The effect of medication and eating habits on the nutritional status and the sense of smell.
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Foreword

This scientific paper was written in the context of our graduation for the Bachelor Nutrition and Dietetics at the Amsterdam University of Applied Sciences. In the geriatrics department of the Slotervaart Hospital a cross-sectional study is conducted in which we looked at the relationship between the sense of smell and the nutritional status of the patients. This study was commissioned by the dietetics and geriatric department of the Slotervaart Hospital in collaboration with the University of Amsterdam.

We have learned to perform a study in a professional setting, were we gained experience in working with geriatric patients. During the process of our study we have gained more experience with using a statistical program and writing a scientific article.

We would like to thank J.P.C.M. van Campen, the supervising geriatrician and C. Pleune, the supervising dietician for their guidance and constructive criticism. We also want to thank M.J.J. de Bos Kuil, our supervising lecturer of the University of Amsterdam for his guidance and advice during the research.

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Karin Koopmans and Grace Kreuzen
The effect of medication and eating habits on the nutritional status and the sense of smell.

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Abstract

Background: This cross-sectional study is a follow-up study designed to investigate the relationship between the sense of smell and the nutritional status, especially in regard to drugs that may influence smell and taste and eating habits in geriatric patients who visited the geriatric diagnostic day clinic or outpatient clinic of the Slotervaart Hospital located in Amsterdam. This study took place between August and December 2013.

Materials and methods: The Mini Nutritional Assessment-Short Form (MNA-SF) was used to assess the nutritional status. To investigate the smell function of the participants the Sniffin’ Sticks – Screening 12 test was assessed in 138 participants (91 females, mean age 80.9, ± 7.6).

Results: Of the participants 44% were at risk of malnutrition, 16% were malnourished and 40% had a normal nutritional status. The smell test showed that 56% of the participants had reduced sense of smell (hyposmic), 32% had absence of smell (anosmic) and 12% had a normal sense of smell (normosmic). A strong negative significant relation between the sense of smell and nutritional status (p= 0.01) was shown by a linear regression analysis. There was no significant relation found between the sense of smell and medication that can affect smell or smell and taste. There was a weak significant correlation between the results of the smell test and the own assessment of the smell function (r= 0.310, p= <0.001).

Conclusions: This study shows that there is a relation between the sense of smell and nutritional status. Medication with potential effect on smell or taste and smell and eating habits do not have significant effects on the sense of smell and nutritional status. Geriatric patients can poorly assess their own smell function.

Key words: Sense of smell, nutritional status, geriatric patients, eating habits, medication.

Introduction:

The fastest growing part of the population in the Netherlands is the age group above 65 years. Currently 15% of the population is above 65 years. It is expected that this will increase to more than 25% in 2040.¹ ² ³ Aging increases the chance of multi morbidity. Among the 65 years and older 1 out of 5 have multiple chronic diseases and in the 75 years and older this is 50%. The most common diseases include visual disturbances, coronary heart disease, osteoarthritis and diabetes mellitus. ⁴ ⁵ Another common condition in elderly is dementia where Alzheimer is the most common form. ⁶ In 2013 there were 250 thousand persons over 55 years with dementia in the Netherlands.⁷ Elderly often face social, psychological and somatic problems, such as widowhood and loneliness. ⁸ Elderly are living longer independently, therefore they are increasingly less institutionalized. In the Netherlands approximately 95% of the 65 years and older still live independently and only 4% live in a care- or nursing home. The remaining 1% lives in different settings. ⁹ Multi morbidity is considered an important risk factor for malnutrition among the elderly. Malnutrition in Geriatric patients is between 32-61%. ¹⁰ ¹¹ ¹² ¹³ Other common causes of malnutrition found in this group are psychological factors such as depression and stress, loneliness and isolation, cognitive decline, gastrointestinal problems and loss of taste and smell.¹⁴ Changes that occur during aging, such as loss of taste and smell, may enhance malnutrition, due to diminished pleasure in eating and food related activities.⁶ ¹⁵ Several attempts to increase the food intake in elderly have been investigated. For instance, communal dining leads to a higher energy intake in comparison to eating alone. ¹⁶ Communal dining is possibly a protective factor for the nutritional status and the sense of smell. Olfactory loss is a common cause of malnutrition among elderly and
increases with age.\textsuperscript{17} There are different stages of olfactory loss. Anosmia is defined as the complete loss of smell, hyposmia as the partial loss of smell.\textsuperscript{13,18} Loss of smell can be caused by upper airway infection, smoking, head trauma, chronic renal failure, liver disease, diabetes mellitus and medication.\textsuperscript{14} Medication that affect the sense of smell include for example the calcium blockers amlodipine, diltiazem and nifedipine, but are numerous, medication that may affect taste or smell is even more frequent, for example enalapril, clozapine and amitriptyline.\textsuperscript{6,19,20,21,22} The relation between the amount of suspected medication and anosmia has never been systematically studied in geriatric patients with co-morbidity and polypharmacy. This article describes a study on the relationship between the sense of smell and nutritional status, especially with regard to drugs that may influence smell and taste, and eating habits especially the absence or presence of diner companions. Furthermore, this study examined to what degree the elderly geriatric patients are aware of their capacity to smell, since this may have implications for interventions.

Materials and methods:
Participants: Participants were recruited on the geriatric diagnostic day clinic or outpatient clinic of the Slotervaart Hospital in Amsterdam during the period from 23-08-2013 until 06-12-2013. This research is a follow up on the study conducted in the period 26-03-2012 until 29-05-2012 on the geriatric diagnostic day clinic or outpatient clinic of the Slotervaart Hospital in Amsterdam. The participants from both studies are combined in order to create a larger study population, except for the variable eating habits which are only included in the second study. The ethical commission of the hospital granted permission for the study protocol. Participants signed an informed consent in which the study was explained in full detail. The nursing staff of the clinic assessed the MMSE, 7 Minute screen (Benton Temporal Orientation, Enhanced Cued Recall, Clock drawing and Verbal Fluency) and the Geriatric Depression Scale (GDS) of the participants.\textsuperscript{23,24} The patients were screened for their comorbidity with the Charlson Comorbidity Index, to predict the short-term mortality or morbidity. Patients were excluded if their MMSE score was 18 or lower. A score lower than 19 suggest that the patient suffers from a serious cognitive disorder, which means that the answers that are given are not reliable.\textsuperscript{25} The prescribed medication with potential negative effect on taste or smell are included. The literature was studied to examine which medication has a potential effect on taste or smell. The medication is divided into 2 separate categories: medication with a potential effect on smell and medication with a potential effect on smell or taste. From all the patients the laboratory results (ferritin, albumin, vitamin B1, vitamin B12 and folate) were taken to investigate if they have an influence on the sense of smell and nutritional status.

Procedure and measurements:
Questionnaire: The nutritional status of the participants was tested by using the Mini Nutritional Assessment-Short Form (MNA-SF). The MNA-SF is designed to assess the nutritional status in elderly patients and includes questions about appetite loss, weight loss, mobility, acute illness or stress, depression or dementia and the Body Mass Index (BMI).\textsuperscript{26} The assessment was conducted in 138 participants (91 females, mean age 80.9, \pm 7.6). The outcome of the MNA-SF can be: normal nutritional status (score 12-14), at risk of malnutrition (score 8-11) or malnourished (score 0-7).\textsuperscript{27} There was a short questionnaire that consisted of 4 questions to assess eating habits and to examine if social eating habits are a protective factor for malnutrition. The 4 questions were: if patients eat their supper alone or together, if the patients still cook their own supper, if they eat a warm meal every day and if this situation applies to every meal.
Table 1. Participant characteristics per group.

<table>
<thead>
<tr>
<th></th>
<th>Patients participated the MNA-SF and the odor test total. (mean, ±SD)</th>
<th>Patients participated the MNA-SF and the odor test in the 2012 research. (mean, ±SD)</th>
<th>Patients participated the MNA-SF and the odor test in the 2013 research. (mean, ±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>138</td>
<td>73</td>
<td>65</td>
</tr>
<tr>
<td>Female</td>
<td>91</td>
<td>53</td>
<td>38</td>
</tr>
<tr>
<td>Male</td>
<td>47</td>
<td>20</td>
<td>27</td>
</tr>
<tr>
<td>Age</td>
<td>80.9, ± 7.6</td>
<td>82.0, ± 6.6</td>
<td>79.8, ± 8.5</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>26.5, ± 4.6</td>
<td>26.8, ± 4.6</td>
<td>26.2, ± 4.6</td>
</tr>
<tr>
<td>MMSE (score)</td>
<td>25.0, ± 3.1</td>
<td>25.0, ± 3.0</td>
<td>25.0, ± 3.2</td>
</tr>
<tr>
<td>GDS (score)</td>
<td>4.9, ± 3.7</td>
<td>4.7, ± 3.5</td>
<td>5.2, ± 1.4</td>
</tr>
<tr>
<td>MNA-SF (score)</td>
<td>10.2, ± 2.7</td>
<td>10.0, ± 2.7</td>
<td>10.4, ± 2.8</td>
</tr>
<tr>
<td>Vitamin B₁ (nmol/l)</td>
<td>138.6, ± 41.2</td>
<td>122.5, ± 33.8</td>
<td>154.4, ± 42.0</td>
</tr>
<tr>
<td>Folate (nmol/l)</td>
<td>18.1, ± 11.6</td>
<td>21.7, ± 12.6</td>
<td>14.6, ± 9.4</td>
</tr>
<tr>
<td>Vitamin B₁₂ (pmol/l)</td>
<td>323.9, ± 207.6</td>
<td>302.6, ± 203.8</td>
<td>342.4, ± 210.9</td>
</tr>
<tr>
<td>Living situation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Independent</td>
<td>116</td>
<td>65</td>
<td>51</td>
</tr>
<tr>
<td>Rest home</td>
<td>20</td>
<td>7</td>
<td>13</td>
</tr>
<tr>
<td>Nursing home</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Patients with Medication</td>
<td>134</td>
<td>70</td>
<td>64</td>
</tr>
<tr>
<td>With effect on smell</td>
<td>59</td>
<td>30</td>
<td>29</td>
</tr>
<tr>
<td>With effect on taste and smell</td>
<td>51</td>
<td>24</td>
<td>27</td>
</tr>
<tr>
<td>Comorbidity</td>
<td>2.3, ± 1.7</td>
<td>2.3, ± 1.6</td>
<td>2.2, ± 1.9</td>
</tr>
</tbody>
</table>

Odor stimuli:
The Sniffin Sticks test contains 12 odors out of daily life, like coffee, banana, leather and fish. This odor identification test takes approximately four minutes. Each odor pen has to be presented at both nostrils for no longer than 3-4 seconds with an interval of 30 seconds between the different pens. For each odor 4 possible answers are presented on a multiple choice card. The patient has to pick the answer that describes the odor best (forced choice). The results of the test can be anosmic (score 0-5), hyposmic (score 6-9) and normosmic (score 10-12).

Statistical analysis:
Results were analysed with SPSS version 20.0 for Windows. To examine the potential relation between the sense of smell and the nutritional status a linear regression analysis was used. The Pearson Correlation test was used to investigate if there is a match between the results of the smell test and the own assessment of the smell function. The Pearson Correlation test was also used to investigate if there is a match between the eating habits and the nutritional status. To establish a possible relation between results of the smell test and the medication with known effect on smell or smell and taste the independent sample t-test was used.

Results:
The outcome of the MNA-SF showed that 44% of the participants (n = 138) were at risk of malnutrition, 16% were malnourished and 40% had a normal nutritional status.

![Figure 1. Total score on the MNA-SF for the participants that were anosmic, hyposmic or normosmic (n = 138). Shown are boxplots with median, 25⁰ and 75⁰ percentile according as minimum and maximum values.](image-url)
There was a small, non-significant difference in the mean MNA-SF score between men and women (9.9, ±2.5 and 10.3, ±2.9, p=0.378). Of the participants 56% turned out to be hyposmic, 32% turned out to be anosmic and 12% was normosmic. Figure 1 illustrates the mean MNA-SF score of the participants. The mean score for patients who were anosmic was 9.8, ± 2.8, hyposmic 10.0, ± 2.7 and normosmic 11.9, ± 2.4. Between MNA-SF and the three smell groups there was a significant difference (p=0.019). There was no significant difference between men and women in the mean score of the smell test (6.6, ± 2.6 and 6.5, ± 2.7, p=0.813). In the 65th to 80th year group the mean score on the smell test was 6.9, ± 2.2 and in the 80+ group it was 6.2, ± 2.8.

**Table 2.** Unstandardized coefficients, 95% confidence intervals and p-values for the relationship between the sense of smell and nutritional status (dependent variable).

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Unstandardized coefficient</th>
<th>95%-CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple analysis</td>
<td>0.227</td>
<td>0.055-0.400</td>
<td>0.01</td>
</tr>
<tr>
<td>Corrected analysis*</td>
<td>0.224</td>
<td>0.052-0.395</td>
<td>0.011</td>
</tr>
<tr>
<td>Corrected analysis**</td>
<td>0.209</td>
<td>0.043-0.375</td>
<td>0.014</td>
</tr>
<tr>
<td>Corrected analysis***</td>
<td>0.165</td>
<td>-0.014-0.344</td>
<td>0.07</td>
</tr>
</tbody>
</table>

* Corrected for polypharmacy and comorbidity
** Corrected for GDS and smoking
*** Corrected for GDS, smoking, gender, age and MMSE

Linear regression analysis showed a strong relation between the sense of smell and the nutritional status (p=0.01). Corrected for polypharmacy and comorbidity the relation remained significant (p=0.011). Corrected for GDS and smoking the relation also remained significant (p=0.014). Corrected for GDS, smoking, gender, age and MMSE the relation was not significant. The unstandardized coefficient shows that for each correct answer in the smell test the MNA-SF score is expected to increase with 0.165 (95%CI -0.014 – 0.344). No significant difference was found in the results of the smell test among participants that had no cognitive disorder, mild cognitive impairment or dementia. Furthermore no significant relations were found between vitamin B1, folate and vitamin B12 levels and the results of the smell test and the nutritional status. There was no significant relation found between the results of the smell test and the medication shown in table 3 that affect the sense of smell or smell and taste. There was no significant relation found between the MNA-SF and polypharmacy, MNA-SF and comorbidity or smell test results and comorbidity. There was a weak correlation between the results of the smell test and the own assessment of the smell function (r= 0.310, p=<0.001), this means that the patients can poorly assess their own smell function. Women show a weaker correlation compared to men (r= 0.267 and r= 0.399). Of the participants 84% still lives independent, 15% lives in a rest home and 1% lives in a nursing home. The eating habits of 65 participants are included. Of all participants 52% eats dinner on their own, 28% eats dinner with a partner and 20% eats their dinner in a nursing or rest home. Of the participants 43% prepares their own dinner and for 57% dinner is prepared by others (family, neighbours or a communal kitchen). The mean score of the smell test for the participants who cook their own dinner is 6.5, ± 3.1 and for the participants who do not cook their own dinner the mean score is 6.0, ± 2.3, p=0.432. The mean score of the MNA-SF is nearly equal for participants who eat their dinner alone (10.3, ± 2.9) or together (10.5, ± 2.8), p=0.180. There was no significant relation between the MNA-SF and eating dinner alone, the MNA-SF and cooking your own dinner and the results of the smell test and cooking your own dinner.
Table 3. Medication in substance and brand name used by the participants.

<table>
<thead>
<tr>
<th>Medication with potential effect on smell</th>
<th>Medication with potential effect on taste or smell</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amlodipine – norvasc</td>
<td>Amitryptiline – saratex</td>
</tr>
<tr>
<td>Atenolol – tenormin</td>
<td>Amiloride/hydrochlorothiazide – biduret</td>
</tr>
<tr>
<td>Bisoprolol – emcor</td>
<td>Baclofen – lioresal</td>
</tr>
<tr>
<td>Doxycycline – vibramycin</td>
<td>Carbamazepine – tegretol</td>
</tr>
<tr>
<td>Diltiazem – tildiem</td>
<td>Didofenac – voltaren</td>
</tr>
<tr>
<td>Enalapril – renitec</td>
<td>Dipyridamol – persantin</td>
</tr>
<tr>
<td>Metoprolol – selokeen</td>
<td>Doxycycline – vibramycin</td>
</tr>
<tr>
<td>Nifedipine – adalat oros</td>
<td>Diltiazem – tildiem</td>
</tr>
<tr>
<td>Nebivolol – nebilet</td>
<td>Enalapril – renitec</td>
</tr>
<tr>
<td>Sotalol - sotalol</td>
<td>Fentanyline - diphantoine</td>
</tr>
<tr>
<td></td>
<td>Hydrochloorthiazide – acuzide</td>
</tr>
<tr>
<td></td>
<td>Lisinopril/hydrochloorthiazide – zestoretic</td>
</tr>
<tr>
<td></td>
<td>Lithium – camcolit</td>
</tr>
<tr>
<td></td>
<td>Nitroglycerine oromucosaal – nitrolingual</td>
</tr>
<tr>
<td></td>
<td>Nifedipine – adalat oros</td>
</tr>
<tr>
<td></td>
<td>Pravastatine – selektine</td>
</tr>
<tr>
<td></td>
<td>Spirinolacton – alactone</td>
</tr>
</tbody>
</table>

Discussion:
This study shows that there is a negative significant relation between the nutritional status and the sense of smell in the elderly visiting the geriatric dayclinic of the Slotervaart hospital in Amsterdam. There is a relation between the sense of smell and ageing. This is found in several studies. Doty RL et al. showed that the smell function is at its best in the 30th through 50th year and after the 70th year it declines considerably. Between the age of 65 and 80 years, more than half of the participants showed evidence of major olfactory impairment. Three-quarters of the 80+ group shows evidence of major olfactory impairment.29 Lafreniere D et al. showed that in the United States more than 35 million people are aged 65 years or older. Of the people aged over 80 years between 62% and 80% have a significant reduction in the sense of smell. This can affect their nutritional status and their safety.29 Smoliner C et al. showed that of the study population 71.7% were females with a mean age of 79.6, ± 6.3 years. In this study 39.3% had hyposmia and 31.9% had anosmia.30 These data are consistent with the data from our study which showed that 56% of the participants were hyposmic and 32% was anosmic. Our data also showed a lower mean score on the smell test in the 80+ group compared to the 65th to 80th group (6.9, ± 2.2 and 6.2, ± 2.8). The relation between the nutritional status and the olfactory function is mentioned in a few studies.

Duffy VB et al. showed that olfactory dysfunction was present in nearly half of the women with a mean age of 76±6. The participants in this study had a lower interest in food related activities (enjoying cooking, eating a wide variety of foods), a lower preference for foods with sour/bitter taste, a higher intake of sweets and a higher risk for cardiac disease.31 Kim WY et al. showed that in a group of 41 elderly women aged 61 to 81 the smell and taste function were lower than in an equal number of young adults. The lower the smell and taste function in this group the more they complained about a decreased appetite, food intake and weight loss as they aged. Thus, olfactory dysfunction may have an effect on food intake and the nutritional status.32 Our results support the relation between nutritional status and impaired olfactory function. Apart from aging, loneliness and comorbidities, the olfactory function can also be influenced by the use of medication. Lotsch J et al. showed that drugs can influence the complex processing of olfactory information, which can lead to a reduced olfactory function.33 Douglas R et al. showed that more than 250 medications can affect the sense of smell or taste in the elderly.34 Kharoubi S showed that drugs which are used for cardiology, like nifedipine, metoprolol and enalapril, are one of the major medications that can lead to dysfunction in smell and taste.35 These data do not correspond to our study, where a significant
relation between medication and olfactory loss was not found. A study of Nordin S et al. showed that 77% of the elderly and 74% of the patients with Alzheimer Disease had smell loss but at the same time, patients reported that there smell sensitivity was normal.\(^36\) Another study of Nordin S et al. that was done in Sweden investigated the odor detection in 1387 volunteers. They found that when age increases the poorer the sensitivity to smell gets and that women had a better sensitivity than men.\(^37\) Another study about ratings and measures of the olfactory function of Welge-Leussen A et al. examined 152 patients with olfactory dysfunction. Of the patients 78 were anosmic, 64 hyposmic and 10 normosmic. Anosmic patients rated the olfactory impairment significantly higher than patients who were hyposmic and normosmic.\(^38\) Our study shows a small non-significant correlation between the ratings of the patients and the measurements of the olfactory function, which means that the patients were unaware of their olfactory loss. Our data show that women had a weaker correlation compared to men (r=0.267 and r=0.399). This can’t be generalized because there are twice as much women as men in our study. A study of Gibbons MD et al. showed that the eating environment has an effect on the eating habits of elderly. Social environment can have a positive effect on the energy intake. A significant difference is shown in the energy intake between the improved and standard eating environments.\(^39\) Nijs K et al. showed that eating together at mealtimes maintained the quality of life, body weight and the physical performance in elderly.\(^40\) Our study did not show a significant relation between the nutritional status and the eating habits. There can be a few comments made on the current study. This study contains more than 100 participants, which leads to the fact that the results are more reliable. The study population consisted of twice as much women as men. As a result, our findings are difficult to generalize, but in the Netherlands there are demographically more women than men in the 65 + group. To decide which cut off point for correct answers on the smell test could be used to determine malnutrition or the risk of malnutrition a ROC curve should be created. In our study the population was too small to find a good specificity and sensibility to determine the cut off point on the ROC curve. This study used the Sniffin’ Stick 12 test to investigate if the patients had a normal or diminished sense of smell. The Sniffin’ Stick 12 is a validated test, but gives only a rough answer whether someone has a normal or diminished sense of smell. The extended version of the Sniffin’ Stick test is more accurate and consists of 48 sticks using 3 subtests like odor thresholds, discrimination and identification. A limitation of the extended version is that it takes 40 minutes to take the test. This would have been too long for the patients in our study population, because they already experience a day at the diagnostic day clinic as long and stressful. In this group it is good to use the short test, because it takes less time and gives a reasonably reflection of the sense of smell.

**Conclusion:**
This study shows a relation between the nutritional status and the sense of smell in geriatric patients. If the sense of smell is reduced, the nutritional status is also reduced. In this population malnutrition is a common problem, as shown in our study results. To ensure an appropriate treatment, we recommend to screen the nutritional status of all the patients with the MNA-SF and to screen all the patients with malnutrition with the Sniffin’ Sticks 12 test. This study shows how important it is to test the olfactory function instead of trusting on their own judgement, because the elderly can’t judge it correctly. Their own judgement of their sense of smell does not correspond with how it really is. Based on those tests the dietician can adjust the treatment so that the treatment is suitable for the patient. The dietician can give recommendations to make the food more appealing, for example to add more colour, serve the food in an appealing way, use spices or herbs and to use different cooking methods to enhance the flavours.
Acknowledgements
We would like thank Margot de Roon and Nicole Toussaint for their work on the first study and for providing us their data to perform this follow-up study. We would also like to thank the nursing staff of the geriatric diagnostic day clinic and the outpatient clinic of the Slotervaart Hospital for their assistance during the study.

References

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