Enhanced odorant localization abilities in congenitally-blind but not in late-blind individuals

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Abstract

Blindness leads to enhanced spatial abilities in the remaining senses. Whether such improved spatial abilities extend to chemosensation remains unexplored. Consequently, the present study aims at determining whether blind subjects have superior odorant localization abilities compared to sighted controls, and whether the time of vision loss onset modulates those abilities. By testing a group of congenitally blind (CB; n=10) and late blind (LB; n=10) individuals as well as matched sighted controls (CB-C; LB-C; n=20), we investigated whether there is a sensitive period for the development of atypical olfactory-spatial abilities. Assessment of chemosensation perception, and more specifically the trigeminal function, was performed by a birhinal localization task using mixed olfactory-trigeminal stimuli. We observed that congenitally blind individuals outperformed late-blind subjects when localizing these stimuli (p = .03). We therefore showed that congenital but not late acquired blindness leads to enhanced localization of the trigeminal component of chemosensory stimuli. In addition to previous studies highlighting enhanced localization abilities in auditory and tactile modalities, our current results extend such enhanced abilities to the chemosensation localization as well.

Keywords: trigeminal function, odor localization, congenitally blind, late blind, sensory compensation

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Conflict of interest

None declared.

Introduction

Sensory deprivation influences perceptual abilities in the remaining senses through experience-dependent mechanisms (Voss, Collignon, Lassonde, & Lepore, 2010). Since vision typically provides the most reliable information for the processing of spatial information (Alais & Burr, 2004; Charbonneau, Veronneau, Boudrias-Fournier, Lepore, & Collignon, 2013), the consequence of blindness on spatial abilities in the remaining senses has been the focus of scientific attention (Collignon, Voss, Lassonde, & Lepore, 2009; Heller & Ballesteros, 2016; Voss et al., 2004). The relative weighting of spatial information obtained through different perceptual modalities is determined by the reliability of the cues provided by each perceptual modality (e.g., the precision of the information specifying an object's location; (Alais & Burr, 2004; Charbonneau et al., 2013; Millar, 1994)). This model posits that, in the absence of vision, other modalities receive greater weight than they otherwise would have. This idea is supported by studies showing enhanced auditory (Voss, 2016) and tactile (Heller & Ballesteros, 2016) spatial abilities in blind people. Interestingly, the presence of these compensatory mechanisms appears to be strongly dependant on the onset time of visual deprivation (Bavelier & Neville, 2002; Voss, Penhune, Wan, Israel, & Burton, 2013). Contrary to congenital blindness or blindness acquired during the first few years of life (i.e. early blindness), late onset blindness gives rise to lower behavioural compensatory mechanisms. For instance, numerous behavioural studies in the auditory and tactile domains have provided evidence of a better performance in participants with early-onset blindness compared with those with a late onset and sighted controls (for a review see Voss et al., 2013).

Studies evaluating the sense of smell in this population is relatively scarce (Beaulieu-Lefebvre, Schneider, Kupers, & Ptito, 2011; Gagnon, Kupers, & Ptito, 2014; Kupers et al., 2011). Although blind individuals rely extensively on touch and audition to interact with their environment (Burton, 2003), they also pay attention to all non-visual cues, including odor cues. One may postulate that blind individuals rely more on chemosensation compared to their sighted counterparts. For example, when vision is lacking, the olfactory sense has an enhanced ecological value for the detection of odors that yield information about the environment (e.g., evaluation of the quality of food). It may also serve to detect landmarks in navigation and thus contribute to spatial cognition (e.g., turn left at the bakery). Verily, results from interviews showed that blind individuals reported using their sense of smell to gain information about the position of an object or attribute in the environment, to understand that certain object or attribute lies within close proximity, and to serve as useful points of reference (Koutsoklenis & Papadopoulos, 2011).

So far, comparative studies between blind and sighted subjects regarding their performance during sensory and perceptual-driven olfactory tasks, as well as tasks soliciting higher-order olfactory functions, revealed inconsistent results (for a systematic review see Sorokowska, Sorokowski, Karwowski, Larsson, & Hummel, 2018). In this meta-analysis, the authors showed no positive effects of visual impairment on odor detection threshold, olfactory discrimination and, free and cued odor identification abilities. However, at the time of this study, chemosensory localization in blind individuals has not yet been investigated.

Chemosensory localization is based on stimulation of the trigeminal system and can be assessed by measuring the ability to determine if an odor is administered in the right or left nostril. Humans are not able to localize pure odorants, which stimulate the sense of smell exclusively, and can only localize odorants that additionally stimulate the intranasal trigeminal system (Frasnelli, Charbonneau, Collignon, & Lepore, 2009; Frasnelli, La Buissonnière Ariza, Collignon, & Lepore, 2010; Kleemann et al., 2009; Wise, Wysocki, & Lundstrom, 2018). As the trigeminal system is sensitive to irritant information and helps to discern between different chemicals component (i.e. burning sensation from capsaicin in chilli peppers, cooling sensation from menthol in peppermint), we can hypothesize that this system could be, for adaptive reasons, especially developed in blind subjects compared to sighted individuals. For example, compared to sighted individuals, blind individuals might relay more on chemosensory information to protect their safety (i.e.; detect the source of smoke in the case of a fire to retrieve to safety) and navigate in their environment. Only recently a novel study investigated whether blind individuals were able to localize chemosensory stimuli on a spectrum of various tasks, and unfortunately, no supra-performances were found (Sorokowska et al., 2019). However, in this study, the authors did not evaluate the impact of blindness onset on their performances. In other words, since an earlier blindness onset has been previously associated with greater supra-performances (Gougoux et al., 2004) compared to a later blindness onset, this is an important factor to keep in mind when exploring potential supra-performances of blind individuals on chemosensory localization tasks.

Therefore, the goal of this study was to evaluate odor localization abilities in congenitally and late-blind individuals. We hypothesize that congenitally blind individuals, will outperform late-blind individuals on an odor localization task. In order to control for unspecific effects of blindness such as differences in detection and perception of odors among blind and sighted individuals, we also administered odor detection and an odor identification tasks.

Experimental procedures

Participants

We tested 10 congenitally-blind (CB; age *M* = 41, *SD* = 14, range 21 to 62 years, 2 women) and 10 late-blind individuals (LB; age *M* = 56, *SD* = 10, range 38 to 66 years, 7 women). Due to large age-differences between the two groups, we established two separate control groups; one for the congenitally blind (CB-C; age *M* = 41, *SD* = 14, range 23 to 58 years, 2 women) and one for the late blind (LB-C; age *M* = 56, *SD* = 9, range 37 to 63 years, 7 women) to match each blind individual respectively in terms of age, gender and smoking habits. Within the CB, all participants were born blind, and half of them had some light perception in at least one of their eyes. Within the LB, 2/10 individuals had light perception in at least one of their eyes. CB and LB were matched with their respective control groups (CB-C and LB-C) in terms of age, gender, and smoking habits. Further detailed description about both blind groups can be found in Table 1. Although the duration of blindness was slightly greater for the CB group (*M* = 41, *SD* = 14) compared to the LB group (*M* = 28, *SD* = 15), it was not statistically significant ($t(18) = 2.02$, $p = .059$), suggesting that both groups have been blind for a similar duration of time. All participants declared that they did not suffer from any medical condition that could affect their sense of smell at the time of the testing. Participants were instructed not to eat or drink anything besides water one hour prior to the experiment. As depicted in Figure 1, all participants had normal olfactory function as ascertained by means of the Sniffin' Sticks identification test (Hummel, Kobal, Gudziol, & Mackay-Sim, 2007; Hummel et al., 1997). Specifically, the Free Recall condition (*M* = 6.35, *S.D.* = 2.84) was easier than the Forced Choice condition (*M* = 13.15, *S.D.* = 1.70; ($F(1, 36) = 221.95$, $p < .001$, $\eta_{partial}^2 = .86$) for all groups. Importantly there was no difference between any of the groups with regards to their average scores $F(3, 36) = 2.06$, $p = .12$, $\eta_{partial}^2 = .15$), indicating that all groups had similar olfactory abilities

Before taking part in the study, subjects gave their written informed consent. After completion, they received a $40 monetary compensation for their participation as well as reimbursement of their travel expenses. The ethics board of the Center for Interdisciplinary Research in Rehabilitation of Greater Montreal (CRIR) approved this study.

[Insert Table 1 here]

[Insert Figure 1 here]

Olfactory evaluation

Odors

We used two specific odorants for the investigation of the localization ability as well as the identification, namely, benzaldehyde (Sigma-Aldrich, St Louis, MO, almond odor, burning/tingling sensation) and eucalyptol (Galenova St-Hyacinthe, Quebec, eucalyptus odors, cooling sensation), in neat concentrations. These two odors are known to largely stimulate the trigeminal system in addition to the olfactory one as well (Viana, 2011). For the detection tasks, odors of strawberry (strawberry aroma, Frey & Lau, Hamburg, Germany) and parmesan cheese were used. These odors tend to recruit the olfactory system more than the trigeminal system, although both systems are implicated.

Since odor edibility was associated with faster reaction times (Boesveldt, Frasnelli, Gordon, & Lundstrom, 2010; Manescu, Frasnelli, Lepore, & Djordjevic, 2014), we thus used these odors for their ecological and edibility properties. To create the parmesan cheese odorant, parmesan cheese was boiled in canola oil, which was then filtered to obtain parmesan cheese infused oil. Before every testing session, the experimenter verified that the odors smelled the same and had the same intensity. Since the quality of the odors didn't alter with time, the same odorants were used throughout the experiment.

Stimulator

Odors were delivered with an adapted computer-controlled air compressor (IBB, University of Münster, Germany), which was used in past studies for administration of time-controlled air pulses (Frasnelli et al., 2010; La Buissonnière-Ariza, Frasnelli, Collignon, & Lepore, 2012). The odors were presented via a six-channel air compressor. It delivered air puffs of 2.5 L/min per channel, as ascertained by a flow meter (Cole Parmer, Montreal, QC). A valve control unit directed air into the air compressor via polyurethane tubing with 8.0 mm outer diameter and an inner diameter of 4.8 mm (Fre-Thane 85A, Freelin-Wade, McMinnville, OR). From the air compressor, polyurethane tubes were connected to the bottles containing the odors. Specifically, for the identification and localization tasks, six tubes were connected to six 60mL glass bottles containing the odors; two bottles filled with benzaldehyde; two bottles filled with eucalyptol, and two empty control bottles (Figure 2). From the six bottles, three polyurethane tubes were directly connected to the left nostril and the other three polyurethane tubes were connected to the right nostril. For the detection task three tubes were connected to three 30mL glass bottles containing the odors; strawberry aroma, parmesan cheese, as well as one empty control bottle.

To administer the odors, an air stream was sent to the compressor, which delivered an air puff into one of the four odor-containing bottles and/or into the two control bottles for the identification and localization tasks or one of the two odor-containing bottes and/or into the control bottle for the detection task. During the inter-stimulus interval, no air was delivered. The Presentation software (Neurobehavioral Systems, Inc, Albany, CA) was used to deliver the chemosensory stimuli as well as record participants responses and reaction times.

[Insert Figure 2 here]

Tasks and Procedures

To test odor localization, participants were placed in front of the computer on a comfortable chair with their chin on chin rest in a ventilated testing booth. They were instructed to press one of two buttons on keyboard if they smelled an odor in their left nostril and the other button if they smelled an odor in their right nostril, independent of the identity of the odor (almond or eucalyptus). Two seconds before odor stimulation a sound was emitted indicating that an odor would be administered. This allowed participants to stop breathing during odor delivery. Odors (eucalyptus or almond, 500ms, 2.5L/min) were delivered to one nostril (randomly chosen per trial), while the other nostril received an odor-free air puff (500ms, 2.5L/min). The inter-stimulus interval was set at 40s to avoid habituation (Hummel & Kobal, 1999). Each odor was presented 16 times to each nostril, divided into two blocks with a 5 minutes break between blocks. We recorded response accuracy (% of total stimuli) and response time for correct responses (ms).

We carried out two additional tasks, to control for unspecific effects of blindness on olfactory processing. First, we measured participants' ability to identify the odorants used in the main task. In this odor identification task, conditions were identical as in the localization task, with the exception that participants had been instructed to press one button if they smelled almond odor and the other button if they smelled eucalyptus odor, independent of the stimulated nostril (left or right). We again recorded response accuracy (% of total stimuli) and response time for correct responses (ms). Second, we assessed participants' ability to detect odors. For this odor detection task, the same conditions as above applied with the following exceptions: Stimuli (strawberry aroma, parmesan cheese odor and odorless control condition) were delivered to both nostrils; each stimulus was presented 15 times. Participants were asked to press on a button as soon as they smelled an odor, and refrain from pressing it if they did not smell anything. To avoid habituation, odor inter-stimulus for the detection task was set at 30s. Since the odors used stimulated less the trigeminal system, a shorter inter-stimulus duration could be used (Hummel & Kobal, 1999). For this task, we solely recorded their response times (ms) to the stimuli.

Each participant completed practice trials before the start of each task to familiarize them with the protocol. The detection task was first administered using the olfactometer followed by the identification and then the localization task. The whole experiment took around three hours from start to finish.

Statistical analysis

For each variable (localization and identification accuracy rates as well as odor detection response times), we examined whether there were any outliers beyond a z-score 3.29 using the Median Absolute Deviation method (MAD; Leys, Ley, Klein, Bernard, & Licata, 2013; Tabachnick & Fidell, 2013). Although traditional methods in dealing with outliers relies on the average, this is problematic since the calculation of the average is influenced by the outliers. To overcome this, more recent methods suggest using the median of the variable to determine the cut-off scores in order to identify outliers in the data. For all identified outliers on all three tasks combined (2.92%), their value was brought to 3.29 to their respected variable (Tabachnick & Fidell, 2013).

In order to compare the CB and LB directly, we used their respective control groups to generate standardized scores. Specifically, for each variable, we subtracted each data point in the CB group from the average and divided the result by the standard deviation of the CB-C. The same was done for the LB and LB-C group. In doing so, every participant of the CB and LB had a score z-score for each odor and task (localization, identification and detection tasks).

Two separate ANOVAs were conducted for the odor localization and odor identification tasks, by using *group* (two levels: CB, LB) as between subject factors and *odor* (two levels: almond, eucalyptus) as within-subject factor.

Similarly, the response time related to the odor detection task was evaluated with a repeated measures ANOVA using *group* (two levels: CB, LB) as between-subject factor and *odor* (two levels: strawberry, parmesan cheese) as within-subject factor. If *F* values were significant, we used t-tests with Bonferroni correction for *post-hoc* comparisons.

Significance level for all statistics was fixed at $p < .05$. All analyses were conducted with SPSS Statistics 25 (IBM, Corp, Armonk, NY).

Results

As shown in Figure 3, the ANOVA conducted for the odor localization task revealed a significant main effect of *group* on the standardized measure of accuracy ($F(1, 18) = 11.79$, $p = .003$, $\eta_{partial}^2 = .40$). More specifically, the CB group ($M = .72$, $S.D. = .45$) was significantly better at localizing both odors (almond and eucalyptus) compared to the LB group ($M = -.52$, $S.D. = .33$). Although not significant, there was a tendency towards an interaction between *odor* and *group* ($F(1, 18) = 4.31$, $p = .053$, $\eta_{partial}^2 = .19$). Further post-hoc analyses revealed that EB localized the almond odor better ($M = 1.14$, $S.D. = .73$) than LB ($M = -.55$, $S.D. = 1.31$; ($t(18) = 3.55$, $p = .013$, corrected). No other comparison was significant after correcting for multiple comparisons ($p > .05$).

To ascertain that the two groups did perceive the odors used in the localization task in a similar fashion, we conducted an ANOVA to evaluate the participants' ability to identify the odors. Here we find no differences between the two *groups* for the standardized measure of accuracy ($F(1, 18) = 3.88$, $p = .07$, $\eta_{partial}^2 = .18$), no main effect of *odor* ($F(1, 18) = .18$, $p = .67$, $\eta_{partial}^2 = .01$) and no interaction between *groups* and *odor* ($F(1, 18) = .39$, $p = .54$, $\eta_{partial}^2 = .02$).

[Insert Figure 3 here]

In order to ascertain that the groups did not differ in terms unspecific odor detection; we compared their response times towards two unrelated odors (strawberry and parmesan cheese odors). We did not observe any *group* differences, ($F(1, 18) = 1.83$, $p = .19$, $\eta_{partial}^2$

= .09), no main effect of *odor* ($F(1, 18) = 1.81$, $p = .20$, $\eta_{partial}^2 = .91$), nor an interaction between *odor* and *groups* ($F(1, 18) = .000$, $p = .96$, $\eta_{partial}^2 < .001$) as illustrated in Figure 4.

[Insert Figure 4 here]

Discussion

In the present study, we found that congenitally blind individuals have a higher capacity to extract spatial information from chemosensory stimuli compared to late blind individuals. More specifically, while all participants were matched in terms of gender and smoking habit, and showed comparable performances in detection and identification tasks, we observed that congenitally blind participants showed selective improvement in localizing mixed trigeminal-olfactory odorants over late blind individuals, even when the age effect was accounted for.

Our results are in line with previous reports portraying enhanced localization abilities among the congenitally blind when soliciting auditory (Lessard, Pare, Lepore, & Lassonde, 1998; Röder et al., 1999; Voss et al., 2004) and tactile (Goldreich & Kanics, 2003; Van Boven, Hamilton, Kauffman, Keenan, & Pascual-Leone, 2000) modalities. This enhanced ability could result from a training effect. More specifically, visual deprivations may lead to an increase in the recruitment of remaining healthy senses (i.e. chemosensory processing) and thus consequently and indirectly train them. Furthermore, it has been demonstrated that training can improve chemosensory localization (Porter et al., 2007) and lateralization abilities (Negoias, Aszmann, Croy, & Hummel, 2013) in sighted individuals. Such behavioral adjustments in blind people may relate to brain plasticity of the chemosensory systems. Although odorant localization is primarily based on activation of the intranasal trigeminal system, according to the olfactory spatial hypothesis of Jacobs (2012), the size of the olfactory bulb may reflect the ability to decode and map patterns of odorants for the purpose of spatial navigation. In this regard, studies have shown stronger recruitment of the olfactory cortex in congenitally blind compared to sighted control subjects during olfactory processing (Kupers et al., 2011) and there is a positive association between olfactory bulb volume and olfactory performance in blind subjects (Rombaux et al., 2010). This raises the hypothesis that the cerebral regions implicated in the processing of chemosensory objects can undergo significant changes due to visual deprivation.

Beyond intramodal plasticity, there is ample evidence that the occipital cortex of blind individuals activates when localizing stimuli in the remaining sense (Collignon et al., 2011, 2009; Dormal, Lepore, & Collignon, 2012), and that such crossmodal recruitment may relate to performance (Gougoux, Zatorre, Lassonde, Voss, & Lepore, 2005). More particularly, it has been shown that localizing information in the remaining senses selectively recruit regions of the right dorsal stream in blind people, regions know to process visuo-spatial information in the sighted. These results support the idea that crossmodal plasticity is constrained by intrinsic computational bias of the deprived visual regions (Collignon et al., 2009; Collignon, Dormal, & Lepore, 2012; Heimler, Striem-Amit, & Amedi, 2015; Ricciardi, Tozzi, Leo, & Pietrini, 2014). However, whether the location of chemosensory information also preferentially recruit occipital regions typically assigned to visuo-spatial processing remains to be investigated.

In line with previous findings (Beaulieu-Lefebvre, Schneider, Kupers, & Ptito, 2011; Çomoğlu et al., 2015; Cuevas et al., 2010; Guducu, Oniz, Ikiz, & Ozgoren, 2016;

Luers et al., 2014; Majchrzak, Eberhard, Kalaus, & Wagner, 2017; Sorokowska, 2016; Sorokowska & Karwowski, 2017), we found no significant difference in olfactory performance between blind and sighted individuals on odor detection and identification tasks. It is therefore possible that the selective improvement of congenitally blind individuals for chemosensory localization but not for odor identification or detection reveal a selective pressure to further develop such skills for coping with visual deprivation in daily life, potentially in relation to the dominant role vision typically plays in spatial processing and navigation. Perceptual enhancement in blind individuals should therefore not be considered as an automatic and general perceptual process but as a compensatory mechanism emerging depending on specific cognitive pressure created by the lack of vision early in life. The fact that such compensation does not emerge in late blind people points towards the fact that such mechanisms interact with the developmental stage of the individual. Thus, our results support the importance of considering the duration and the age of onset of vision loss when doing research on compensatory mechanisms. Compared to the recent study conducted by Sorokowska et al. (2019) where no supra-performances of chemosensory localization and lateralization were found in blind individuals, we evaluated two distinct groups of blind participants (i.e. congenitally vs late blind) with comparable durations of vision loss. Consequently, our results highlight the importance of a sensitive period for the enhancement of odor localization abilities among visually deprived individuals.

In summary, the findings of the present study suggest that the trigeminal component of chemosensory objects is processed differently among blind individuals, i.e., congenitally blind individuals are better at localizing olfactory-trigeminal objects than late blind subjects. Future neuroimaging studies could provide a better understanding of the underlying mechanisms of the current findings, (i.e., the brain reorganization of congenitally blind individuals that contributes to the enhancement of trigeminal processing of chemosensory stimuli).

References

Bavelier, D. &, & Neville, H. J. (2002). Cross-modal plasticity: Where and how? *Nature Reviews Neuroscience*, *3*(6), 443–452. http://doi.org/10.1038/nrn848

Beaulieu-Lefebvre, M., Schneider, F. C., Kupers, R., & Ptito, M. (2011). Odor perception and odor awareness in congenital blindness. *Brain Research Bulletin*, *84*(3), 206–209. http://doi.org/10.1016/j.brainresbull.2010.12.014

Burton, H. (2003). Visual cortex activity in early and late blind people. *Journal of Neuroscience*, *23*(10), 4005–4011.

Çomoğlu, Ş., Orhan, K. S., Kocaman, S. Ü., Çelik, M., Keleş, N., & Değer, K. (2015). Olfactory Function Assessment of Blind Subjects Using the Sniffin Sticks Test. *Otolaryngology - Head and Neck Surgery*, *153*(2), 286–290. http://doi.org/10.1177/0194599815583975

Cuevas, I., Plaza, P., Rombaux, P., Collignon, O., De Volder, A., & Renier, L. (2010). Do People Who Became Blind Early in Life Develop a Better Sense of Smell? A Psychophysical Study. *Journal of Visual Impairment & Blindness*, *104*(6), 369–379.

Frasnelli, J., Charbonneau, G., Collignon, O., & Lepore, F. (2009). Odor localization and sniffing. *Chemical Senses*, *34*(2), 139–144. http://doi.org/10.1093/chemse/bjn068

Frasnelli, J., Collignon, O., Voss, P., & Lepore, F. (2011). Crossmodal plasticity in sensory loss. *Progress in Brain Research*, *191*, 233–249. http://doi.org/10.1016/B978-0-444-53752-2.00002-3

Frasnelli, J., La Buissonnière Ariza, V., Collignon, O., & Lepore, F. (2010). Localisation of unilateral nasal stimuli across sensory systems. *Neuroscience Letters*, *478*(2), 102–106. http://doi.org/10.1016/j.neulet.2010.04.074

Frasnelli, J., Lundström, J. N., Schöpf, V., Negoias, S., Hummel, T., & Lepore, F. (2012). Dual processing streams in chemosensory perception, *6*(October), 1–9. http://doi.org/10.3389/fnhum.2012.00288

Frasnelli, J., & Manescu, S. (2017). The Intranasal Trigeminal System. In Buettner, A. (Ed.), *Springer Handbook of Odor* (pp. 113–114). Cham: Springer International.

Frasnelli, J., Schuster, B., & Hummel, T. (2007). Subjects with congenital anosmia have larger peripheral but similar central trigeminal responses. *Cerebral Cortex*, *17*(2), 370–377. http://doi.org/10.1093/cercor/bhj154

Goldreich, D., & Kanics, I. M. (2003). Tactile acuity is enhanced in blindness. *Journal of Neuroscience*, *23*(8), 3439–3445. http://doi.org/10.1097/WNR.0b013e32802b70f8

Guducu, C., Oniz, A., Ikiz, A. O., & Ozgoren, M. (2016). Chemosensory Function in Congenitally Blind or Deaf Teenagers. *Chemosensory Perception*, *9*(1), 8–13. http://doi.org/10.1007/s12078-015-9199-2

Heller M., Ballesteros S. (2016) Visually-Impaired Touch. In Prescott T., Ahissar E., Izhikevich E. (Eds.), *Scholarpedia of Touch* (pp.387-397). Paris: Atlantis Press.

Hummel, T., Kobal, G., Gudziol, H., & Mackay-Sim, A. (2007). Normative data for the "Sniffin' Sticks" including tests of odor identification, odor discrimination, and olfactory thresholds: An upgrade based on a group of more than 3,000 subjects." *European Archives of Otorhinolaryngology*, *264*(3), 237–243. http://doi.org/10.1007/s00405-006-0173-0

Hummel, T., Sekinger, B., Wolf, S. R., Pauli, E., Kobal, G., & Hummel, T. (1997). "Sniffin' Sticks": Olfactory Performance Assessed by the Combined Testing of Odor Identification, Odor Discrimination and Olfactory Threshold. *Chemical Senses*, *22*,

39–52.
Jacobs, L. F. (2012). From chemotaxis to the cognitive map: The function of olfaction. *Proceedings of the National Academy of Sciences*, *109*, 10693–10700. http://doi.org/10.1073/pnas.1201880109
Jacobs, L. F., Arter, J., Cook, A., & Sulloway, F. J. (2015). Olfactory orientation and navigation in humans. *PLoS ONE*, *10*(6). http://doi.org/10.1371/journal.pone.0129387
Kéïta, L., Frasnelli, J., La Buissonnière-Ariza, V., & Lepore, F. (2013). Response times and response accuracy for odor localization and identification. *Neuroscience*, *238*, 82–86. http://doi.org/10.1016/J.NEUROSCIENCE.2013.02.018
Kleemann, A. M., Albrecht, J., Schöpf, V., Haegler, K., Kopietz, R., Hempel, J. M., … Wiesmann, M. (2009). Physiology & Behavior Trigeminal perception is necessary to localize odors. *Physiology & Behavior*, *97*(3–4), 401–405. http://doi.org/10.1016/j.physbeh.2009.03.013
Koutsoklenis, A., & Papadopoulos, K. (2011). Olfactory Cues Used for Wayfinding in Urban Environments by Individuals. *Journal of Visual Impairment & Blindness*, *105*(November), 692–702.
Kupers, R., Beaulieu-Lefebvre, M., Schneider, F., Kassuba, T., Paulson, O., Siebner, H. R., & Ptito, M. (2011). Neural correlates of olfactory processing in congenital blindness. *Neuropsychologia*, *49*(7), 2037–2044. http://doi.org/10.1016/J.NEUROPSYCHOLOGIA.2011.03.033
Kupers, R., & Ptito, M. (2011). Insights from darkness. what the study of blindness has taught us about brain structure and function. *Progress in Brain Research*, *192*, 17–31. http://doi.org/10.1016/B978-0-444-53355-5.00002-6
La Buissonnière-Ariza, V., Frasnelli, J., Collignon, O., & Lepore, F. (2012). Neuroscience Letters Olfactory priming leads to faster sound localization. *Neuroscience Letters*, *506*(2), 188–192. http://doi.org/10.1016/j.neulet.2011.11.002
Lessard, N., Pare, M., Lepore, F., & Lassonde, M. (1998). Early blind human subjects localise sound sources better than sighted subjects. *Nature*, *395*(September), 278–280.
Luers, J. C., Mikolajczak, S., Hahn, M., Wittekindt, C., Beutner, D., Hüttenbrink, K. B., & Damm, M. (2014). Do the blinds smell better? *European Archives of Oto-Rhino-Laryngology*, *271*(7), 1933–1937. http://doi.org/10.1007/s00405-013-2816-2
Majchrzak, D., Eberhard, J., Kalaus, B., & Wagner, K. H. (2017). Do Visually Impaired People Develop Superior Smell Ability? *Perception*, *46*(10), 1171–1182. http://doi.org/10.1177/0301006617717942
Millar, S. (1994). *Understanding and Representing Space Theory and Evidence from Studies with Blind and Sighted Children*. Oxford University Press.
Porter, J., Craven, B., Khan, R. M., Chang, S. J., Kang, I., Judkewitz, B., … Sobel, N. (2007). Mechanisms of scent-tracking in humans. *Nature Neuroscience*, *10*(1), 27–29. http://doi.org/10.1038/nn1819
Röder, B., Teder-Sälejärvi, W., Sterr, A., Rösler, F., Hillyard, S. A., & Neville, H. J. (1999). Improved auditory spatial tuning in blind humans. *Nature*, *400*(6740), 162–166. http://doi.org/10.1038/22106
Rombaux, P., Huart, C., De Volder, A. G., Cuevas, I., Renier, L., Duprez, T., & Grandin, C. (2010). Increased olfactory bulb volume and olfactory function in early blind

subjects. *NeuroReport*, *21*(17), 1069–1073. http://doi.org/10.1097/WNR.0b013e32833fcb8a
Rosenbluth, R., Grossman, E. S., & Kaitz, M. (2000). Performance of early-blind and sighted children on olfactory tasks. *Perception*, *29*(1), 101–110. http://doi.org/10.1068/p3001
Sorokowska, A. (2016). Olfactory Performance in a Large Sample of Early-Blind and Late-Blind Individuals. *Chemical Senses*, *41*(8), 703–709. http://doi.org/10.1093/chemse/bjw081
Sorokowska, A., & Karwowski, M. (2017). No sensory compensation for olfactory memory: Differences between blind and sighted people. *Frontiers in Psychology*, *8*(DEC), 2127. http://doi.org/10.3389/fpsyg.2017.02127
Sorokowska, A., Oleszkiewicz, A., Stefańczyk, M., Płachetka, J., Dudojć, O., Ziembik, K., ... & Hummel, T. (2019). Odor lateralization and spatial localization: Null effects of blindness. *Attention, Perception, & Psychophysics*, 1-10. https://doi.org/10.3758/s13414-019-01717-4
Sorokowska, A., Sorokowski, P., Karwowski, M., Larsson, M., & Hummel, T. (2018). Olfactory perception and blindness: a systematic review and meta- analysis. *Psychological Research* , 1-17. http://doi.org/10.1007/s00426-018-1035-2Van Boven, R. W., Hamilton, R. H., Kauffman, T., Keenan, J. P., & Pascual-Leone, A. (2000). Tactile spatial resolution in blind braille readers. *Neurology*, *54*(12), 2230–6. http://doi.org/10.1212/WNL.54.12.2230
Voss, P. (2016). Auditory Spatial Perception without Vision. *Frontiers in Psychology*, *07*, 1960. http://doi.org/10.3389/fpsyg.2016.01960
Voss, P., Collignon, O., Lassonde, M., & Lepore, F. (2010). Adaptation to sensory loss. *Wiley Interdisciplinary Reviews: Cognitive Science*, *1*(3), 308–328. http://doi.org/10.1002/wcs.13
Voss, P., Lassonde, M., Gougoux, F., Fortin, M., Guillemot, J.-P., & Lepore, F. (2004). Early- and Late-Onset Blind Individuals Show Supra-Normal Auditory Abilities in Far-Space. *Current Biology*, *14*(19), 1734–1738. http://doi.org/10.1016/J.CUB.2004.09.051
Voss, P., Penhune, V., Wan, C. Y., Israel, B., & Burton, H. (2013). Sensitive and critical periods in visual sensory deprivation, *4*(September), 1–13. http://doi.org/10.3389/fpsyg.2013.00664
Wise, P. M., Wysocki, C. J., & Lundstro, J. N. (2018). Stimulus Selection for Intranasal Sensory Isolation : Eugenol Is an Irritant, (August), 509–514. http://doi.org/10.1093/chemse/bjs002