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Factors associated with odour identification in older Indonesian and white Australian adults

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Abstract

Background and aims—Among older adults, olfactory dysfunction is associated with cognitive impairment, lower quality of life, and increased mortality. While age is a risk factor for olfactory dysfunction, other risk factors are less well understood, and may vary between ethno-regional groups. This study investigated how associations between odour identification (OI) and various risk factors, as well as cognition and language ability, differed or were similar in two distinct ethno-regional groups of older adults.

Methods—This cross-sectional study used data from two cohorts: 470 Indonesians (aged 67.4 ± 7.4 years) and 819 white Australians (aged 78.7 ± 4.8 years). Univariate and multivariate analyses explored whether OI test scores were associated with age, sex, education, cholesterol levels, apolipoprotein E ε4 status, smoking, diabetes, hypertension and depression scale scores, or with Mini-Mental State Examination (MMSE) and language test performance.

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Author contributions YT, DL: study concept and design. HB, PS, NK: design of the cohort studies and data acquisition. IS, TS: analysis and interpretation of data. YT, DL: drafting the manuscript. YH, JR, HB, PS, NK: critical revision of the manuscript. PSS, HB: obtaining the funding.

Conflict of interest There are no financial or personal conflicts of interest to report.

Statement of human ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the University of New South Wales Human Research Ethics Committee (Approval #14327) for MAS, and from the School of Medicine and Health Sciences Atma Jaya Catholic University of Indonesia Ethics Committee (Approval 03/04/2014&01/05/2015) for AJ.

Informed consent Written informed consent was obtained from each participant.

Results—Univariate analyses identified some factors associated with OI scores in both Indonesians and white Australians, including older age and smoking with lower scores, and MMSE and language test performance with higher scores. Multivariate analyses yielded different and mutually exclusive patterns of associations in the two ethno-regional groups, with language test scores significantly associated with higher OI scores in Indonesians, and age, being male, smoking, having diabetes and higher depression scale scores significantly associated with lower OI scores in white Australians.

Conclusion—Ethno-regional differences may need consideration in the attempt to fully understand associations between OI and negative outcomes like dementia and mortality, and interventions for olfactory dysfunction might need to be tailored to specific ethno-regional groups. However, the difference in mean age between cohorts is a limitation of this study, and future studies should aim to compare populations with similar age distributions.

Keywords

Odour identification; Olfactory; Language; MMSE; Risk factors

Introduction

Among older adults, worse olfactory functioning has been associated with lower quality of life, depression and loneliness, cognitive impairment, and increased risk of dementia and mortality [1–6]. Implicated in some of these associations is an effect of impaired olfactory functioning on the taste of food and appetite, which can promote malnutrition and frailty [7]. While older age is itself a prominent risk factor for olfactory impairment [8–13] another that appears influential is being male [9–12, 14, 15]. Lower levels of education have also been associated with olfactory impairment [8, 9, 12, 16, 17], but other studies have found either the opposite [10, 11] or no effect [18]. Findings for a range of other risk factors, including medical and genetic, have also been mixed, though the evidence for deleterious effects of smoking [19] and diabetes [18] is more established.

While methodological differences may contribute to inconsistent associations between olfactory impairment and some factors, another potential, though little researched, influence is an effect of race or ethno-regional group. Two recent studies have compared risk factors for olfactory impairment in overlapping samples of blacks and whites [10, 17]. Poorer olfaction was consistently associated with older age among both blacks and whites. However, associations with being male were found for both blacks and whites in one study [10] but only for blacks in the other [17], whereas associations with having less education were found for both blacks and whites in one study [17] but only for whites in the other [10]. Associations for other factors were dependent on race, with the particularly striking finding of one study that having an apolipoprotein (APOE) ε4 allele was associated with poor olfaction among whites but with good olfaction among blacks [17]. There is some research on risk factors for olfactory impairment specifically in Asian populations. An association between older age and poorer olfaction has been reported for samples of Chinese [20] and Japanese [21]. A study of Japanese-Americans also reported this association with age, but found no association between APOE genotype and olfactory test scores [22]. Studies with Asian samples investigating a wider range of potential risk factors for olfactory impairment

are limited in having used self-reported olfactory dysfunction rather than olfactory test scores [23, 24].

In the present study, we aimed to expand the limited literature on racial and ethno-regional differences or similarities in risk factors for olfactory impairment. Olfactory ability was based on odour identification (OI) test scores, rather than self-reported dysfunction. We investigated demographic and health factors in two samples, one comprising Indonesians and the other white Australians. We also investigated and compared these groups on how olfactory ability was associated with general cognitive functioning and verbal ability. An association between OI and verbal ability has been previously described [1, 25, 26], with both possibly involving the same cognitive domain [27], as well as there being evidence for an integrated odour/lexical system in the brain [28].

Methods

Study participants

Retrospective baseline data for this cross-sectional study were obtained from two members of the Cohort Studies of Memory in an International Consortium (COSMIC) [29] that had measured olfactory ability: Atma Jaya Cognitive and Ageing Research (AJ) from Jakarta, Indonesia and the Sydney Memory and Ageing Study (MAS) from Sydney, Australia. Full details of the recruitment process are available elsewhere for AJ [6] and MAS [30]. Briefly, AJ participants were Indonesians aged ≥ 60 years old and without physical or mental health conditions that could affect assessments; this population typically has low education levels, but all participants had sufficient reading ability to understand and complete the assessments. MAS participants were population-based individuals aged 70–90 years, and without dementia or other conditions that could affect assessments. Of the 1037 MAS participants, only 866 (83.5%) who were white and of an English-speaking background were included in this study. Both AJ and MAS provided data for age, sex and education, which we classified as either less than or at least 9 years of formal schooling. Any participant without olfactory ability data was excluded: 75/545 (13.8%) of individuals in AJ, and 48/866 (5.5%) of the eligible individuals in MAS. There was no significant difference in any of the characteristics listed in Table 1 between included participants and individuals without olfactory data in AJ. For MAS, included participants had higher levels of high-density lipoprotein (HDL) cholesterol (1.46 mmol/L vs 1.30 mmol/L, $t = 2.18$, $p = 0.030$) and a lower prevalence of APOE ε4 positivity (22.4% vs 38.1%, $\chi^2 = 5.53$, $p = 0.019$) than individuals without olfactory data; there were no significant differences for any of the other characteristics listed in Table 1. A total of 1289 individuals were included in this study, 470 from AJ and 819 from MAS.

Olfactory ability tests

Familiarity with particular odours is influenced by culture [31] and thus different but culturally appropriate OI tests were used in AJ and MAS. In AJ, this was a 10-item test of odours commonly found in Indonesia [32], and in MAS it was the 12-item Brief Smell Identification Test [33]. For both tests, the assessments involved participants being given a single olfactory stimulus at a time and instructed to choose the correct odour name from four

possible answers. The tests thus had similar operational procedures and verbal demands, and were considered to be comparable.

Clinical risk factors

Depression was assessed with the Geriatric Depression Scale in both AJ and MAS [34]. Blood samples were used in both studies to determine levels of low-density lipoprotein (LDL) cholesterol, HDL cholesterol, and fasting plasma glucose, as well as APOE genotype. Diabetes was defined in both studies as a history of, or being treated for diabetes, or having a fasting plasma glucose level ≥ 7 mmol [35]. Hypertension was defined in AJ as a systolic blood pressure (BP) ≥ 140 mmHg and/or a diastolic BP ≥ 90 mmHg [36], and in MAS using the same BP cutoffs or either of a previous diagnosis or current treatment. Participants were defined as smokers if current smokers when assessed (past smoking was not investigated as this information was only collected in MAS). APOE ε4 carrier status was classified as either positive or negative. Other potential risk factors that were not assessed in both AJ and MAS were not included.

Language and cognitive status tests

Both AJ and MAS administered language tests that included a semantic fluency test (animals named in 60 s) [37], and either a 15-item (AJ) or 30-item (MAS) version of the Boston Naming Test (BNT) [38]. As a measure of cognitive status, both studies also administered the Mini-Mental State Examination (MMSE) [39].

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS for Windows version 20.0). For comparisons between AJ and MAS, normally distributed continuous data were analysed using independent *t* tests, and non-normally distributed continuous and categorical data were analysed using Mann–Whitney and Chi-square tests.

For each study, we used univariate general linear models to investigate the extent to which OI scores were associated with each risk factor and cognitive test scores. Study-specific multivariate regression models featuring all risk factors and cognitive test scores were then also conducted (using the Enter method in SPSS). Inspection of P–P plots suggested no significant deviation from multivariate normality, and multicollinearity tests indicated that none of the included independent variables were highly linearly related.

Results

Table 1 shows the characteristics of the subjects, including the results of statistical comparisons. Compared to the Indonesian group, the white Australian group was older, and had more years of education and a greater percentage of males. White participants also had lower mean LDL cholesterol levels and GDS scores. The prevalence of smoking and diabetes was lower among whites, but the prevalence of hypertension was higher. HDL cholesterol levels and APOE ε4 positivity did not differ significantly between the groups. Mean MMSE and fluency scores were higher among whites than Indonesians.

Univariate analyses (Table 2) revealed significant associations with OI ability that were similar among Indonesians and whites Australians for some factors. In both groups, older age and smoking were associated with lower OI scores, while higher BNT, fluency and MMSE scores were associated with higher OI scores. Other significant associations with OI ability were found only within one of the groups. For Indonesians, having less than 9 years of education was associated with lower OI scores, and higher LDL cholesterol levels were associated with higher OI scores. For white Australians, being male, having diabetes and higher GDS scores were all associated with lower OI scores. HDL cholesterol levels, APOE ε4 positivity and hypertension were not significantly associated with OI ability in either group.

The results of multivariate analyses that included all factors investigated are shown in Table 3. For Indonesians, the only variables identified in univariate analyses that remained significantly associated with OI scores were language test scores. For white Australians, the demographic and health variables identified in univariate analyses remained significantly associated with OI scores, but language test and MMSE scores did not.

Discussion

We investigated factors associated with olfactory functioning (specifically OI) in two ethno-regional groups, Indonesians and white Australians. Univariate analyses revealed some common factors associated with OI scores in Indonesians and white Australians. However, multivariate analyses that adjusted for possible confounding by the other factors revealed patterns of effects that differed between the groups, and it is these results that we focus on here. Older age was associated with poorer OI ability only in white Australians after multivariate analyses. Older age is an established risk factor for olfactory impairment [8–12, 20–22], and has many potential causes, including changes in non-olfactory elements and in any or all of the olfactory epithelium, bulb or cortical processing regions [13]. Men commonly have poorer olfactory functioning than women [9–12, 14, 15], but this effect can be more apparent in older individuals [40, 41]. The relatively young mean age of our Indonesian group may thus explain why we did not find age or sex effects in this group. Two previous studies reporting no difference between men and women featured Asian samples (Chinese and Koreans), and in both, the mean age was also relatively low [23, 24]. However, these studies also relied on self-reported olfactory or chemosensory dysfunction rather than olfactory test scores. Potential reasons for women having better olfactory functioning than men include the presence of more neurons and non-neuronal cells in the olfactory bulb [42], and beneficial effects of female, but deleterious effects of male, sex hormones [43]. Verbal ability was associated with OI scores in Indonesians, reflecting previous reports linking lower language test scores to olfactory dysfunction [26, 27, 44] and neuroimaging evidence for close linkages between olfactory and lexical brain systems [28]. Education was not associated with OI scores in multivariate analyses, possibly because any effects of education on OI ability [8, 9, 12, 16, 17] may be through enhancing verbal ability.

Recent reviews support our observed association between depression and poorer olfactory functioning in white Australians [45, 46]. Depression may share or invoke physiological changes that affect olfaction [47] including thinner olfactory epithelium and less olfactory

receptor neurons [47]. Depression might also result in less attention to olfactory stimuli [48] or conceivably be a result of loss of smell affecting quality of life. White Australians also exhibited an association between diabetes and poorer OI. There is increasing evidence for an association between diabetes and olfactory dysfunction [25], with potential mechanisms including the effects of hyperglycemia, macrovascular disease, and insulin resistance on the olfactory apparatus and/or brain [9, 48]. While one study not finding an association between diabetes and olfactory functioning used a non-white sample [49], another found that patients with diabetes for more than 10 years had lower OI scores than patients with diabetes for 10 or less years [50]. The whites in our study were an average 10 years older than the Indonesians, and this difference may have contributed to finding an effect of diabetes in the former but not the latter.

Smoking was only associated with poorer OI in white Australians after multivariate analyses. An association between smoking and OI scores is consistent with a recent meta-analysis finding that smoking is a reversible risk factor for olfactory impairment [19]. Multivariate analyses found no associations between OI scores and cholesterol, hypertension or APOE ε4 status. The null cholesterol finding is consistent with some previous reports [12, 51, 52], and while some studies have reported deleterious effects of hypertension [9, 19, 53], others have found no effect [48, 49]. Similarly, some studies have found an association between the APOE ε4 allele and olfactory dysfunction [10, 12] but others, including one in a sample of Japanese-Americans, have not [22, 54, 55], and further investigation is warranted.

Some previous studies have identified differences in olfactory functioning between racial/ethnic groups, including poorer OI among blacks, Asians and Hispanics than among whites [9–11]. Unfortunately, the use of different, but culturally appropriate, OI tests prevented us from directly comparing performance between our Indonesian and white Australian samples. Other limitations of our study include the groups not being more closely matched in age, and not considering the use of medication for relevant risk factors, including diabetes, hypertension, high cholesterol and depression. Not being able to include past smoking means one reason for lower OI scores may have been missed, as while past smoking has smaller effects than current smoking [19], recovery of olfactory function after quitting smoking can take some years depending on the amount smoked [56]. We also did not investigate associations between OI ability and memory, which would be of particular interest given reported associations between lower hippocampus volume and poorer OI test scores [44, 57]. Longitudinal studies are needed to determine the extent to which some of the factors we found to be associated with OI scores either contribute to or are a result of olfactory ability.

This study is the first to investigate and compare associations between olfactory functioning and various demographic, clinical and cognitive factors in Indonesians and white Australians. While our univariate analyses revealed some common factors associated with OI scores in Indonesians and white Australians, our multivariate analyses revealed patterns of effects that differed between the groups, with only language test scores remaining to be associated with OI ability in Indonesians and only demographic and health variables remaining to be associated with OI ability in white Australians. Some of these differences could stem from the different demographic characteristics of the cohorts, particularly the

older age of MAS compared to AJ, and studies should ideally aim to compare populations with similar age distributions. The existence of ethno-regional differences in associations between risk factors for olfactory ability or dysfunction could help explain mixed findings in the literature. Worse olfactory functioning has been associated with many negative outcomes, including an increased risk of dementia and mortality [1, 4, 5]. Future research could investigate whether differences in associations between risk factors and OI ability influence associations between OI ability and negative outcomes in different ethno-regional groups. Further, interventions for olfactory dysfunction might need to be tailored to specific ethno-regional groups.

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Table 1

Subjects characteristics

Factor	Indonesians (*n* = 470)	White Australians (*n* = 819)	*p* value
Age, mean ± SD	67.4 ± 7.4	78.7 ± 4.8	< 0.001
Female, *n* (%)	316 (67.2)	465 (56.8)	< 0.001
Education < 9 years, *n* (%)	304 (64.7)	120 (14.7)	< 0.001
HDL, mmol/L, mean ± SD	1.4 ± 0.4	1.5 ± 0.5	0.126
LDL, mmol/L, mean ± SD	3.6 ± 1.0	2.8 ± 0.9	< 0.001
APOE ε4+, *n* (%)	98 (24.6)	170 (22.4)	0.429
Smoker, *n* (%)	76 (16.2)	23 (2.8)	< 0.001
Diabetes, *n* (%)	95 (20.2)	107 (13.1)	0.001
Hypertension, *n* (%)	253 (59.1)	676 (82.5)	< 0.001
GDS score, mean ± SD	3.4 ± 2.7	2.2 ± 2.0	< 0.001
BNT score, mean ± SD[a]	12.0 ± 3.3	25.0 ± 3.5	–
Fluency score, mean ± SD	14.7 ± 4.8	15.0 ± 4.3	< 0.001
MMSE score, mean ± SD	23.0 ± 4.9	28.1 ± 1.4	< 0.001
OI score, mean ± SD[b]	5.4 ± 2.6	9.2 ± 2.2	–

[a]The BNT was 15 items for Indonesians and 30 items for white Australians

[b]Different OI tests were used, with the maximum score 10 for Indonesians and 12 for white Australians

APOE apolipoprotein E, *BNT* Boston Naming Test, *GDS* Geriatric Depression Scale, *HDL* high-density lipoprotein cholesterol, *LDL* low-density lipoprotein cholesterol, *MMSE* Mini-Mental State Examination, *OI* odour identification, *SD* standard deviation

Table 2

Univariate associations with odour identification scores

Factor	Indonesians		White Australians	
	B	***p* value**	***B***	***p* value**
Age, years	−0.047	0.004	−0.100	< 0.001
Female	0.225	0.875	0.888	< 0.001
Education < 9 years	−1.285	< 0.001	−0.260	0.223
HDL, mmol/L	0.413	0.164	−0.017	0.918
LDL, mmol/L	0.280	0.010	0.142	0.110
APOE ε4+	−0.208	0.495	−0.218	0.238
Smoker	−0.694	0.034	−1.089	0.017
Diabetes	0.491	0.102	−0.732	0.001
Hypertension	0.100	0.627	−0.131	0.510
GDS score	−0.039	0.397	−0.122	0.001
BNT score	0.167	< 0.001	0.073	0.001
Fluency score	0.121	< 0.001	0.054	0.002
MMSE score	0.122	< 0.001	0.163	0.002

APOE apolipoprotein E, *BNT* Boston Naming Test, *GDS* Geriatric Depression Scale, *HDL* high-density lipoprotein cholesterol, *LDL* low-density lipoprotein cholesterol, *MMSE* Mini-Mental State Examination

Table 3

Multivariate associations with odour identification scores

Factor	Indonesians		White Australians	
	B	*p* value	B	*p* value
Age, years	−0.021	0.197	−0.073	< 0.001
Female	0.179	0.521	0.862	< 0.001
Education < 9 years	−0.216	0.418	−0.085	0.699
HDL, mmol/L	0.193	0.578	−0.222	0.212
LDL, mmol/L	0.202	0.092	0.008	0.928
APOE ε4+	−0.172	0.507	−0.222	0.212
Smoker	−0.249	0.469	−0.964	0.038
Diabetes	0.201	0.449	−0.798	0.001
Hypertension	0.189	0.397	0.060	0.762
GDS score	0.047	0.288	−0.088	0.020
BNT score	0.089	0.047	0.042	0.089
Fluency score	0.069	0.011	0.006	0.767
MMSE score	0.008	0.800	0.021	0.707

APOE apolipoprotein E, *BNT* Boston Naming Test, *GDS* Geriatric Depression Scale, *HDL* high-density lipoprotein cholesterol, *LDL* low-density lipoprotein cholesterol, *MMSE* Mini-Mental State Examination