RESEARCH ARTICLE

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Olfactory training with older people

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Background/objectives: Loss of olfactory function is largely found with aging. Such a reduction in olfactory function affects quality of life and enhances likelihood of depressive symptoms. Furthermore, it has been shown that reduction in olfactory function is associated with cognitive impairment and several diseases such as major depression. Because several studies suggest that discontinuous exposure to odors may improve general olfactory function, the primary aim of this study was to investigate whether such "olfactory training" has positive effects on subjective well-being and cognitive function.

Design: We performed a controlled, unblinded, longitudinal study

Setting: The study took place at an outpatients' clinic of a Department of Otorhinolaryngology at a Medical University.

Participants: A total of 91 participants (age 50 to 84 years) completed testing. They were randomly assigned to an olfactory training (OT) group ($N = 60$) and a control group ($N = 31$). The study included two appointments at the Smell and Taste Clinic.

Measurements: Olfactory and cognitive function as well as subjective well-being was tested using standardized tests.

Intervention: During the 5-month interval between sessions, the OT group completed daily olfactory exposure. During the same time, the control group completed daily Sudoku problems.

Results: Analyses show a significant improvement of olfactory function for participants in the OT group and improved verbal function and subjective well-being. In addition, results indicated a decrease of depressive symptoms.

Conclusion: Based on the present results, OT may constitute an inexpensive, simple way to improve quality of life in older people.

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Introduction

A decrease of the sense of smell may substantially affect quality of life with several studies showing this relation; an overview is given by Croy *et al.* (2014a). In addition, for example, Pause *et al.* (2001) were able to demonstrate that people with diagnosed depression had a reduced olfactory performance. Also, a negative correlation between the olfactory function and depressive symptoms has been detected (Pause *et al.*, 2001; Negoias *et al.*, 2010). In addition, olfactory abilities decrease with age (Murphy *et al.*, 2002; Vennemann *et al.*, 2008; Pinto *et al.*, 2014), and a reduction of olfactory function correlates with cognitive impairment (e.g., Murphy *et al.*, 2002). On the positive side, it has been reported that regular short-term exposure to odors (so-called "olfactory training," OT) can improve general olfactory function in patients with olfactory loss (Hummel *et al.*, 2009a; Sohrabi *et al.*, 2012; Konstantinidis *et al.*, 2013; Damm *et al.*, 2014); in people between 55 and 96 years of age, OT may prevent olfactory decline (Schriever *et al.*, 2014).

In summarizing the current study situation, it seems that OT improves olfactory function in patients with

olfactory loss. Also, patients with signs of depression (Croy and Hummel, 2017) and neurodegenerative diseases often exhibit and suffer from an olfactory loss (Doty *et al.*, 1988; Haehner *et al.*, 2009) and hence a loss of life quality. This leads to the question, whether OT in older people may also modulate subjective well-being and cognitive function.

Hypotheses

We hypothesized that OT would improve olfactory function, which would be accompanied by an improvement of cognitive function in older people. Secondary hypotheses were that (1) OT would improve life quality in older people and (2) that OT would have a positive effect on depressive symptoms.

Methods

Participants

Initially, 121 patients were included in an OT group and a control group, whereof 91 completed the whole study. Participants who did and did not complete the study did not differ with respect to age, sex, or olfactory function. Dropouts were equally distributed on both study groups. The 91 participants were aged between 50 to 84 years (M = 61.1, SD ± 8.7). They were randomly assigned to the OT group (N = 60, age M = 60.8 years, SD ± 7.7, range 50–76 days, sex: 45 women, 15 men) and the control group (N = 31, age M = 61.4 years, SD ± 10.5, range 50–84 days, sex: 26 women, 5 men). The two groups showed no significant differences for number of drugs taken, education, smoking habits, or contact with potential chemical toxic agents. OT was performed over a period of 155 days (SD ± 19, range: 125–242 days). Actually, 90% of our participants were tested in a time frame between 133 and 192 days. Importantly, there were no significant differences of test–retest interval between the OT group and the Sudoku group (p = 0.62).

Inclusion criteria, exclusion criteria, and ethics

Inclusion criteria were as follows: an age between 50 and 85 years, absence of acute or chronic nasal diseases like chronic rhinosinusitis, and normal olfactory function. Normal olfactory function is defined for an age between 30 and 53 years with a cutoff of the Threshold-Discrimination-Identification (TDI) score >29 points. From an age over 53 years, the TDI score has a cutoff of >28 points (Hummel *et al.*, 2007). Exclusion criteria were as follows: neurodegenerative disease, such as Alzheimer's disease, and metabolic diseases, for instance, diabetes mellitus. A standardized medical history was taken to exclude major pathologies that might be accompanied by smell loss, for example, neurodegenerative disease, diabetes mellitus II, or renal or liver disease (Welge-Luessen *et al.*, 2013). Nasal endoscopy using a rigid 30° endoscope (Storz, Tuttlingen, Germany) was performed in all subjects to exclude nasal pathology, which might have interfered with smelling. A Beck Depression Inventory-1 (BDI-1) score of ≥11 was considered as mild subclinical depression (Hautzinger *et al.*, 1995).

All participants gave written informed consent and received a moderate financial reward. The study was conducted according to the Declaration of Helsinki (WMA, 1997) and was approved by the local Ethics Committee (EK 116042013).

Procedure

The study included two appointments where olfactory and cognitive function as well as subjective well-being was assessed using standardized tests. The same tests were applied again after 5 months (see discussion earlier). The OT group completed daily OT, while the control group completed daily Sudoku tasks. After 3 months of OT, the participants were contacted to check on their compliance.

Olfactory training was performed by the participants, twice a day. In the morning and the evening, they smelled four odors (citronellal, eugenol, eucalyptus, and phenyl ethyl alcohol = odors of lime, cloves, eucalyptus, and rose; all odors from Sigma, Deisenhofen, Germany) (Hummel *et al.*, 2009a) and noted odor intensities in a "smell diary" (Damm *et al.*, 2014). This note was used after the training to evaluate whether OT was performed regularly.

The control group solved Sudoku tasks twice daily, in the morning and the evening, over 5 months. We employed an easy Sudoku task, which was provided in paperback form (Bromleigh House Ltd., "Das Megadicke Sudoku Taschenbuch," 2013, Germany). The Sudoku task was performed as long as the OT in the other group of patients. At the end of the study, the control group was asked to show the solved Sudoku tasks. All included participants could prove regular Sudoku training because they filled in all the tasks in the booklet. This procedure was chosen because Owen *et al.* (2010) had reported that a 6-week Sudoku exercise has no significant effect on cognitive function.

Test material

Testing of sensory function

Olfactory testing. All participants received nasal endoscopy to exclude nasal pathology. Assessment of olfactory function was performed using the "Sniffin' Sticks" (Burghart, Wedel, Germany) (Kobal *et al.*, 1996; Hummel *et al.*, 1997). This procedure allows to measure odor thresholds (T), discrimination (D), and identification (I). Results are summated in the TDI score. A reduced TDI score indicates reduced olfactory function (Hummel *et al.*, 2007). Olfactory testing was performed at baseline and after 5-month OT/Sudoku.

The Sniffin' Sticks are odor-dispensing devices based on felt-tip pens. The odors are presented for approximately 3 s each, 2 cm distance in front of both nostrils. For the threshold and the discrimination tasks, participants were blindfolded. Threshold testing was performed for phenyl ethyl alcohol odor using a single-staircase, three-alternative forced choice procedure. Two pens contained the odorless solvent (propylene glycol); one was filled with phenyl ethyl alcohol in a certain concentration; 16 dilution steps are available. The participant's task was to detect the pen containing odor. Odor threshold measurements followed a staircase: If the odor had not been detected, the concentration was increased. If the odor was detected twice in a row, its concentration was decreased. After seven turning points, the average of the last four was used as a threshold estimate.

The discrimination task measured the participant's ability to discriminate between odors. In each of the 16 tasks, two pens were filled with the same odor, one with a different odor. Participants had to detect the one pen that smelled different. Correct answers were summated as discrimination score (D).

The third part of the test was the identification task. Participants were asked to identify the odor from a list of four descriptors. The number of correct answers was summated as identification score (I). Finally, the scores from the three subtests were summated as "TDI score" (Wolfensberger and Schnieper, 1999). An increase of the TDI score of ≥5.5 points was defined as improvement of olfactory function (Gudziol *et al.*, 2006).

Auditory test. Auditory testing was performed to control whether the assumed beneficial effects of OT are domain specific or whether they generalize to other sensory domains. The test setting was a single-staircase design at 1 and 4 kHz (MA 11 Screening Audiometer; Präcitronic, Dresden, Germany). Frequencies were presented separately for each ear in a single-staircase procedure, in 5-dB steps. Measurements were performed three times in a row; the results of which were averaged. Volunteers wearing hearing aid ($N = 10$) were tested without.

Importance of olfaction

The "importance of olfaction questionnaire" (Croy *et al.*, 2010) is divided in three categories: "association," "application," and "consequence." "Association" is related to odor-associated unconscious emotions and memories. "Application" describes how much the sense of smell is used in everyday life. Finally, "consequence" describes whether an odor has direct consequences, for example, on behavior.

Neuropsychological testing

Several neuropsychological tests were performed in order to assess whether OT impacts on cognitive domains.

The Montreal Cognitive Assessment (MoCA) is a screening test to indicate *mild cognitive impairment*. Results ≥26/30 are considered normal (cutoff was 26 points). The test is standardized for participants with ≤12 education years. It was performed to exclude participants with mild cognitive impairment and to detect a possible influence of OT on cognitive function; test sensitivity is 90% (Nasreddine *et al.*, 2005).

The Controlled Oral Word Association Test (COWA; test–retest reliability $r = 0.74$; $p < 0.001$) measures the formal lexical verbal fluency and semantic-categorical fluency (Ruff *et al.*, 1996b). For the measurement of the formal lexical verbal fluency, participants were asked to name as many words possible starting with the letter B, F, or L within 1 min. For the semantic-categorical verbal fluency, participants listed as many words on a topic as possible within 1 min (Ruff *et al.*, 1996a).

The *Auditory Verbal Learning Test* was used in an adapted form. Only the part "Learninglist" was used to explore the short-term memory function (Helmstaeder *et al.*, 2001). The list consists of 15 words, semantically and phonetically independent. The list was slowly read aloud once. Thereafter, the subject should repeat all the remembered words.

The revised d2 *attention and concentration test* measures speed and accuracy to distinguish visual

stimuli. This relates to concentration and attention performance (Brickenkamp *et al.*, 2009). The "concentration power" (combining measures of speed and accuracy) and the percentage of errors (indicating performance accuracy) were analysed.

Depression scale. The BDI-1 (Hautzinger *et al.*, 1995) assesses depressive symptoms. The test assesses the presence of depressive symptoms during the last week based on 21 questions, for example, in the areas of insomnia, loss of appetite, or fatigue. Mild subclinical major depression is assumed for a score of >9 points. The BDI was used because it is documented so well although future studies might rather refer to the updated version BDI-II.

Life quality. The five-question WHO Well-Being Index (Heun *et al.*, 2001) was presented to the subjects on a 6-point Likert scale with the anchor points 5 ("all the time") to 0 ("at no time"). The questions related to the general condition of the last 2 weeks. The test score is the sum of the responses, with 0 points indicating the lowest well-being and 25 points the greatest well-being.

Cognitive age. The cognitive age questionnaire (Barak and Schiffman, 1981) is divided into four basic elements: The "perceived age" evaluates in four items how old a person feels. The "extrinsic age" asks how old a person judges their outer appearance. The "activity age" evaluates whether a person's activities are similar to people within the same age group. The "interest age" evaluates whether a person's interests are similar to people within the same age group.

Statistical analysis

The statistical analysis was performed with SPSS (version 23; SPSS Inc., Chicago, IL, USA). All data were investigated for normal distribution.

Whenever possible, results were analysed with an analysis of variance for repeated measurements. In case data exhibited a nonparametric distribution (e.g., olfactory identification score and BDI score), they were analysed with Mann–Whitney *U*-test. Further, the initial TDI score was correlated to the neuropsychological tests and tests of emotional condition. In order for the effect of age to be excluded, correlations were performed as partial correlations, including age as covariate. The alpha level was set to 0.05 for all results, and a $p < 0.1$ is reported as a trend. Results of the analysis of variance are reported after Greenhouse–Geisser correction, and *post hoc* testing was performed with *t*-tests for dependent samples. Bonferroni correction was applied in addition to non-corrected *p*-values and is indicated by "p_{corr}." The factor of correction was 3 for the three measures of olfactory function, 4 for the four measures of cognitive function, 2 for the measures of depressive symptoms, and 4 for the perceived age.

Sample size calculation was performed with the sample size calculator (UCSF Clinical and Science Institute; http://www.sample-size.net/sample-size-means/). Based on a previous publication (Hummel *et al.*, 2009b) on the effects of smell training on olfactory function, a medium effect size (d = 0.5) and a standard deviation of the outcome of SD = 0.8 were assumed. The total sample size for two unequal groups (one-thirds versus two-thirds) was calculated for 90 participants (a power of 1-β = 0.8; α = 0.05).

Results

Sensory function. Evaluation of the *TDI score* showed a main effect of time (F = 16.4, $p < 0.001$), group (F = 8.6, $p = 0.004$), and an interaction (F = 15.12, $p < 0.001$; effect size 0.96). The training group improved during the course of training ($t = 6.8$, $p < 0.001$), while the controls did not ($p = 0.9$); 20% of the training group participants improved their smelling function by 5.5 points or more, indicating significant individual improvement, whereas only 10% of the control group exhibited such improvement. Evaluation of the *olfactory threshold* showed a main effect of time (F = 20.8, $p < 0.001$) and group (F = 5.2, $p = 0.02$; effect size 0.73) and an interaction (F = 9.8, $p < 0.003$). *Post hoc* testing verified that the training group improved during training ($t = 7.0$, $p < 0.001$), while the controls did not ($t = 0.86$, $p = 0.3$) (Figure 1). In contrast, the *discrimination ability* showed no significant main effect of time (F = 0.3, $p = 0.8$) but a main effect of group (F = 5.4, $p = 0.022$; effect size 0.78). The interaction effect reached a significant level (F = 11.1, $p = 0.001$). *Post hoc* testing verified that the training group improved in the course of training ($t = 2.86$, $p = 0.006$, $p_{corr} = 0.018$), while the controls exhibited a decrease of the discrimination score ($t = 2.06$, $p = 0.05$, p_{corr} = n.s.). The nonparametric evaluation of the *identification ability* before the training showed no difference between the training group and controls ($z = 0.6$, $p = 0.6$); also, after OT, odor identification was not different between groups ($z = 1.12$, $p = 0.2$).

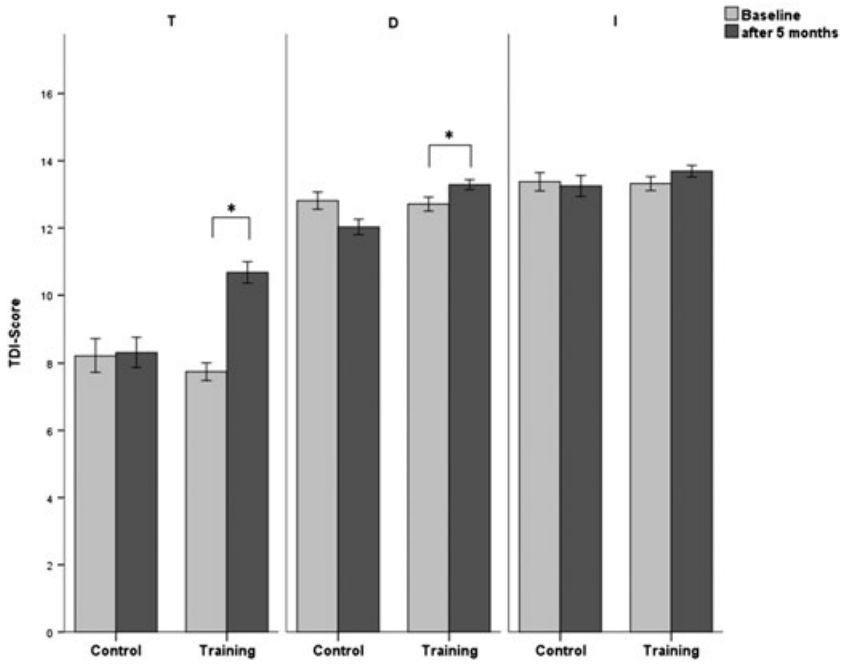

Figure 1 Evaluation of the Transition Dyspnea Index (TDI) score—results (means and standard errors of means) from olfactory testing before (light grey bars) and after the 5-month training period (dark grey bars), using the "Sniffin' Sticks" tests for odor threshold (T), odor discrimination (D), and odor identification (I). The olfactory testing group improved at the level of odor threshold level and the ability to discriminate odors (significant effects indicated by asterisks [*]).

The results of the importance of smell questionnaire did not mirror the objective olfactory testing. There was no significant interaction (F = 0.6, p = 0.44) and no significant main effect of time (F = 1.9, p = 0.17). Similarly, ratings of the intensity of the trained odors showed no significant difference after OT. Finally, the measurement of the auditory functions before and after OT showed no significant difference.

Neuropsychological testing. An evaluation of the overall COWA value showed no significant difference between the two groups. However, an evaluation of the semantic-categorical verbal fluency showed a significant effect of time (F = 19.2, $p < 0.001$). Although the main factor group showed no significant effect (F = 0.5, p = 0.5), there was a significant interaction group * time (F = 4.3, p = 0.04), indicating that the training group improved in the course of training (t = 5.8, $p < 0.001$, p_{corr} = 0.004), while the control did not (t = 1.4, p = 0.1) (Figure 2).

There was no significant interaction effect on the overall MoCA value. However, the short-term memory subscore showed a significant effect of time (F = 32.0, $p < 0.001$); although the main factor group showed no significant effect (F = 0.002, p = 1.0), there was a significant interaction group * time (F = 4.2, p = 0.045). *Post hoc* testing revealed that both groups showed a significant effect in the course of training (training group: $t = -6.7$, $p < 0.001$, p_{corr} = 0.004; comparison group: $t = -2.49$, p = 0.02, p_{corr} = n.s.) but that this was much more pronounced in the group that performed the OT.

The measurement of the short-term memory using the Auditory Verbal Learning Test showed no significant results; neither did the measurement of attentiveness using the d2 attention test.

Testing on emotional condition. The BDI-1 was analysed in the subgroup of patients suffering from at least mild depressive symptoms. No difference between the two groups was found at baseline ($z = -8.09$, p = 1.0). The second testing indicated a significant difference ($z = -2.21$, p = 0.02, p_{corr} = 0.04; effect size 0.23). The training group exhibited a decrease of their depression score by about four points. This subgroup of the whole sample also showed a significant improvement of the TDI score (p = 0.026, p_{corr} = 0.052) (Figure 3).

No significant change was found according to the WHO-5 Well-Being questionnaire (interaction effect: F = 1.8, p = 0.2). The evaluation of the BDI-1 cutoff group showed no significant effect of time (F = 2.5, p = 0.13) or group (F = 0.12, p = 0.73), but a trend

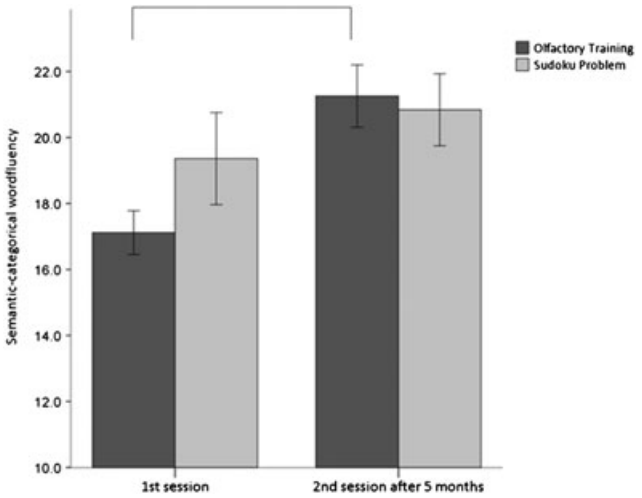

Figure 2 Evaluation of the semantic-categorical verbal fluency—results (means, standard errors of means) of the Controlled Oral Word Association Test score, before (first session) and after the olfactory testing (second session after 5 months). The training group (dark grey bar) improved their ability of semantic-categorical verbal fluency, while the comparison group showed no significant differences (significant effects indicated by asterisks [*]).

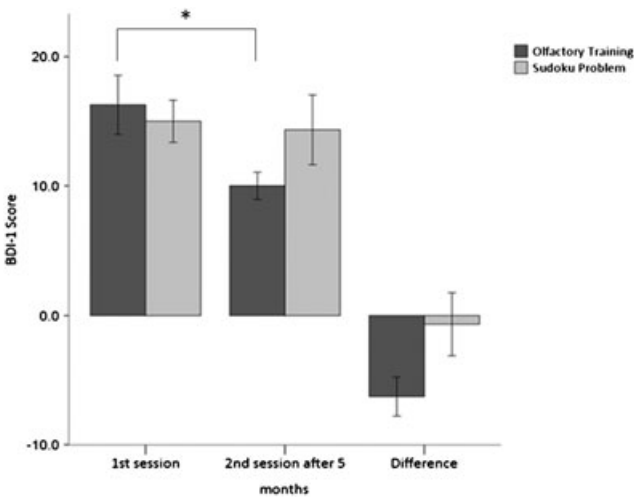

Figure 3 Evaluation on emotional condition—results of the Beck Depression Inventory-1 (BDI-1) score (means and standard errors of means). Participants with a subclinical depression (BDI-1 ≥ 11) (dark grey bars) at baseline (first session) reduced their BDI-1 score after the training (second session after 5 months), while the comparison group (BDI-1 ≥ 11) showed no significant differences after the training (significant effects indicated by asterisks [*]).

for the interaction effect (F = 3.7, $p = 0.07$). *Post hoc* testing verified that the training group improved in the course of training ($t = 2.5$, $p = 0.02$, $p_{corr} = 0.04$), while the control group did not ($t = 0.3$, $p = 0.8$). When looking only at those participants who scored higher than nine points at the baseline BDI, subjects performing the OT exhibited a significantly higher score on the WHO-5 Well-Being than the controls (Mann–Whitney *U*-test—$p = 0.022$, $p_{corr} = 0.04$; effect size 0.36).

Evaluation of the cognitive age questionnaire detected no changes for the perceived age, the extrinsic age, or the interest age. However, activity age showed no significant main effect of time (F = 3.1, $p = 0.6$) or group (F = 0.4, $p = 0.5$), but a significant interaction effect (F = 6.4, $p = 0.014$) (Figure 4).

Discussion

This study showed a positive effect of OT in older people on olfactory function, which extended to general mood and depressive symptoms. Especially, the subgroup of participants with subclinical depression profited from OT. For cognitive function, a positive effect on verbal fluency was observed, but no effect on short-term memory or attentiveness.

Sensory function. After 5 months of regular exposure to odors, 20% of the training group exhibited improvement of their TDI score on an individual level for more than 5.5 points, while only 10% in the comparison group improved by more than 5.5 points. In particular, on a group level, significant improvements were found for olfactory thresholds and odor discrimination ability. An improvement of

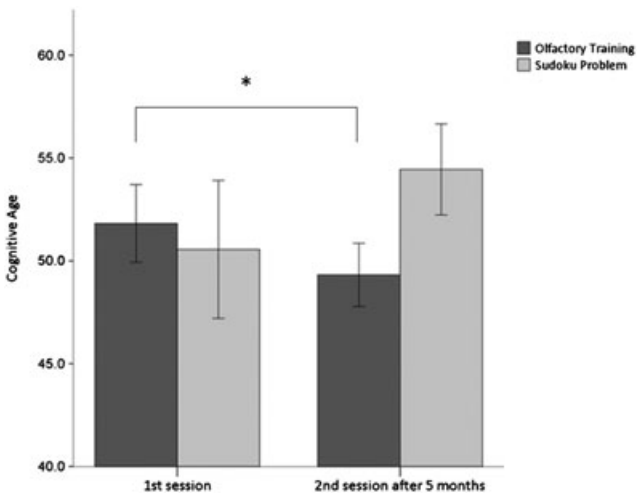

Figure 4 Evaluation of the cognitive age—results of the cognitive age questionnaire (means and standard errors of means). After the olfactory testing, the training group (dark grey bar) indicated their activity age 6 years younger than the comparison group (significant effects indicated by asterisks [*]).

odor threshold after OT was also found in recent studies (Youngentob and Kent, 1995; Wang *et al.*, 2004; Hummel *et al.*, 2009b). The discrimination ability improves in the course of training. In the control group, a decrease in discrimination ability could be observed. This could also be described in a study by Schriever *et al.* (2014) in older people. The OT showed little or no effect on the identification ability. The absence of an effect of OT on odor identification has also been observed in previous studies (Kollndorfer *et al.*, 2013; Geissler *et al.*, 2014). In the present study, a ceiling effect might be the reason for the absence of an effect. As an effect on the side, we did not find a significant effect of OT on auditory function. Overall, however, OT specifically improved measured olfactory function in the training group.

Neuropsychological testing. Olfactory training improved semantic-categorical verbal fluency. This association between cognitive function and olfactory sensitivity was also present in the correlation between initial TDI scores and the semantic-categorical verbal fluency. Similarly, Haehner *et al.* (2013) showed that patients with Parkinson's disease with an impairment of verbal fluency improved after OT. Also, Parrao *et al.* (2012) assumed a close association between cognitive function and olfactory function in Parkinson's disease.

The short-term memory as measured with the MoCA showed a significant improvement in the course of training. This effect has also been shown in patients with Parkinson's disease from the study mentioned earlier (Haehner *et al.*, 2013). However, results from the short-term memory test showed no significant change during OT. This missing congruence may be because both VLMT and MoCA have not been used in a clinical diagnostic setting but have been introduced as screening tools. Thus, more specific studies are needed to explore the possible positive effect of OT on short-term-memory.

Moreover, OT showed a positive effect on the activity age. This also supports the findings in terms of cognitive function in patients performing the OT.

Olfactory training had no effect on the participants' attention and concentration. This may indicate a specific effect of OT on verbal functions, possible on the basis that a major function of the sense of smell lies in social communication (Stevenson, 2010).

The hypotheses that OT improves overall olfactory function and goes along with an improvement of aspects of cognitive function in older people can be confirmed by the available data.

Testing on emotional condition. Olfactory training significantly improved general well-being, scores on the WHO-5 Well-Being test, and depression in those people who were impaired prior to testing.

Recent studies provide evidence that patients with major depression exhibit a decreased olfactory function (Pause *et al.*, 2001; Croy *et al.*, 2014b; Croy and Hummel, 2017), which is even seen on a structural level in terms of a diminished volume of the olfactory bulb (Negoias *et al.*, 2010). In the present investigation, OT participants with mild subclinical depression showed a decrease of depressive symptoms. Thus, OT appears to have a positive effect on the emotional state—albeit the study sample was relatively small. It seems likely that these effects are mediated through the connection between olfactory eloquent structures and structures like amygdala and orbitofrontal cortex (Gottfried, 2006), which play a decisive role in the development of depressive symptoms (Palazidou, 2012). Similar effects of odors in major depression have also been reported in a double-blind study where lemon odor was reported to be as effective as antidepressants in a 4- to 11-week treatment period (Komori *et al.*, 1995).

The results of the study support the hypotheses that OT improves quality of life in older people and seems to have a positive effect on depressive symptoms.

Limitations. (1) Regarding the sex distribution of subjects participating in the study, a higher woman rate was observed. In this study, the rate of men in the training group was 27% and 18% in the control. The higher rate of women has been taken into account. However, this study did not include a sex-specific question. (2) The improvement of depressive symptoms in this study is shown in older people. The question is whether the data in this study are transferable to younger people. (3) In addition, the incidence of patients with subclinical depression who could benefit from the OT is very low. At this point, there is a need for further studies. (4) Also, a factor that is influencing the results of this study is the participant's compliance according to the OT. This question cannot be answered, although "smell diaries" were kept and controlled. An attempt was made to strengthen compliance by means of an attractively designed book and regular contact to the participants.

Conclusions

Five-month OT in people over 50 years of age improved general olfactory. This effect is selective

and does not expand to auditory sensory function. OT further showed a positive effect on semantic-categorical verbal fluency and improvement in terms of emotional well-being and depressive symptoms in people at risk. Although further studies are needed, OT seems to constitute an inexpensive and simple way to improve quality of life in older people.

Conflict of interest

None declared.

Key points

- Loss of olfactory function is largely found with aging.
- Discontinuous exposure to odors was performed with older people, over 5 months.
- Discontinuous exposure to odors improves general olfactory function.
- Olfactory training in older people improved general olfactory function, verbal function, subjective well-being, and, in a subgroup, also depressive symptoms.
- Results indicated a decrease of depressive symptoms.

Acknowledgement

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Author contributions

All authors (W. B. A., C. I., A. H., and T. H.) contributed to the design, preparation, and write-up of the study. W. B. A. collected all the data.

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