; Singer, Ogilvy, & Rordorf, 2019; Suarez et al., 2006). An aSAH is characterized by an accumulation of blood in the subarachnoid space due to a ruptured intracranial aneurysm, whereas the subarachnoid space is normally filled with cerebrospinal fluid (Al-Khindi, Macdonald, & Schweizer, 2010; Burke, Hughes, Carr, Javadpour, & Pender, 2018).

Following aSAH, many patients suffer from cognitive- and functional impairments even after a substantial period of time (Burke et al., 2018; Reijmer et al., 2018). Patients suffering from cognitive impairments can experience problems with regard to attention, memory, language, visuospatial functioning and executive functioning (Al-Khindi et al, 2010; Burke et al., 2018; Mayer et al, 2002).

Executive functioning is a frequently observed cognitive impairment in aSAH patients and can remain impaired for a longer period of time (Buunk et al., 2016; Haug et al., 2007; Wong et al., 2013). The prevalence of executive dysfunction in aSAH patients has been found

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between 3 and 76 percent. This wide prevalence range can be a consequence of treating executive functioning as a unitary construct instead of differentiating between aspects of executive functioning. As a consequence of executive dysfunction, the patients' occupational reintegration or rehabilitation might be compromised (Al-Khindi et al., 2010; De Avellar, Junior, De Albuquerque, Macedo, & Dellaretti, 2016). Executive functioning can be characterized as a set of higher order cognitive abilities that allow us to engage independently and goal-oriented, also involving mental control and self-regulation. It is comprised of multiple neurologically-based skills such as inhibition, planning, working memory, cognitive flexibility and problem solving (Cooper-Kahn & Dietzel, 2008; de Assis Faria, Dias Alves, & Charchat-Fichman, 2015; Lezak, Howieson, Bigler, & Tranel, 2012; Najdowski, Persicke, & Kung, 2014). However, most studies do not differentiate between these different aspects of executive functioning but consider it as a unitary concept. Nonetheless, it has been found that that some of these aspects can be impaired in patients with aSAH, namely cognitive flexibility, planning, problem solving and inhibition, depending on various aspects such as localization of the aneurysm or the amount of grey- and white matter volume loss (Al-Khindi et al., 2010; Burke et al., 2018; Manning, Pierot, & Dufour, 2005). In all these aspects of executive functioning the prefrontal cortex is involved. It is suggested that the orbitofrontal cortex is activated during response inhibition. Moreover, the medial prefrontal cortex is suggested to be mainly involved in cognitive flexibility, whereas the dorsolateral prefrontal cortex is involved in planning (Fagundo et al, 2015; Kolb, Whishaw, Campbell-Teskey, 2016; Owen, 1997; Sigurdardottir et al., 2016; Takeuchi et al., 2012; Zald & Andreotti, 2010).

Similarly, to executive functioning, olfactory function also relies on the prefrontal cortex. In addition, olfactory dysfunction is also a common symptom in patients with aSAH. As a result, the quality of life of patients might be compromised, possibly due to its broad

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function such as social communication, detecting flavors and mate choice (Croy, Negoias, Novakova, Landis, & Hummel, 2012; De Vries, Menovsky, & Ingels, 2007; Martin et al., 2009; Sigurdardottir et al., 2016). Olfactory functioning can be divided into three components; odor threshold, odor discrimination and odor identification. Odor threshold implies the point at which someone can smell an odor. Odor discrimination is the ability to differentiate between different odors and odor identification the ability to identify different odors (Fagundo et al., 2015). It is found that olfactory dysfunction is associated with changes in the frontotemporal brain regions on a neuropathological level with in particular the orbitofrontal cortex (Sigurdardottir et al., 2016). The ipsilateral olfactory bulb transfers information to the pyriform cortex, amygdala and entorhinal cortex via the lateral olfactory tract. Thereafter, the pyriform cortex sends information to the dorsomedial nucleus in the thalamus. Lastly, the orbitofrontal cortex receives input from the dorsomedial nucleus in the thalamus (Herman, Critchley, & Duka, 2018; Kolb & Wishaw, 2015; Rolls, 2004). Whereas odor detection mainly relies on the olfactory bulb and primary olfactory regions, odor discrimination and odor identification relies predominantly on the orbitofrontal cortex (Herman et al., 2018). Despite the fact that olfactory function mainly relies on the orbitofrontal cortex of the prefrontal cortex, in patients with olfactory dysfunction, structural differences of grey matter also have been found in other areas such as the medial prefrontal cortex, medial dorsolateral prefrontal cortex, insular cortex and piriform cortex. This indicates that other areas besides the orbitofrontal cortex might also be involved in olfactory function (Sigurdardottir et al., 2016).

Thus, the prefrontal cortex, particularly the orbitofrontal cortex is involved in olfactory function as well as in different domains of executive functioning (Rolls, 2004; Yahiaoui-Doktor et al., 2019). With regard to previous conducted research, associations between

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olfactory- and executive functioning have been found. Most studies selected however either older adults or patients with diagnosed diseases/cognitive impairments (Compton et al., 2006; Yahiaoui-Doktor et al., 2019). Several studies found that cognitive impairment is related to olfactory function in the middle aged and elderly without severe neurological diseases, in particular to odor discrimination and odor identification (Jin et al., 2016, Liang et al, 2016; Tian, Resnick, Studenski, 2017). Other studies only found associations between odor identification and cognitive flexibility, inhibition response and decision making (Fagundo et al., 2015). Additionally, the study of Herman et al. (2018) found that lower odor discrimination goes hand in hand with lower planning abilities. Fagundo et al. (2015) suspects that odor identification is linked to brain regions associated with executive functioning, whereas Jin et al. (2016) assumes that odor discrimination and odor identification are linked to areas in the central nervous system. Though both Jin et al. (2016) and Fagundo et al. (2015) suspect that odor threshold is linked to sensory areas. Furthermore, both olfactory dysfunction and impairments in executive functioning usually manifest as a result of frontal lobe lesions (De Guise et al, 2015; Singh et al, 2018). Based on these findings, but also taking into account that both olfactory function and executive functioning rest on overlapping brain regions, it might be possible that an association is present between executive functioning and olfactory function (Fagundo et al., 2015).

In addition, olfactory functioning, including odor discrimination, declines with age. This might be due to reduced activation of the orbitofrontal cortex in older people if a stimulus is presented (Boyce & Shone, 2006; Murphy et al., 2002). Peak performance of olfactory function has been found in the age group 21 to 30 years old (0% anosmia, 9.6% hyposmia, 79.4% normosmia & 11% supersmellers). This performance seems to decline with age, with a most pronounced decrease at the age of 60-71 years old (Oleszkiewicz, Schriever,

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Croy, Hähner, & Hummel, 2019). Executive functioning also deteriorates when someone ages. After the age of 20 the amount of grey matter volume reduces due to atrophy. A decrease in white matter volume is also present. Both structural brain changes are most noticeable in the prefrontal cortex and could be related to a decrease in executive functioning (Harada, Natelson Love, & Triebel, 2013; Fjell, Sneve, Grydeland, Storsve, & Walhovd, 2017).

If there is a relationship between olfactory functions and executive functioning in healthy adults, this could imply that olfactory dysfunction is a predictor for problems with executive functioning. This can be beneficial since aSAH patients often suffer from fatigue, causing difficulties in administering complete neuropsychological assessment (Al-Khindi et al., 2010; Powell, Kitchen, Heslin, & Greenwood, 2002). Additionally, when assessing executive functioning using neuropsychological tests, usually other cognitive functions are also indirectly involved. This implies that measuring solely executive functions is complicated (Jurado & Rosselli, 2007). In sum, if more is known about the role of olfactory dysfunction in relation to executive functioning, it might show the importance of taking olfactory functioning into account when assessing these patients, since this is still not part of the standard routine of assessment (Sigurdardottir et al., 2016)

Therefore, the purpose of this study is to research if there is a correlation between olfactory function and executive functioning. If this relationship is found in healthy adults, it is possible that this is also the case in patients suffering from aSAH. Since aSAH might occur in both younger and older adults this study will focus on both age groups, also taking the previously mentioned aging process into account. Thus, this study will also investigate if older adults perform significantly worse on different domains of executive functioning and olfactory functioning in comparison to younger adults. Since aSAH patients suffering from

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problems with their executive functioning often experience problems with planning, inhibition and cognitive flexibility, this study will mainly focus on these three subdomains of executive functioning (Burke et al., 2018; Manning, Pierot, & Dufour, 2005). This leads to the following research question: Is there a relationship between different domains of executive functioning and olfactory function in healthy controls (either in older or younger controls)?

It is expected that there is a significant positive correlation between olfactory function (odor discrimination and odor identification) and all measured subdomains of executive functioning (with in particular inhibition) in older adults. Additionally, the expectation is that this positive correlation is also found in younger adults. Contrarily, it is hypothesized that there is no significant correlation between odor threshold and all measured subdomains of executive functioning on both younger and older adults. Another expectation is that older adults will perform significantly lower on all domains of executive functioning in comparison to younger adults. Moreover, it is hypothesized that older adults will also perform significantly lower on olfactory function in comparison to younger adults.

Method

Sample

The sample of this study has been compiled by convenience sampling to include healthy adults that were divided into two groups ranging from 20 to 30 and 50 to 60 years old, with the aim of equal group sizes and male/female distribution. Participants were excluded from the study if they have a history of neurological or psychiatric disorders or known olfactory disturbances. An additional exclusion criterion was an insufficiency in Dutch. It was also checked if participants did not suffer from color blindness, because of to the D-KEFS Color Word Interference task that was administered. Recruitment of the participants was done by requesting acquaintances to participate in the study.

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Design

This study is part of a larger research project of Utrecht University and the Universitair Medisch Centrum Utrecht (UMCU) investigating olfactory functions in relation to cognitive functioning in healthy adults. A cross-sectional correlational design was used in this study. The participants were divided into two groups depending on their age. In the first group the age ranged between 20 to 30 years old and was assigned as the ‘younger’ adult’ group, whereas in the second group the age ranged between 50 and 60 and was assigned as the ‘older adult’ group.

Procedure

All participants underwent neuropsychological testing at the Universitair Medisch Centrum Utrecht (UMCU) or at participants’ homes. It was ensured that no disturbances and little or no distracting odors were present. Before testing participants were informed that they were not allowed to eat or drink anything besides water 15 minutes prior to and during testing. Due to anonymization of test results, no informed consent was needed. However, participants were informed about the purpose of the study and that they were allowed to quit testing at any time. First clinical information including gender, age, highest achieved educational level and medical history was obtained from participants. Thereafter, neuropsychological testing included the Burghart Sniffin’ Sticks Threshold Test, Brughart Sniffin’ Sticks Discrimination Test, Brughart Sniffin’ Sticks Identification Test, D-KEFS Color Word Interference Test and lastly D-KEFS Tower Test. Since this study is part of a larger project, the total time to administer the neuropsychological tests was approximately 60-90 minutes, depending on the response time and number of presented pens in the Burghart Sniffin’ Sticks odor threshold subtest. Participants received an VVV-check of 20 euros for participating in the study. No formal ethical assessment was necessary for this study.

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Materials

Executive functioning was measured by administering multiple tests of the Delis-Kaplan Executive Function System (D-KEFS) so that three different domains of executive functioning could be assessed (Delis, Kaplan, & Kramer, 2001). Measures of ‘inhibition’ and ‘cognitive flexibility’ were obtained using the D-KEFS Color Word Interference test. In total, the D-KEFS Color Word Interference test consists of four conditions each containing 48 stimuli. During condition 1 (color condition), participants had to name in which color the square is printed, for example red or green. In condition 2 (word condition) participants had to read words printed in black ink referring to colors. Condition 3 (inhibition) consists of words referring to a color which is printed in an incongruent color, where participants had to name the latter. For example, when seeing a word referring to green but printed in red, they had to answer red. During condition 4 (switching), participants were instructed to do the same as in condition 3, but when the word is outlined to do the opposite. Thus, switching between naming incongruent ink colors and reading the word itself. Participants were asked to complete each condition as fast as possible, but also making as few mistakes as possible. The time taken to complete each condition was registered. The longer time needed to complete the trial implies a worse performance. Raw scores (time to complete one condition) were converted into scaled scores using normative data corrected by age of the D-KEFS Color Word Interference test with an average score of 10 and standard deviation of 3. Thus, scaled contrast scores below 7 indicated worse performance on higher order tasks (condition 3 and 4) in comparison to baseline measurements. Scaled contrast scores between 8 and 12 indicated an equal performance on both higher order tasks and baseline measurements, whereas scaled contrast scores higher than 13 indicated worse performance on baseline measurements in comparison to higher order tasks (Delis, Kaplan, & Kramer, 2001; Kreutzer, DeLuca, &

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Caplan, 2011). The scaled contrast scores for inhibition/switching vs. inhibition were used as scores on the variable 'cognitive flexibility'. Additionally, scaled contrast scores for inhibition vs. color naming were used as scores on the variable 'inhibition'.

Planning skills were measured using the D-KEFS Tower Test. The materials of the test contained five disks varying in sizes and a board with three pins. The test consists of nine trials where participants have to rebuild the tower on the right pin which was presented at a stimulus card as fast as possible with as few steps as possible. Trials ranged in difficulty from easy (containing two disks) to hard (containing five disks). The participants were instructed to only use one hand, move just one disk at a time and that it is not allowed to place a larger disk one that is smaller. Number of steps and rule violations, time taken to complete the trial, time to complete the first step, and whether it is the right tower or not was registered. Scaled scores for accuracy of steps-ratio were used as scores on the variable 'planning' (Delis, Kaplan, & Kramer, 2001; Kreutzer, DeLuca, & Caplan, 2011).

Olfactory function was assessed by using the Burghart Sniffin' Sticks test. This test is comprised of three different subtests to measure odor threshold (T), odor discrimination (D) and odor identification(I). The scores of these three subtests combined indicates the TDI global olfactory score. Each subtest utilizes pens with impregnated tips containing 4 milliliters of antibacterial agents and either odorant fluid or odor substances which is dissolved in propylene glycol. Participants were blindfolded during the test. Also, the examiner wore cotton gloves of neutral odor. The duration of completing all three subtests is 30 to 40 minutes.

The subtest measuring odor threshold consisted of 16 triplets of pens, with in each triplet one pen impregnated with phenylethylalcohol with various concentrations whereas the other two pens were odorless. Concentrations ranged from 4% (pen number 1) to 1.2 ppm_v

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(pen number 16) with a 1:2 volume per volume (v/v) (Denzer et al., 2014). Pens from each triplet were presented in a randomized order. Participants were asked to identify which pen contains the odor. Concentrations were lowered when participants correctly identified the pen with the odorant twice and heightened when they chose incorrectly. This shifting between higher and lower concentrations was done seven times. The odor threshold score consisted of the average score of the last four trials and could range between 1-16. Higher scores indicated a higher odor threshold (Rumeau, Nguyen, & Jankowski, 2016).

The odor discrimination subtests also consisted of 16 triplets of pens. In each triplet two pens contained identical odors whereas the other contained a different odor. Pens from each triplet were presented in a randomized order. Participants were asked to identify which pen contained the different odorant. Scores ranged between 0-16, consisting of the sum of correctly identified trials. Higher scores indicated a higher odor discrimination capacity.

The odor identification subtest contained 16 pens with each pen smelling differently. The following everyday odorants were presented: orange, leather, cinnamon, peppermint, banana, lemon, white spirit, garlic, coffee, clove, apple, pineapple, anise and fish. Participants were asked to identify which smell the pen contained, choosing from a multiple-choice card with four choices. Therefore, participants were not blindfolded during this subtest. Scores ranged between 0-16, consisting of the sum of correctly identified trials. Higher scores indicated a higher odor identification capacity.

The TDI global olfactory score is comprised of the sum of the scores from the three subtests (threshold, discrimination and identification). Scores ranged between 0-48.

Statistical analysis

All data analyses were conducted using IBM SPSS statistics version 25. First, descriptive statistics were used to summarize demographic factors (age, gender and

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educational years) as well as neuropsychological results (results of the Burghart Sniffin' Sticks test, D-KEFS Color Word Interference test and D-KEFS Tower Test). Continuous variables were presented as mean +/- standard deviation (SD), categorical variables were presented as proportions.

Second, it was checked if all assumptions were met. To ascertain if the assumption of homogeneity of error variances was met, Levene's test of equality of error variances was conducted. It was also ensured that the assumption of normally distributed scores was being met using the Shapiro-Wilk Test, or is robust against violation by including sufficient participants.

Third, to analyse if older adults perform significantly lower on both executive functioning and olfactory functioning in comparison to younger adults a one-way multivariate analysis of variance (MANOVA) was computed provided that the assumptions are being met. The one-way MANOVA contained four dependent variables (each subdomain of executive functioning and the TDI score representing olfactory function) and one independent variable (age group). Considering that one's level of education and gender could possibly influence the results on the neuropsychological tests, also a one-way multivariate analysis of covariance (MANCOVA) was computed with educational level and gender as covariates (Hummel, Kobal, Gudziol, & Mackay-Sim, 2007). The same dependent- and independent variables were used as in the one-way multivariate analysis of variance (MANOVA).

To answer the main research question of this study, Pearson's correlation between olfactory functioning (odor threshold, odor discrimination, odor identification and total TDI score) and scores on different tests for executive functioning (inhibition, planning and cognitive flexibility) in total, but also in both the younger adult group and the older adult group were computed. These analyses were computed to see if there is a correlation between

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different domains of olfactory functioning and different subdomains of executive functioning. First, correlations were computed without taking age group into account. Second, different age groups were added to check whether the correlation between odor function and executive functioning is as strong in the younger age group as in the older age group.

Results

In total, 32 participants were included. The participants that were part of this study comprised of 8 men and 8 women in both the young group and older adults group ($M_{\text{age young}} = 22.12$, $SD = 1.75$; $M_{\text{age older}} = 53.88$, $SD = 3.50$). Additional descriptive statistics of participants are presented in Table 1. Neuropsychological results of the Burghart Sniffin' Sticks Test, D-KEFS Color Word Interference Test and D-KEFS Tower test can be found in tables 2,3 and 4 respectively.

The assumption of normally distributed scores are met for the variables odor threshold, odor discrimination and planning using the Shapiro-Wilk Test ($p_{\text{odor threshold}} = .293$, $p_{\text{odor discrimination}} = .134$, $p_{\text{planning}} = .054$). Other variables are however robust against violation ($df_w \geq 30$) (Pallant, 2013). The assumption of homogeneity of variances was met in all analyses, except when analyzing inhibition ($p_{\text{MANOVA}} = 0.025$, $p_{\text{MANCOVA}} = 0.022$). However, the test was robust against violation of this assumption (largest $n_k < 1,5$ times smallest n_k). The assumption of equality of covariance matrices was violated in both analyses using Box's Test ($p_{\text{MANOVA}} = 0.029$, $p_{\text{MANCOVA}} = 0.029$), but was robust against violation due to equal number of observations for each variable.

In the one-way multivariate analysis of variance (MANOVA) no significant effect of age group on olfactory function (TDI score) or executive functioning (planning, inhibition and cognitive flexibility) was found using Wilks' statistic ($\Lambda = .886$, $F(4, 27) = .866$, $p = .497$, $\eta^2 = .114$) (Table 5).

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Also when taking gender and educational level into account, no significant effect of age group on olfactory function (TDI score) or executive functioning (planning, inhibition and cognitive flexibility) was found using Wilks' statistic using a one-way multivariate analysis of covariance (MANCOVA) ($\Lambda = .921$, $F(4, 25) = .537$, $p = .710$, $\eta^2 = .079$). Results of the multivariate analysis of covariance are presented in Table 6.

To analyse if there is a relationship present between different aspects of olfactory functioning and executive functioning, first Pearson's correlation was computed without taking age group into account. Only a moderate to large significant relationship between odor discrimination and planning has been found ($r = .358$ [0.03, 0.65]) (Figure 1). As shown in Table 7, no other significant relationships have been found. Thereafter, it was analysed if this correlation was found in both the younger as in the older adult group. In the younger adult group, no significant relationships have been found between scores on olfactory function (odor threshold, odor discrimination, odor identification and TDI score) and scores on executive functioning (inhibition, cognitive flexibility, and planning) using Pearson's correlation (see Table 8). However, in the older adult group large significant relationships have been found between odor discrimination and inhibition ($r = -.539$ [-0.78, -0.15]), odor identification and inhibition ($r = -.561$ [-0.82, 0.05]), odor discrimination and planning ($r = .541$ [0.02, 0.83]) and TDI global olfactory score and planning ($r = .620$ [0.14, 0.92]) (see Figure 2). No other significant relationships have been found in the older adult group (Table 9).

Discussion

This study assessed the relationship between different domains of executive functioning and olfactory function in healthy adults. It was also assessed if there were differences present with regard to performance on executive functioning and olfactory

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function in younger and older adults. Descriptive statistics show that the younger adults perform better on every domain of olfactory functioning when compared to older adults, except for odor identification. It also shows that when taking age into account, younger adults perform better on baseline measurements (conditions 1 and 2 of the Color Word Interference Test) in comparison to older adults. On the other hand, older adults perform better on higher order functioning (conditions 3 and 4 of the Color Word Interference Test) in comparison to younger adults. Older adults performed also better on planning tasks. However, based on the multivariate analysis of variance (MANOVA) no significant differences were found between both groups on olfactory function (TDI score) and all domains of executive functioning (inhibition, planning & cognitive flexibility). The same conclusion can be stated regarding the results of the multivariate analysis of covariance (MANCOVA). Thus, the hypothesis that older adults will perform significantly lower on all domains of executive functioning in comparison to younger adults as well as the hypothesis that older adults will also perform significantly lower on olfactory function in comparison to younger adults cannot be confirmed based on the results of this research, since no group differences were found. A possible explanation is that multiple aspects of olfactory function and executive functioning (including inhibition, cognitive flexibility and planning) are found to mainly deteriorate after the age of 60-71 and 70, respectively. Therefore, it is possible that the chosen age group for the older adults might have been too young to see any significant differences (Best, Miller, & Jones, 2009; Oleszkiewicz et al., 2019).

Regarding the results of the Pearson correlations, the hypothesis that there is a significant positive correlation between olfactory function (odor discrimination and odor identification) and all measured subdomains of executive functioning in older adults can be partly confirmed. Based on the results of this research only positive relationships between

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odor discrimination/TDI score and planning have been found. Relationships were also found between odor discrimination/identification and inhibition, but were however negative. It remains however unclear why this negative relationship has been found. Contrarily, the hypothesis that this previous mentioned positive correlation is also found in younger adults cannot be supported by the results of this research, since no significant relationships were found in the younger adult group. This indicates that the relationship that has been found between odor discrimination and planning when not taking age group into account can be mainly explained by the effects in the older age group. The hypothesis that there is no significant correlation between odor threshold and all measured subdomains of executive functioning on both younger and older adults can however be confirmed by the results of this research. Thus, participants did not score significantly lower on odor threshold when they score higher/lower on any subdomain of executive functioning or vice versa.

Previous conducted research partly supports the results of this study. In accordance with this study, the study of Herman et al. (2018) also found that lower odor discrimination goes hand in hand with lower planning abilities. Fagundo et al. (2015) found associations between odor identification and inhibition in healthy adults, but not between odor discrimination in females with various ages. Contrarily to this study, they found a positive relationship whereas this study found negative relationships between odor discrimination/identification and inhibition. Although they only assessed females with various ages, no significant differences in scores between male and females were found in this study which indicates that the same results should have been expected. Additionally, they also used different neuropsychological measures to assess executive functioning. The study of Yahiaoui-Doktor et al. (2019) found that better scores on olfactory tests were associated with better scores on executive functioning, which is to some extent in line with the results of this

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study. They however did not differentiate between different aspects of executive functioning and olfactory function. On the contrary, different research did not find any relationship between different aspects of olfactory function and executive functioning. Though they did use different neuropsychological measures to assess executive functioning and did not differentiate between different aspects of executive functioning (Hedner, Larsson, Arnold, Zucco, & Hummel, 2010). It is notable that previously found research did not take odor threshold into account when studying the relationship between olfactory function and executive functioning, or did not find a relationship between these two aspects (Blanco, Sanromán, Pérez-Calvo, Velasco, & Peñacoba, 2018; Fagundo et al., 2015; De Guise et al., 2015; Hedner et al., 2010). Despite this fact, looking at the results of this study and previous conducted studies, it seems that odor discrimination and -identification depends on cognitive-based brain areas, with in particular the prefrontal cortex, whereas odor threshold is more associated with sensory areas of the brain. This finding can be supported, since odor threshold has been found to be related to the volume of the olfactory bulb, whereas odor discrimination and -identification did not (Fagundo et al., 2015; Haehner, Rodewald, Gerber, & Hummel, 2008; Jin et al., 2016).

This study did have several limitations which might have caused the differences in results in comparison to previously conducted research. For one, this study is comprised of a small sample size and thus it might not directly generalizable. Due to a moderate effect size when correcting for gender and educational level ($\eta^2 = .079$), it might have been possible that this study did not find a significant effect, whereas there might be a significant effect present in the studied population. Secondly, little research is available about the relationship between different aspects of olfactory function and executive functioning in healthy adults. It is most frequently studied in patients with diagnosed diseases/cognitive impairments. Therefore not

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much information was available to support the hypotheses of this study. Furthermore, no neurological imaging was collected that captures which brain areas are activated during the administered tests. This imaging data could have provided additional support for the results that were found in this research if it shows that the same brain areas are activated when using olfactory function and executive functioning. Also, only Caucasian people participated in this research, whereas in the normal population there are more cultures present which might have affected the generalizability of the results, since results on executive functioning might differentiate between cultures (Lewis et al., 2009; Roos, Flannery, Beauchamp, & Fisher, 2017).

On the other hand, one of the strengths of this research is that the selection of participants was not constraint to one area, since participants were selected from different provinces of the Netherlands. Also participants with various educational levels were selected to participate in this study. These two aspects increased however the generalizability of the results that were found in this study. Additionally, this study differentiates between different aspects of executive functioning. The chosen aspects of executive functioning are in line with those that are often impaired in aSAH patients. Furthermore, standardized methods for differentiating between different components of olfactory function have been chosen, which is also considered a validated method to differentiate between different aspects of olfactory function (Rumeau et al., 2016).

It can be recommended that future research includes a bigger sample size to enhance the statistical power of the analyses that are done by applying a larger time span to administer neuropsychological testing. Additionally, when selecting patients for neuropsychological testing, a collaboration of multiple hospitals might be taken into consideration in order to include more patients in a smaller period of time, but also to include patients from different

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cultures and different areas. It is also important that olfactory function of aSAH patients (and how this relates to different cognitive functions) is better studied in the future, since not much is known about olfactory functions in aSAH patients but might have a severe impact on the quality of life of these patients. Furthermore, additional research is necessary about the relationship between different aspects of executive functioning and olfactory function in healthy participants. It is recommended to be researched in various age groups, for example also including participants or patients who are older than 60 years old, since this study shows that different relationships can be found in different age groups.

The results of this study and previous conducted studies reveals important implications for clinical practice. Since some relationships were found between higher-order functions of olfaction and different aspects of executive functioning, it shows the importance of implying tests for olfactory functioning in the standard routine of neuro(psycho)logical assessment. Since impairments in odor discrimination/-identification often go hand in hand with problems in executive functioning, dysfunctions in higher-order components of olfaction can be cautiously considered as a predictor for problems with different aspects of executive functioning. Using olfactory functions as a predictor can be beneficial, since patients often suffer from fatigue (among which aSAH patients) and assessing olfactory functions of patients is less cognitively demanding.

Conclusion

To conclude, no differences in scores of olfactory function and executive functioning have been found between younger and older adults. The relationship between odor discrimination and planning could be mostly accounted for by the older adults, since this relationship was only found in the older adult group but not in the younger adult group. Also, relationships between odor discrimination/-identification and inhibition and odor discrimination/TDI score

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and planning have been found in the older adult group, whereas no relationship was found in the younger adult group. No relationships between odor threshold and any of the aspects of executive functioning have been found. Based on the results of this study and previous conducted research, it can be stated that odor discrimination and odor identification mostly rely on brain areas that support our cognitive capacities, with in particular the prefrontal cortex, whereas odor threshold relies on sensory areas such as the olfactory bulb (Fagundo et al., 2015; Herman et al., 2018). Thus, it seems that executive functioning and higher order aspects of olfaction rely on overlapping brain areas. Taking this into account and also that various relationships have been found between these two variables, olfactory function could be cautiously used as a predictor of executive functioning. However, additional research is necessary in both healthy participants as in aSAH patients with various age groups for better understanding about the relationship between olfactory function and executive functioning.

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Appendix

Table 1.

Frequencies, means and standard deviations of clinical characteristics and demographic information

	Sample size (%)	Mean	Standard deviation
Gender			
Men/Women	16/16 (50.0%)	-	-
Age			
Younger adults	-	22.1	1.75
Older adults	-	53.9	3.50
Educational level			
Younger adults	-	5.8	1.04
Older adults	-	6.3	0.9
		5.3	0.9

Note. Educational level is based on the level of education scale from Verhage ranging from 1 (less than 6 years of primary school) to 7 (university degree).

Table 2.

Scores of participants on olfactory measures

	Young age group (20-30 years)			Older age group (50-60 years)		
	Mean	Standard deviation	Range	Mean	Standard deviation	Range
Odor Threshold	8.4	2.1	8.5	6.7	2.8	10.0
Odor discrimination	12.8	2.1	9.0	11.9	1.7	6.0
Odor identification	12.3	2.3	9.0	13.4	1.5	5.0
TDI score	33.5	4.9	19.5	31.9	3.6	13.5

Note. For normative data see Hummel et al. (2007).

Table 3.

Scores of participants on the D-KEFS Color Word Interference Test

	Young age group		Older age group	
	Mean	Standard deviation	Mean	Standard deviation
Condition 1 Color naming raw score	28.5	5.3	31.7	5.3
Condition 2 Word reading raw score	20.0	2.9	22.4	3.8
Condition 3 Inhibition raw score	46.2	9.7	53.0	8.5
Condition 4 Inhibition/switching raw score	55.8	10.6	62.8	20.3
Condition 1 scaled score	9.6	2.6	9.3	2.2
Condition 2 scaled score	11.2	1.8	10.4	2.3
Condition 3 scaled score	11.1	2.4	11.5	1.8
Condition 4 scaled score	10.2	2.4	11.3	3.0
Inhibition vs. Color naming scaled score	11.5	2.7	12.2	1.3
Inhibition/switching vs. Inhibition scaled score	9.1	2.6	9.8	2.8

Note. Raw scores are displayed in seconds.

Table 4.

Scores of participants on the D-KEFS Tower Test

	Young age group		Older age group	
	Mean	Standard deviation	Mean	Standard deviation
Number of executed items	8.9	0.3	8.8	0.6
Total time first step	25.1	19.2	22.8	14.6
Total steps taken	135.8	30.0	132.0	42.6
Total rule violations	0.3	0.8	0.6	0.9
Total time all items	365.8	132.4	363.3	137.9
Performance score	17.9	3.2	18.9	2.2
Performance score (scaled)	10.6	2.1	11.8	1.5
Step accuracy-ratio (scaled)	9.9	2.0	9.0	2.3

Table 5.
Multivariate analysis of variance

Variable	N	Main effect of age group		
		F	P	η
TDI score	32	1.103	.302	.035
Inhibition	32	.857	.362	.028
Cognitive flexibility	32	.621	.437	.020
Planning	32	1.296	.264	.041

Wilks' Lambda $\Lambda = .886$, $F(4, 27) = .866$, $p = .497$, $\eta^2 = .114$

Note. * $p < .05$. ** $p < .01$.

Table 6.
Multivariate analysis of covariance

Variable	N	Main effect of age group		
		F	P	η
TDI score	32	.094	.762	.003
Inhibition	32	.261	.614	.009
Cognitive flexibility	32	.264	.611	.009
Planning	32	2.095	.159	.070

Wilks' Lambda $\Lambda = .921$, $F(4, 25) = .537$, $p = .710$, $\eta^2 = .079$

Note. * $p < .05$. ** $p < .01$.

Table 7.
Pearson's correlation between scaled scores of three domains of executive functioning and different levels of olfactory functioning in total

	Odor threshold	Odor discrimination	Odor identification	TDI score
Inhibition	-.034	-.248	.188	-.046
Cognitive flexibility	.064	.026	.086	.090
Planning	.302	.358*	-.147	.278

Note. * $p < .05$, ** $p < .01$

Table 8.
Pearson's correlation between scaled scores of three domains of executive functioning and different levels of olfactory functioning in younger adults

	Odor threshold	Odor discrimination	Odor identification	TDI score
Inhibition	-.052	-.100	-.372	.109
Cognitive flexibility	.187	.298	.188	.297
Planning	.059	.135	-.277	-.046

Note. * $p < .05$, ** $p < .01$

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Table 9.

Pearson's correlation between scaled scores of three domains of executive functioning and different levels of olfactory functioning in older adults

	Odor threshold	Odor discrimination	Odor identification	TDI score
Inhibition	.151	-.539*	-.561*	-.374
Cognitive flexibility	.074	-.200	-.140	-.096
Planning	.384	.541*	.135	.620*

Note. * $p < .05$, ** $p < .01$

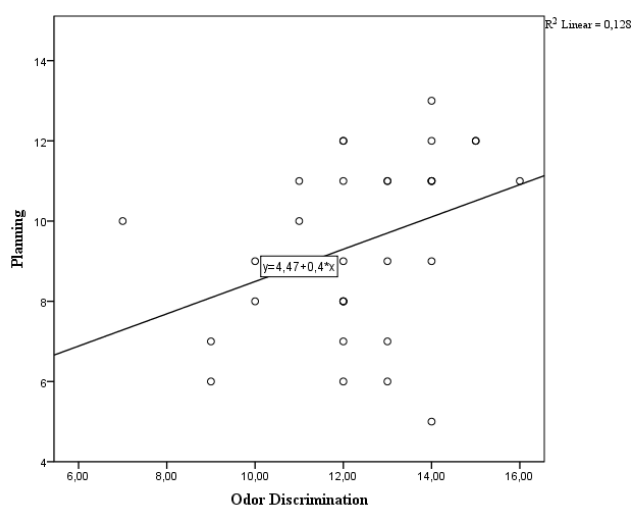


Figure 1. Scatter-plot for the significant relationship between the odor discrimination score on the Burghart Sniffin' Sticks test and the scaled score on planning in total.

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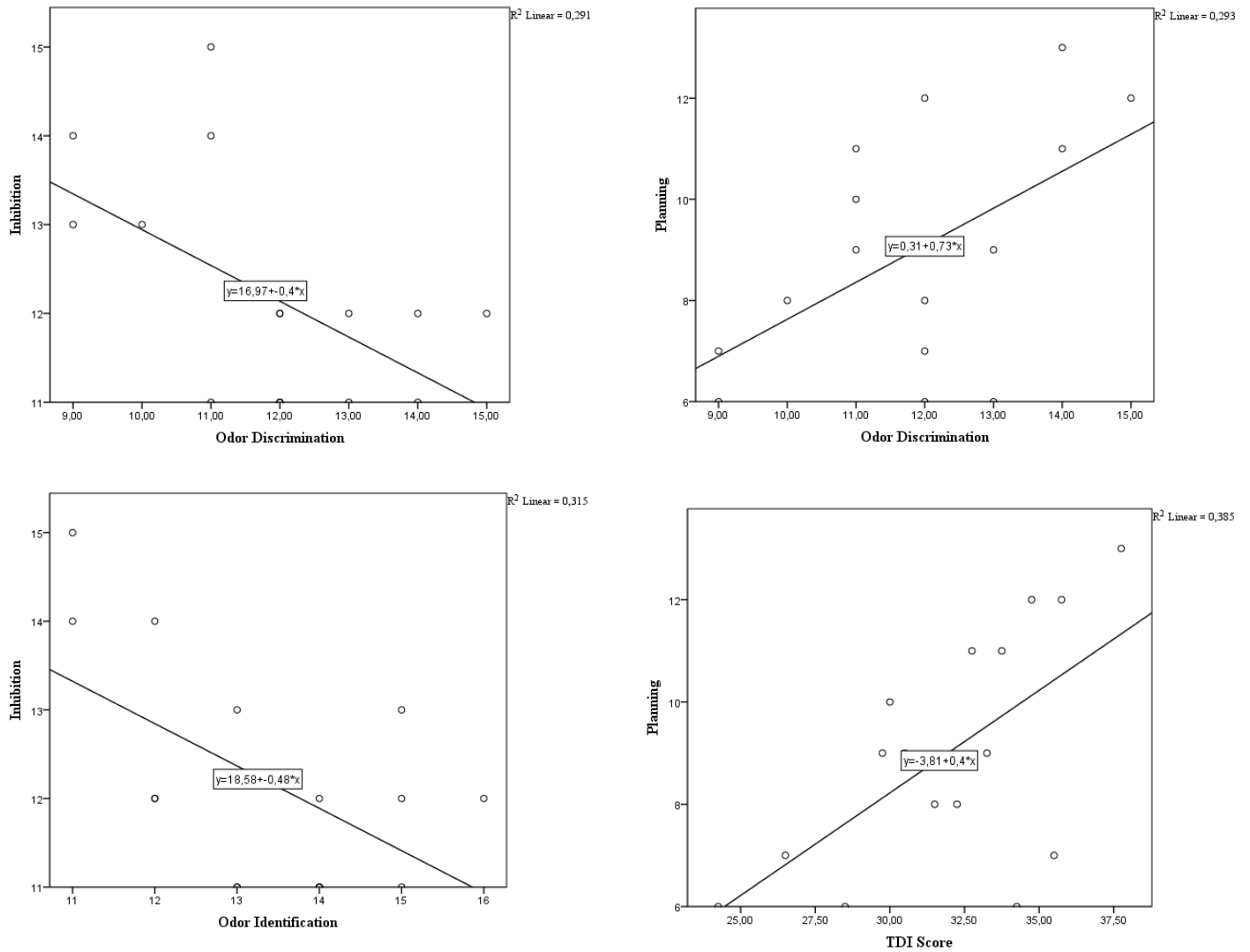


Figure 2. Scatter-plots for the significant relationships between odor discrimination and inhibition/planning, odor identification and inhibition, and TDI score and planning in older adults.