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# Beyond Olfaction: Beneficial Effects of Olfactory Training Extend to Aging-Related Cognitive Decline

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Studies on olfactory training (OT) outcomes have mostly been limited to olfactory performance, while direct neural connections between olfactory system and amygdala–hippocampal complex allow expecting OT to have psychological effects. To address this hypothesis, we examined olfactory, cognitive and emotional effects of OT in the group of 68 subjects aged between 50 and 88 years ($M_{age}$ = 62.8 ± 8.9 years; 28 males) who are likely to experience an age-related decline in olfactory and cognitive performance. We diversified stimuli used in the OT to verify whether odor mixtures result in more effective activation of olfactory receptor neurons than single molecule odors. Subjects were randomly assigned to one of the experimental conditions: (a) simple OT utilizing single-molecule odors; (b) mixtures OT using odor mixtures; (c) control group without OT. Results indicate beneficent effects of the simple OT on cognitive assessment, cognitive decline symptoms, and olfactory sensitivity. OT can be adapted from otorhinolaryngological practice to successfully serve neurocognitive research and in supporting the cognitive-related aging process.

*Keywords:* olfaction, olfactory training, olfactory threshold, cognitive decline, aging



Humans interact with chemical properties of their environment through the olfactory system. Detection of odorants starts in the nasal cavity where olfactory receptors (ORs) are located (Rinaldi, 2007). An odor-specific cellular response is converted into an electrical signal and further transmitted to the olfactory bulb where olfactory processing takes place. Next, the signals from the olfactory bulb are transmitted to the olfactory cortex (Ache & Young, 2005; Buck, 2004; Kay & Sherman, 2007) and other cortical areas including those involved in the processing of emotions, memories, hearing and seeing, such as amygdala, hippocampus, retina, and auditory cortex (Royet & Plailly, 2004; Wesson & Wilson, 2011). Interestingly, the thalamus relays only portions of the olfactory input. In part, olfactory information is sent directly and immediately to the amygdala–hippocampal complex, suggesting a primal effect of olfactory information on cognition and emotions (Cahill et al., 1995). None of the remaining sensory modalities have direct access to these brain structures. Therefore, the unique meaning of the sense of smell is rooted in its strong limbic projections of the olfactory pathways (Brand, 1999; Savic, 2001; van Toller, 1988). For this reason, certain odors can interact with cognition and emotions (Ehrlichman & Bastone, 1992; Kirk-Smith & Booth, 1987; Spangenberg et al., 1996) usually in a way that more pleasant odorants are followed by positive emotions or enhanced cognitive performance whilst unpleasant odors elicit negative emotions and decreased cognitive performance (Millot et al., 2002). Valence and frequency of olfactory stimulation have a large effect on cognition. It has been found that both pleasant and unpleasant smells decrease reaction time to visual and auditory stimuli, as compared to no-odor conditions (Millot et al., 2002), suggesting highly efficient arousal potential of the human chemosensory environment.

The olfactory system exhibits plasticity and susceptibility to systematic rehabilitation. The olfactory bulb, a key structure linking peripheral and central processing of olfactory stimulation, changes its volume as a function of exposure to peripheral olfactory input (Gudziol et al., 2009; Huart et al., 2013; Hummel et al., 2015; Rombaux et al., 2010), although it might also be affected by top down processes (Croy et al., 2013; Negoias et al., 2010, 2016; Thomann et al., 2009) further suggesting an interplay between chemosensory perception and higher order neural processes. Changes in olfactory bulb in association with exposure to olfactory enriched environments can be observed even at early stages of neurogenesis (Rochefort et al., 2002). Olfactory receptor neurons (ORNs) are able to regenerate and increase activation capacity when exposed to frequent short-term exposures to odors over a period of at least 12 weeks (Schwob et al., 1999; Youngentob & Kent, 1995). All these signs of olfactory system plasticity have been observed to improve in the course of olfactory training (OT) (Huart et al., 2013; Hummel et al., 2018; Kim et al., 2020; Negoias et al., 2017; Sorokowska et al., 2017). Many questions about the usefulness

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The experiment was not preregistered.

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The authors declare no conflict of interest.

Relevant raw data will be freely available to any researcher wishing to use them for noncommercial purposes, without breaching participants confidentiality.

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of this noninvasive method of brain stimulation are open, including its psychological effects—specifically in the cognitive and emotional domains that have strong neural connections to the olfactory system.

The vast majority of experimental evidence on OT concerned olfaction-related effects of this method with special attention paid to otorhniolaryngological patients and the relationship between olfactory loss etiology and OT outcomes (Damm et al., 2014; Fleiner et al., 2012; Hummel et al., 2009; Pekala et al., 2016; Sorokowska et al., 2017). Although aging constitutes the major cause of olfactory loss (Hummel & Oleszkiewicz, 2020), older subjects remain poorly explored within the context of OT. The few reports on OT effects among older subjects are incoherent. While one study showed no significant improvement of olfactory function among older subjects with an age range between 50 and 88 years (yet no deterioration that would be likely in this age group without OT; Schriever et al., 2014), another report showed enhanced olfactory performance, improved well-being and verbal functions in subjects aged 50–84 years (Wegener et al., 2018). Simply because age-related olfactory loss affects such a large number of people it appears to be vital to further examine effects of OT on cognitive and emotional functioning in this particular group, where rapid decline in these domains is plausible (Brunoni & Vanderhasselt, 2014). To date, cognitive processing has been known to enhance during regular electrical and magnetic stimulation (Brunoni & Vanderhasselt, 2014; Hamani et al., 2008; Schneider et al., 2003), however, no studies on a regular, intermittent olfactory stimulation (OT) with this regard have been done, despite the compelling evidence for the neural connections between olfaction and cognitive functions. Therefore, the present study is of great importance to establish an innovative, simple, easy and inexpensive method to provide support in the cognitive aging process. To this end, we performed an experimental study investigating effects of OT on cognitive and emotional functions among subjects likely to exhibit aging-related cognitive and emotional decline. We hypothesized that odor mixtures may be more efficient in activating ORNs than single odors, and thus yield stronger cognitive and emotional effects of OT, due to the documented individual variation in ORNs expression (Verbeurgt et al., 2014; Croy et al., 2015) and degeneration of peripheral olfactory system as a result of aging (Robinson et al., 2002).

## Material and Method

### Ethics Statement

The study was performed in accordance to the Declaration of Helsinki on Biomedical Studies Involving Human Subjects. Informed written consent was obtained from all participants. The study design and consent approach were approved by the Ethics Review Board at the TU Dresden (EK21022018) and the Institutional Review Board at the University of Wroclaw.

### Participants

We determined sample size by utilizing G*Power software (Faul et al., 2007). Within the repeated measures design with between-within group interactions (described in detail in the *Statistical approach* section), to obtain power of .95 with α level set to .05 to detect moderate effects of $f = .25$ (Sorokowska et al., 2017), the projected sample size was at least 66 subjects. Due to the possibility of dropouts in our sample, we initially recruited approximately 78 subjects. Of those 10 did not complete the study procedure (i.e. did not show up for the post-training measurement; $M_{age} = 58.3 \pm 4.03$ years; 5 males; dropping out was independent from experimental condition assignment, $\chi^2(2) = .40$, $p = .82$). The final sample was 68 subjects ($M_{age} = 62.8 \pm 8.9$ years; 28 males). The excluded subjects were about the same age as the included subjects, $t(73) = -1.24$, $p = .22$, [−11.67; 2.68] and had a similar baseline olfactory performance, $t(62) = -.92$, $p = .36$, [−6.97; 2.58]).

### Procedure

All participants took part in two sessions—before and after OT. During the first session, a standardized medical interview was conducted to monitor factors potentially undermining olfactory performance such as head traumas, diabetes or smoking (Welge-Lüssen et al., 2013). In both sessions olfactory function was comprehensively assessed using the Sniffin' Sticks test battery (Hummel et al., 1997; Oleszkiewicz et al., 2019). The Sniffin' Sticks battery comprises three subtests: (a) threshold which reflects the lowest concentration detected by the subjects that is established in a three alternative forced choice paradigm. Subject is presented with the triplets of pens and has to discriminate one pen containing an odorous solution from two blanks filled with the solvent. Sixteen concentrations are created by stepwise diluting previous ones by 1:2 (beginning with the highest concentration of 4%). Starting with the lowest odor concentration, a staircase paradigm is used where two subsequent correct identifications of the odorous pen or one incorrect navigate a decrease or increase of the concentration (respectively); (b) the discrimination subtest comprises 16 triplets of pens; however, they are administered in ascending order of numbers. Within each triplet two odors are identical and one is different. Subject is asked to indicate the nonpaired odor; (c) identification subtest wherein subject labels the smell, using four alternative descriptors for each pen. Detailed instruction can be found in Hummel et al. (1997) and normative data (Oleszkiewicz et al., 2019). Subjects were asked to rate their olfactory function using a visual analogue scale (0 = no sense of smell, 100 = excellent sense of smell). Several other tests focused on cognitive and emotional functions. Cognitive function was assessed with Montreal Cognitive Assessment (MOCA) (Nasreddine et al., 2005), Dementia Screening Interview (AD8) (Galvin et al., 2005) and Controlled Oral Word Association Test (COWAT) (Hall et al., 2010). Emotional functioning was measured with Beck Depression Inventory (BDI) (Beck et al., 1988), Positive and Negative Affect Schedule (PANAS) (Watson et al., 1988).

The duration of OT ranged from 3 to 6 months ($M = 4.13$, $SD = .42$ months). Participants were randomly assigned to one of the three experimental conditions: (a) "simple" training comprising nine single-molecule substances ($n = 26$); (b) "mixtures" training involving nine odor mixtures (multi-molecule substances provided by the Smell Lab, Geneva, Switzerland; $n = 27$); (c) control group with no OT at all ($n = 15$). Odors used in the study are summarized in Table 1. The selection of odors aimed to provide olfactory and trigeminal stimulation and evoke memories and associations (e.g. sea breeze, freshly mown hay, homemade pastries). Odors were selected arbitrary by a panel of experts to be likely to evoke pleasant memories and positive associations, and to present

**Table 1**
*Odors Used in the Two Experimental Conditions*

| Single-molecule odors [order number] | Odor mixtures (region of origin) [order number] |
|---|---|
| Eugenol W246700[1] | Clove bud essential oil (Indonesia)[4] |
| Eucalyptol C80601[1] | Eucalyptus essential oil (China)[4] |
| Citral 27450[3] | Yellow mandarine blend (France)[4] |
| Menthol 2416[2] | Peppermint oil[7] |
| Anethol 11870[1] | Star anise essential oil (South Europe)[4] |
| Ethylvanillin 4985001[4] | vanilla mauvais essential oil (Comores) [5] |
| Cumarine 4185001[4] | Tonka beans absolute (South America)[4] |
| Calone 3194201[4] | Sea odor [PRT10391 15%][6] |
| Butanol B7906[1] | Burnt rubber [PRT10390 AE 5%][6] |

Manufacturers: 1—Sigma Aldrich, Taufkirchen, Germany; 2—Caelo, Hilden, Germany; 3—Fluka, München, Germany; 4—Givaudan, Dübendorf, Switzerland; Argenteuil, France; 5—Atelier Français des Matières, Archamps, France; 6—symrise, Holzminden, Germany; 7—Lichtwer Pharma, Berlin, Germany

similar intensity. Isointensity of the odors was further assured by the subjects, who rated odor intensity over the training period in the smell diaries using 11-point Likert type scale where 0 meant *not intense* at all and 10 meant *very intense*.

Odors were used at neat concentrations. They were distributed in brown glass bottles of 60 ml volume, height 65 mm, diameter of opening 35 mm containing a cotton ball soaked with 4 ml of an odorous substance. Subjects were asked to sniff each odor twice a day, moving the bottle from one nostril to another and back for 20 s. They sniffed in the morning and in the evening, before or at least 30 min after a meal. During the training period, participants had to fill out a "smell journal" on a weekly basis to assure training compliance and to write down possible irregularities in OT. Compliance to the OT regimen was quantified with the Likert-type scale ranging from 0 (*no compliance*) to 7 (*absolute compliance*) for morning and evening routine. These two ratings were summed, and the total compliance score could range from 0 to 14 points. The protocol for the post-training measurement after completion of OT was identical to the pre-training session described above.

## Statistical Analyses

Compliance between the two OT groups was compared with the nonparametric *U* Mann–Whitney test due to the negative skewness (most subjects declared maximum compliance). We examined whether intensity ratings varied between experimental groups over the period of first 3 and last 3 weeks of the OT (due to the varying between-session interval we limited the analysis to these 6 weeks) in order to assure that the odors did not fade over time. For this purpose, we ran general linear model examining the effect of group (simple vs mixtures) and week (ordinal number) on intensity ratings of odors involved in OT. Further, we examined whether the three experimental groups differed in terms of age or the length of OT with Bonferroni corrected one-way analysis of variance and compared sex distribution across the groups with the chi-square distribution test. We performed repeated measures analysis of variance to investigate if the OT had a significant effect on olfactory, cognitive and emotional domains. We were interested in the interaction of within-subject factor measurement (pre-training vs post-training measurement) and between-subjects factor OT regimen (simple OT vs. mixtures OT vs. control group). Multiple pairwise comparisons were Bonferroni corrected. Values in squared brackets describe 95% confidence intervals. We examined the relationship between changes in the outcome variables affected by OT with Pearson's *r* correlation coefficients.

## Results

Compliance to the OT regimen in simple OT group ($Mdn = 14$) was similar to this in the mixtures OT group ($Mdn = 14$), $U = 340.5$, $p = .72$. Odors were perceived as similarly intense by the two experimental groups $F(1,2687) = .72$, $p = .40$ throughout the first and last 3 weeks of OT period $F(5,2687) = 1.51$, $p = .18$ and these two factos did not interact with each other, $F(5,2687) = 1.68$, $p = 14$, pointing to the constant and equal intensity perception of the odorants sets involved in simple and mixtures training regimen.

The three experimental groups did not differ in terms of age, $F(2,65) = .07$, $p = .93$. The pairwise comparisons for the one-way analysis of variance testing the difference in duration of between-session interval revealed that this period in the control group was on average $M = 13.7 \pm 4.95$ days longer than in the group performing OT with mixtures ($p = .02$ [1.56; 25.83]), but similar to the between-session interval in the experimental group performing simple OT ($p = .08$ [−.92; 23.6]). There was no difference between session intervals in simple OT and mixtures OT groups ($p = 1$ [−8.02, 12.75]). Sex was evenly distributed across the experimental conditions, $\chi^2(2) = 1.01$, $p = .60$.

Analysis of variance revealed significant interaction effect between measurement and training regimen on olfactory sensitivity. There was an improvement of olfactory sensitivity (i.e. olfactory threshold), $F(2,56) = 3.31$, $p = .044$, $\eta^2 = .11$ in the experimental group performing simple OT (increase of $M = 1.2 \pm .59$ points, [.03; 2.4], $p = .045$) while the experimental group performing mixtures OT ($p = .83$) and control group ($p = .09$) did not exhibit any changes between the pre- and post-training measurements. There was no difference in threshold between the three experimental groups at the baseline measurement ($p > .23$), but after the training was concluded, the simple condition group presented significantly higher scores than mixtures group ($M_{diff} = 2.21 \pm .72$ [.44; 3.98], $p = .009$) and control group ($M_{diff} = 2.61 \pm .83$ [.56; 4.65] $p = .008$). The post-training difference between mixtures and control groups was not significant ($p = 1$).

We observed a significant interaction effect between measurement and training regimen on AD8 score, $F(2, 65) = 4$, $p = .029$, $\eta^2 = .13$. Post-hoc comparisons revealed that the control group exhibited significant increase of cognitive decline symptoms (increase of $M = .77 \pm .3$ points, [.18; 1.35], $p = .01$) whereas groups performing simple ($p = .41$) and mixtures ($p = .24$) OT regimens did not show such changes in cognitive decline symptoms. There were no between group differences at pre- ($p > .77$) or post-training measurements ($p > .50$). We assured the robustness of the simple effect of the lack of OT on dementia symptoms in the control group by running an additional nonparametric test for repeated measures within the control group. The increase of dementia symptoms in the control group was further confirmed by Friedman test, $\chi^2(1) = 4.5$, $p = .034$ (pre-training mean rank = 1.3 points, post-training mean rank = 1.7 points).

Finally, there was a significant interaction effect between measurement and OT group on MOCA score, $F(2, 54) = 3.18$, $p = .049$., $\eta^2 = .11$. Pairwise comparisons indicated significantly increased MOCA scores in the experimental group performing simple OT (increase of $M = .76 \pm .37$ points, [.15; 1.51], $p = .046$) whereas the experimental group performing mixtures OT ($p = .72$) and control group ($p = .15$) did not exhibit any changes between the pre- and post-training measurements. There were no between-group differences in MOCA scores at the pre-training measurement ($p > .24$), but after OT completion subjects who performed simple training regimen scored significantly higher than the control group ($p = .04$), but not mixtures group ($p = 1$). The mixtures group was not better after the OT than control group ($p = .10$). There were no other significant interaction effects within the tested model. Significant effects of OT are summarized in Figure 1. Descriptive statistics for all measurements and post-hoc comparisons are presented in Table 2.

Changes in olfactory threshold, cognitive decline symptoms and cognitive assessment were not related to each other across the experimental groups (all $p > .32$) with an exception of the relationship between the difference in olfactory threshold score and the difference in MOCA score that was significantly and positively correlated $r = .58$, $p = .003$ in the mixtures OT condition.

## Discussion

The results of the present study confirm our hypothesis that effectiveness of OT improves olfactory performance and extends to the age-related decline in cognitive assessment in middle-aged and older adults. This replicates the former notion that OT increases olfactory performance (Damm et al., 2014; Hummel et al., 2009). However, in our sample this effect was limited to olfactory sensitivity which may be due to a decreasing plasticity of the olfactory system with increasing age (Conley et al., 2003; Suzukawa et al., 2011). Contrary to the results of a metaanalysis, we did not observe OT effects on cognition-related olfactory domains, i.e., discrimination and identification (Sorokowska et al., 2017). A potential explanation of our null result refers to the specificity of our sample. Aging people experience more dynamic drop of olfactory threshold with age as compared to odor discrimination and identification (Cain & Stevens, 1989; Oleszkiewicz et al., 2019). Thus, in the case of participants of our sample, OT was more likely to cause a positive effect on olfactory sensitivity whereas changes in the relatively stable abilities to discriminate and recognize odors were more difficult to capture within the training period.

Stimulation of olfactory pathways affects brain areas responsible for cognitive processing, such as temporal, frontal and parietal cortices (Cheewakriengkrai et al., 2014), and hippocampus (Kaye et al., 1997). In our cohort, middle-aged and older people subjected to OT did not present increased cognitive decline as opposed to the control group. Therefore, OT may have the potential to slow down development of cognitive decline symptoms as a result of aging. However, this effect requires replication, ideally with an objective assessment of cognitive decline symptoms, as we employed only self-reported data. To confirm true positive effect of OT on cognitive decline symptoms, the issue of expectancies and the general enjoyment of the OT reflected in the improved self-reports needs to be ruled out. OT turned out to be beneficial for cognitive assessment (boosting MOCA score). Our results corroborate the single previous study presenting preliminary evidence for an improvement in semantic–categorical verbal fluency accompanying the improvement of olfactory abilities in older people as function of OT (Wegener et al., 2018). Interestingly, the group exposed to odor mixtures exhibited a robust, positive relationship between the change in olfactory threshold and MOCA scores, suggesting a complex change in the peripheral and central systems. This correlation lays a promising foundation for neuroimaging studies potent to capture causal effects.

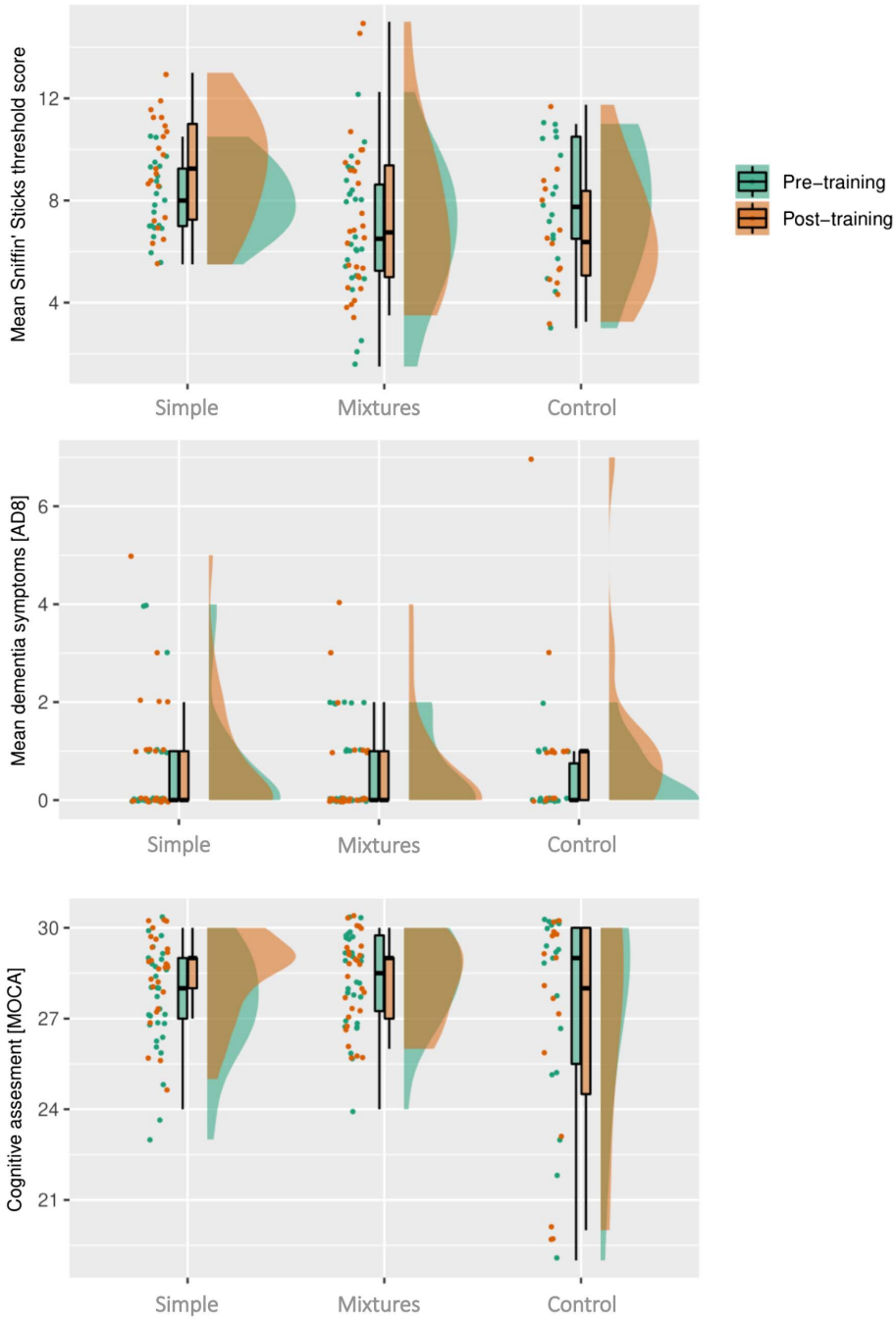
In the present study, we manipulated the complexity of olfactory stimuli included in the OT. The hypothesis of a more effective activation of ONRs by more complex olfactory stimuli has been addressed in the past. The studies yielded inconsistent findings with some reports suggesting that the complexity of OT boosts its effects (Altundag et al., 2015) and the other showing null results for the use of odor mixtures or the use of a broader spectrum of odors (Oleszkiewicz et al., 2018). However, these studies were limited to the effects of OT with relation to olfactory performance and included otolaryngological patients. Here we found that the simple olfactory stimuli yielded significant results on all the dependent variables that benefited from the OT: olfactory sensitivity, cognitive decline, and cognitive assessment, whereas the odor mixtures were only effective in the case of cognitive decline symptoms where we did not observe deterioration in our sample. Thus, at least in the present study, the single-molecule stimuli appear to be more efficient in terms of olfactory and cognitive outcomes than the odor mixtures and this difference in efficiency depending on the complexity of stimuli (simple vs mixtures) could not be explained by the intensity of odorants. This conclusion is, however, limited to middle-aged and older people. Our findings concur with the previous reports showing aging-related insensitivity to heavy-molecule odorants and odors mixtures as compared to light-molecule odorants and mixtures (Sinding et al., 2014) and extend it by showing that this age-related insensitivity may translate into lesser effectiveness of OT in the same age group. Further investigations linking degradation of olfactory system with age and the effectiveness of OT could be helpful to gain better insights into the neural mechanism underlying translation from olfactory stimulation to cognitive enhancement.

The present study could be improved with the delayed measurement aimed to monitor stability of the OT effects in time. Previous study confirmed stability of OT effects on olfactory performance over time (Konstantinidis et al., 2016), but to our best knowledge the durability of cognition-related effects of OT has not been monitored. However, longitudinal design requires a larger study sample recruited a priori to reduce the negative consequences of participants dropping out. In the present study, we did not monitor training compliance otherwise than the paper-and-pencil smell journals filled in everyday by the subjects and the occasional telephone contact. We decided to use only this subtle reminder about OT because most of our subjects volunteered for this study and were highly enthusiastic about knowing the results. High compliance is somehow reflected in the relatively low, random dropout rate (<10%).

The selected set of methods is usually (but not exclusively) used as clinical screening tools. However, the aim of our study was to replicate the effects of OT on olfactory function and explore its assumed benefits for cognitive performance. We have selected most

**Figure 1**

*Significant Effects of OT on AD8, MOCA and Sniffin' Sticks Threshold Scores as a Function of Pre- vs Post-Training Measurement*




Error bars present estimated marginal means ± standard error of the mean $^{*}p < .05$. The effect of OT on cognitive decline symptoms in the control group was not driven by the outlier marked with an arrow (→)—it remained significant after the outlying observation was removed. See the online article for the color version of this figure.

basic, widely acknowledged and commonly used screening tests for olfactory and cognitive functions to be able to refer our results to the former studies linking olfaction and cognition. In our view, the selection of methods we present creates a solid base for further research focused on enhancement of cognitive performance via olfactory stimulation and more broadly on the cross-modal correspondences including vision, hearing and olfaction. With the results we have reported in the manuscript, bolder hypotheses can be

posited and tested with more sophisticated and sensitive methods, including neuroimaging techniques. Longer between-session interval in the control group as compared to the odor mixtures OT group did not yield any significant differences, presumably because the control group was not involved in any type of training activity. Nevertheless, future studies should strive to standardize the training period at both individual and group levels.

Although OT is an inexpensive, quick, enjoyable, and easy method that can be applied in practically every laboratory and private premises, to date its use has been limited to the neuroscientific and clinical purposes due to the lack of evidence on its efficacy in cognitive domains. Here we present preliminary evidence that OT can be successfully used in neurocognitive research and in various interventions.

**Table 2**

*Descriptive Statistics for the Pre- and Post-Training Measurements Across the Three Experimental Groups With Pairwise Comparison Between pre-and Post-Training Measurements*

| Measure | OT stimuli | Measurement | Mean | Std. Error | 95% Confidence Interval | | Pairwise comparison | Measurement*OT regimen interaction |
|---|---|---|---|---|---|---|---|---|
| | | | | | Lower Bound | Upper Bound | | |
| Olfactory threshold [Sniffin' Sticks] | Simple | Pre-training | 8.07 | .48 | 7.11 | 9.03 | .045 | $F(2,56)=3.31$, $p=.044$ |
| | | Post-training | 9.29 | .52 | 8.24 | 10.34 | | |
| | Complex | Pre-training | 7.07 | .46 | 6.15 | 7.98 | .834 | |
| | | Post-training | 7.18 | .50 | 6.18 | 8.19 | | |
| | Control group | Pre-training | 7.83 | .61 | 6.60 | 9.05 | .088 | |
| | | Post-training | 6.52 | .67 | 5.18 | 7.85 | | |
| Olfactory discrimination [Sniffin' Sticks] | Simple | Pre-training | 12.67 | .45 | 11.77 | 13.56 | .108 | $F(2,65)=2.64$, $p=.079$ |
| | | Post-training | 11.95 | .46 | 11.03 | 12.88 | | |
| | Complex | Pre-training | 11.39 | .43 | 10.53 | 12.25 | .151 | |
| | | Post-training | 12.00 | .44 | 11.12 | 12.88 | | |
| | Control group | Pre-training | 11.46 | .57 | 10.32 | 12.60 | .273 | |
| | | Post-training | 10.85 | .59 | 9.67 | 12.02 | | |
| Olfactory identification [Sniffin' Sticks] | Simple | Pre-training | 13.33 | .49 | 12.35 | 14.32 | .128 | $F(2,65)=1.51$, $p=.229$ |
| | | Post-training | 13.90 | .42 | 13.06 | 14.75 | | |
| | Complex | Pre-training | 12.70 | .47 | 11.76 | 13.64 | .464 | |
| | | Post-training | 12.43 | .40 | 11.63 | 13.24 | | |
| | Control group | Pre-training | 12.85 | .62 | 11.60 | 14.10 | .745 | |
| | | Post-training | 13.00 | .53 | 11.93 | 14.07 | | |
| Self-rated olfactory function | Simple | Pre-training | 34.14 | 1.60 | 30.93 | 37.36 | .027[a] | $F(2,65)=1.08$, $p=.346$ |
| | | Post-training | 31.67 | 1.57 | 28.52 | 34.81 | | |
| | Complex | Pre-training | 33.57 | 1.53 | 30.49 | 36.64 | .174 | |
| | | Post-training | 32.13 | 1.50 | 29.12 | 35.14 | | |
| | Control group | Pre-training | 32.08 | 2.04 | 27.99 | 36.16 | .825 | |
| | | Post-training | 31.77 | 1.99 | 27.77 | 35.77 | | |
| Cognitve assessment [MOCA] | Simple | Pre-training | 27.62 | .49 | 26.64 | 28.60 | .046 | $F(2,65)=4.26$, $p=.018$ |
| | | Post-training | 28.38 | .49 | 27.40 | 29.37 | | |
| | Complex | Pre-training | 28.43 | .47 | 27.50 | 29.37 | .715 | |
| | | Post-training | 28.30 | .47 | 27.36 | 29.25 | | |
| | Control group | Pre-training | 26.85 | .62 | 25.60 | 28.09 | .149 | |
| | | Post-training | 26.15 | .62 | 24.90 | 27.41 | | |
| Cognitive decline | Simple | Pre-training | .43 | .16 | .10 | .75 | .411 | $F(2,65)=3.74$, $p=.029$ |
| | | Post-training | .62 | .24 | .14 | 1.10 | | |

**Table 2** (*continued*)

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| symptoms [AD8] | Complex | Pre-training | .57 | .15 | .26 | .87 | .240 | |
| | | Post-training | .30 | .23 | -.15 | .76 | | |
| | Control group | Pre-training | .31 | .21 | -.10 | .72 | .011 | |
| | | Post-training | 1.08 | .30 | .47 | 1.69 | | |
| Verbal skills [COWA-B*] | Simple | Pre-training | 12.48 | .74 | 10.99 | 13.96 | .570 | |
| | | Post-training | 12.05 | .78 | 10.47 | 13.62 | | |
| | Complex | Pre-training | 13.78 | .71 | 12.36 | 15.20 | .208 | $F(2,65)=.80$, $p=.456$ |
| | | Post-training | 14.70 | .75 | 13.19 | 16.20 | | |
| | Control group | Pre-training | 12.23 | .94 | 10.34 | 14.12 | .379 | |
| | | Post-training | 13.08 | 1.00 | 11.08 | 15.08 | | |
| Verbal skills [COWA-F*] | Simple | Pre-training | 9.76 | .73 | 8.29 | 11.23 | .167 | |
| | | Post-training | 10.95 | .94 | 9.06 | 12.84 | | |
| | Complex | Pre-training | 12.70 | .70 | 11.29 | 14.10 | .873 | $F(2,64)=.91$, $p=.409$ |
| | | Post-training | 12.83 | .90 | 11.02 | 14.63 | | |
| | Control group | Pre-training | 11.46 | .93 | 9.60 | 13.33 | .437 | |
| | | Post-training | 12.31 | 1.20 | 9.91 | 14.71 | | |
| Verbal skills [COWA-L*] | Simple | Pre-training | 12.33 | .81 | 10.71 | 13.96 | .217 | |
| | | Post-training | 13.29 | .84 | 11.61 | 14.96 | | |
| | Complex | Pre-training | 13.78 | .77 | 12.23 | 15.33 | .070 | $F(2,64)=.08$, $p=.928$ |
| | | Post-training | 15.13 | .80 | 13.53 | 16.73 | | |
| | Control group | Pre-training | 12.85 | 1.03 | 10.78 | 14.91 | .581 | |
| | | Post-training | 13.38 | 1.06 | 11.26 | 15.51 | | |
| Deprssive symptoms [BDI] | Simple | Pre-training | 6.00 | 1.04 | 3.91 | 8.09 | .660 | |
| | | Post-training | 6.29 | 1.06 | 4.17 | 8.40 | | |
| | Complex | Pre-training | 6.61 | 1.00 | 4.61 | 8.60 | .295 | $F(2,65)=.79$, $p=.460$ |
| | | Post-training | 5.96 | 1.01 | 3.93 | 7.98 | | |
| | Control group | Pre-training | 5.38 | 1.32 | 2.73 | 8.04 | .515 | |
| | | Post-training | 5.92 | 1.34 | 3.23 | 8.62 | | |
| Positive affect [PANAS] | Simple | Pre-training | 34.52 | 1.23 | 32.06 | 36.98 | .397 | |
| | | Post-training | 35.52 | 1.40 | 32.72 | 38.33 | | |
| | Complex | Pre-training | 34.61 | 1.17 | 32.26 | 36.96 | .699 | $F(2,65)=.79$, $p=.460$ |
| | | Post-training | 35.04 | 1.34 | 32.36 | 37.73 | | |
| | Control group | Pre-training | 35.31 | 1.56 | 32.18 | 38.43 | .719 | |
| | | Post-training | 34.77 | 1.78 | 31.20 | 38.34 | | |
| Negative affect [PANAS] | Simple | Pre-training | 17.19 | 1.09 | 15.00 | 19.38 | .704 | |
| | | Post-training | 17.48 | 1.07 | 15.33 | 19.62 | | |
| | Complex | Pre-training | 14.78 | 1.04 | 12.69 | 16.87 | .809 | $F(2,65)=.30$, $p=.744$ |
| | | Post-training | 14.96 | 1.02 | 12.90 | 17.01 | | |
| | Control group | Pre-training | 18.08 | 1.39 | 15.29 | 20.86 | .809 | |
| | | Post-training | 17.85 | 1.36 | 15.12 | 20.58 | | |

*Note*. * Denotes letter used in the test; grey color denotes olfactory-related measures, blue—cognitive measures and green—emotional measures.

[a] although the pairwise comparison for pre- and post-training measurement in the simple OT stimuli is significant for the individual significance of olfaction, the overall ANOVA effect was not significant, therefore we do not interpret this post-hoc result. See the online article for the color version of this figure.

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