

Original Article

Subjective cognitive and olfactory impairments predict different prospective dementia outcomes

Nira Cedres^{1,2,3,*}, Jonas K. Olofsson¹

¹Department of Psychology, Sensory Cognitive Interaction Laboratory (SCI-Lab), Stockholm University, Stockholm, Sweden

²Department of Psychology, Faculty of Health Sciences, University Fernando Pessoa Canarias, Las Palmas de Gran Canaria, Spain

³Division of Clinical Geriatrics, Centre for Alzheimer Research, Department of Neurobiology, Care Sciences, and Society, Karolinska Institutet, Stockholm, Sweden

*Corresponding author: Department of Psychology, Sensory Cognitive Interaction Laboratory (SCI-Lab), Stockholm University, Albanovägen 12, 114 19 Stockholm, Sweden. Email: nira.cedres@psychology.su.se

Self-reported measures emerge as potential indicators for early detection of dementia and mortality. We investigated the predictive value of different self-reported measures, including subjective cognitive decline (SCD), subjective olfactory impairment (SOI), subjective taste impairment (STI), and self-reported poor health (SPH), in order to determine the risk of progressing to Alzheimer's disease (AD) dementia, Parkinson's disease (PD) dementia, or any-other-cause dementia. A total of 6,028 cognitively unimpaired individuals from the 8th wave of the English Longitudinal Study of Ageing (ELSA) were included as the baseline sample and 5,297 individuals from the 9th wave were included as 2-year follow-up sample. Self-rated measures were assessed using questions from the ELSA structured interview. Three logistic regression models were fitted to predict different dementia outcomes. SCD based on memory complaints (OR = 11.145; $P < 0.001$), and older age (OR = 1.108, $P < 0.001$) significantly predicted the progression to AD dementia at follow-up. SOI (OR = 7.440; $P < 0.001$) and older age (OR = 1.065, $P = 0.035$) significantly predicted the progression to PD dementia at follow-up. Furthermore, SCD based on memory complaints (OR = 4.448; $P < 0.001$) jointly with complaints in other (non-memory) mental abilities (OR = 6.662; $P < 0.001$), and older age (OR = 1.147, $P < 0.001$) significantly predicted the progression to dementia of any other cause. Different types of complaints are specifically associated with different dementia outcomes. Our study demonstrates that self-reported measures are a useful and accessible tool when screening for individuals at risk of dementia in the general population.

Key words: self-reported measures, subjective cognitive decline, screening, dementia, olfaction.

Introduction

The growth of the elderly population globally increases the prevalence of age-associated neurodegenerative diseases, such as Alzheimer's disease (AD) or Parkinson's disease (PD), among others (Li et al. 2022). The progressive neurodegeneration in both AD and PD results in the onset of dementia in the later stages of these diseases. However, current efforts to develop drug-based treatments have not reached substantial therapeutic benefits for these conditions once present (Karran and Hardy 2014; Zhang et al. 2023). Furthermore, the available drug-based treatments yield side effects which renders leading to cautious consideration (Daly 2023). This highlights the importance of early detection and preventive approaches to identify individuals at risk of neurodegenerative diseases.

Self-reported measures have emerged as potential indicators for early detection and prediction of dementia and mortality (DeSalvo et al. 2006; Jylhä et al. 2006). In the context of predictive, preventive, and personalized medicine, the inclusion of subjective assessments could provide a cost-effective tool to identify individuals at risk, potentially decreasing the social and economic impact of the associated diseases (Golubnitschaja et al. 2014). Especially, subjective cognitive complaints have shown promise as early markers

of cognitive decline and potential predictors of dementia (Slot et al. 2019). Individuals reporting subjective cognitive decline (SCD) often experience difficulties in cognitive function, despite standardized neuropsychological evaluations failing to detect objective impairment (Jessen et al. 2014, 2020). These self-reported cognitive complaints have been associated with underlying brain pathologies, such as increased amyloidosis and neurodegeneration (Buckley et al. 2017; Müller et al. 2017; Cedres et al. 2021), and have been linked to an elevated risk of future cognitive impairment and dementia, especially the context of AD (Slot et al. 2019; Wang et al. 2021). Most of SCD research has focused on amnesic cognitive complaints (Rabin et al. 2015). Nevertheless, complaints in other domains are also prevalent, with different phenotype-dependent neurodegenerative patterns (Diaz-Galvan et al. 2021). A recent review and meta-analysis shows increased cerebrovascular disease markers in individuals with SCD, proposing the condition not only as a preclinical symptom of AD but also of vascular cognitive impairment (VCI) (Pitti et al. 2022).

On average, SCD individuals may have normal olfactory abilities (Cedres et al. 2023). However, olfactory impairment is present among some people with SCD, and, in a recent meta-analysis, the combination of olfactory impairment and

SCD was proposed as a potential early marker of dementia. The authors suggested combining SCD with sensory assessments in order to increase predictive sensitivity (Jobin et al. 2021). However, older adults who have already an objectively established cognitive impairment are typically unaware of any olfactory impairments and their olfactory self-assessment is uninformative (Ekström et al. 2019). Furthermore, decreased cortical responses to taste stimuli were recently reported in cognitively impaired older adults (El Kadiri et al. 2023). Thus, the combination of SCD and subjective sensory complaints might be beneficial for predicting dementia outcomes in adults without objective cognitive impairment. In this context, subjective olfactory impairment (SOI) has gathered attention as potential predictor of cognitive decline and dementia (Cedres et al. 2023). SOI is characterized by self-reported difficulties in perceiving smells and is associated with an increased risk of future dementia and mortality (Stanciu et al. 2014), even after accounting for objective olfactory performance levels. It has been noted that SOI does not correlate strongly with objective olfactory tests, and SOI may instead be affected by nasal air-flow or emotional reactivity (Landis et al. 2003; Knaapila et al. 2008). This lack of a strong association may be due to a lack of clear benchmark for judging how one's own olfactory performance compares to those of others, or the fact that objective olfactory tests often measure identification ability, whereas subjective olfactory assessments typically regard the perceived ability to detect faint odors (Ekström et al. 2019). Indeed, it is difficult to judge how your score on an olfactory test will compare to those of other, unknown people. The literature suggests that SOI assessments might still carry useful information about the olfactory system. Ekström and colleagues (2019) suggested that subjective olfactory assessments are performed based on perceived intra-individual changes over time. SOI, viewed thus as reflecting noticeable, significant olfactory loss or decline, explains why such assessments would possess predictive utility and may capture early olfactory deficits that are not yet evident in objective assessments (Cedres et al. 2023).

In addition to SCD and SOI, other self-reported complaints hold potential value as indicators of neurodegenerative diseases. One such complaint is subjective taste (gustatory) impairment (STI). Experiences of gustatory impairment could reflect underlying neurodegenerative processes and be reported as changes in gustatory function (Kouzuki et al. 2020). Food aromas coming from the mouth during ingestion are often mislabeled as tastes due to a phenomenon called "oral referral" (Spence 2016). For this reason, STI might be confounded such that it also reflects a poor sense of smell. However, emerging research suggests that STI, when combined with other cognitive and sensory assessments, could contribute to a more comprehensive understanding of an individual's cognitive health trajectory (STI) (Kouzuki et al. 2018). Another subjective indicator is self-reported poor health (SPH), which has also been proposed as a global measure associated to future dementia outcomes (Clarke et al. 2020). SPH refers to individuals' perceptions of their overall health status, and it provides insights into their physical, mental, and emotional well-being (Bombak 2013). Given the heterogeneous presentations of neurodegenerative diseases, the inclusion of SPH in predictive models could enhance their accuracy by accounting for multiple additional health-related factors that may contribute to disease progression. As such, considering STI and SPH alongside other subjective complaints could enrich the predictive

utility of such assessments, offering a more nuanced perspective on the early identification of dementia-related outcomes.

Little is known about how these subjective measures, when used together, may predict distinct prospective outcomes. This issue is critical because, due to the subjective nature of the tests, there is a risk that they reflect the same thing (e.g. poor overall health, rather than domain-specific impairments), in which case these complaints would not be predictive of distinct outcomes. Thus, the current study aims to investigate the predictive value of different self-reported measures, combining SCD based on amnesic complaints and non-amnesic complaints, SOI, subjective taste impairment (STI), and SPH, in order to determine the risk of progressing to AD or PD dementia. By exploring the associations between these self-reported measures and the subsequent development of neurodegenerative diseases, we aim to contribute to the growing body of knowledge regarding early detection and prediction of disease progression.

Materials and methods

Participants

The study sample belongs to the English Longitudinal Study of Ageing (ELSA), a population-based sample to study the older adult men and women living in England (Stepptoe et al. 2013). ELSA data is publically available upon request. We used data from 2 years follow-up from wave 8 (i.e. 2016) to wave 9 (i.e. 2018). A total of 6,028 participants were retrieved from wave 8 of whom 5,297 were followed up until wave 9. Gender was operationalized based on self-reported gender identity. Level of education was operationalized based on the age individuals finished their formal education and categorized as: (0) no formal education; (1) up to 14 years old; (2) between 15 and 18 years old; (3) and 19 or over.

According to the SCD-Initiative (Jessen et al. 2014), participants with (i) Objective cognitive decline, dementia, and/or impaired functionality; history of (ii) AD diagnosis; (iii) PD diagnosis; (iv) cardiovascular or cerebrovascular problems; (v) neurodegenerative disease or psychiatric disease were excluded from the baseline sample (i.e. wave 8).

Self-reported measures assessment

Self-rated complaints were assessed using different questions from a structured interview (Stepptoe et al. 2013). SCD was assessed by two different questions that referred to (i) subjective memory performance and (ii) other mental abilities performance in the present compared to previous status (Table 1). SOI, STI, and SPH status were assessed by asking individuals to complete three different sentences, rating each ability separately (Table 1).

All five questions about self-reported measures were rated in a 5-point Likert scale according to degree of ability (i.e. 1- excellent to 5- poor). Following a conservative approach, responses equal, or below 4 (i.e. from "fair" to "excellent") were classified as not self-reported complaint. Responses equal to 5 (i.e. "poor") were classified as self-reported complaint.

Dementia diagnosis at follow-up

Dementia diagnosis in ELSA cohort is ascertained at each wave through the combination of self-reported or informant-reported physician-made diagnosis of dementia. In addition, when participants are unable to respond to the full assessment of ELSA, an informant (i.e. family member or caregiver)

Table 1. Self-reported complaints questions.

Subjective cognitive decline (SCD)	How would you rate your memory at the present time? How would you rate your other mental abilities (not memory), such as thinking clearly or solving problems at the present time?
Subjective olfactory impairment (SOI)	Is your sense of smell...
Subjective taste impairment (STI)	Is your sense of taste...
Self-reported poorer health (SPH)	Would you say your health is...

All five questions about self-reported measures were rated in a 5-point Likert scale according to degree of ability (i.e. 1- excellent to 5- poor).

completes the short form of IQCODE questionnaire, and the threshold score of 3.38 is used to classify the participants as dementia patients (Jorm 1994; Duffner et al. 2022; Ajnakina et al. 2023; Kontari et al. 2023). The dependent variable of the current study is the onset of AD dementia, PD dementia or dementia of any other cause at 2-year follow-up (from wave 8 to wave 9).

Statistical analysis

To report the distribution of the different types of self-reported measures, frequencies and descriptive analysis were performed. Paired sample *T*-test and chi-square analysis were performed to compare the sample characteristics at baseline and follow-up.

Three logistic regression models using the backward stepwise conditional method for predictor inclusion were performed independently to predict the risk of developing AD dementia, PD dementia, or dementia of any other cause at follow-up. SCD was operationalized separately based on complaints regarding memory and general cognitive abilities; SOI, STI, and SPH were included as predictors for each logistic regression model, together with age, gender, education, and ethnicity. Interactions between the self-reported measures were also tested. The overall predictive capacities of the models were examined through the omnibus test of model coefficients, Nagelkerke R^2 and Hosmer–Lemeshow test for each model goodness-of-fit.

All statistical analyses were carried out using SPSS v.26 (IBM Statistics, Chicago, IL, USA). All *P*-values were two-tailed and the level of significance was set at $P < 0.05$. Benjamini–Hochberg correction was applied to correct for multiple comparisons.

Results

Sample characteristics

Demographic and self-reported measures data are given in Table 2. Of the 6,028 participants at baseline (i.e. wave 8), 5,297 were available at 2-year-follow-up (i.e. wave 9). The participants available at follow-up were comparable to the baseline sample in terms of proportion of sex ($\chi^2 = 1.44$; $P = 0.230$), education ($\chi^2 = 1.25$; $P = 0.740$), and ethnicity ($\chi^2 = 0.02$; $P = 0.895$). First, we assessed the frequency

Table 2. Demographic information of the study sample.

	Wave 8	Wave 9
<i>N</i> (females/males)	3407/2621	2989/2308
Age (mean (SD)) ^a	68.2(9.21)	69.8(8.70)
Ethnicity (white/nonwhite)	5802/226	5103/194
Amnesic SCD	335	308
Non-amnesic SCD	74	68
SOI	287	285
STI	87	85
SPH	233	235

Amnesic-SCD: Amnesic subjective cognitive decline; non-amnesic SCD: non-amnesic subjective cognitive decline; SOI: subjective olfactory impairment; STI: subjective taste impairment; SPH: self-reported poorer health.

of each self-reported measure in the baseline sample. Subjective memory complaints (i.e. amnesic SCD) were present in 5.56% ($N = 335$) of the participants, whereas subjective complaints in other mental abilities-not memory (i.e. non-amnesic SCD) were present in 1.22% ($N = 74$) of the participants. Regarding the other self-reported measures, SOI was present in 4.76% ($N = 287$) of the participants, STI in 1.44% ($N = 87$) and SPH was present in 3.87% ($N = 233$). Amnesic SCD and non-amnesic SCD complaints were moderately overlapped with each other ($\chi^2 = 3024.3$; $P < 0.001$), as well as SOI and STI complaints ($\chi^2 = 860.9$; $P < 0.001$) (Fig. 1). The interaction term among predictors was included in the regression models. Regarding the incidence of dementia after 2 years follow-up, a total of 15 participants developed AD dementia (0.65%), other 15 participants developed PD (0.65%), and finally, 34 participants developed any-other-cause dementia non-AD/non-PD (1.48%).

Predictors of incidence of Alzheimer’s disease dementia

A logistic regression model was used to identify predictors of AD dementia incidence at a 2-year follow-up. The following predictors were considered including interaction effect among self-reported measures: amnesic SCD, non-amnesic SCD, SOI, STI, SPH, age, gender, education, and ethnicity.

Using the backward conditional variable inclusion method, two significant predictors remained significant in the model at step 18, with an $R^2 = 20.2\%$ and an adequate goodness-of-fit based on the Hosmer–Lemeshow test ($\chi^2_{(8)} = 6.42$; $P = 0.600$) (Fig. 2). Additionally, the overall predictive capacity of the model was examined through the omnibus test of model coefficients, yielding a $\chi^2_{(6)} = 41.06$ ($P < 0.001$) and a $-2\log$ likelihood = 164.89. Amnesic SCD showed a strong association with AD dementia (OR = 8.235; $P = 0.001$), indicating that individuals reporting subjective memory complaints at baseline were substantially more likely to progress to AD dementia. Furthermore, age was linked to a significantly increased risk (OR = 1.107, $P = 0.008$), with each incremental year associated with a higher likelihood of developing AD dementia. Education and the interaction term between amnesic SCD and SOI (Exp(B) = OR, $P = 0.054$) remained in the final model showing a trend toward significance. The rest of the variables were excluded from the equation.

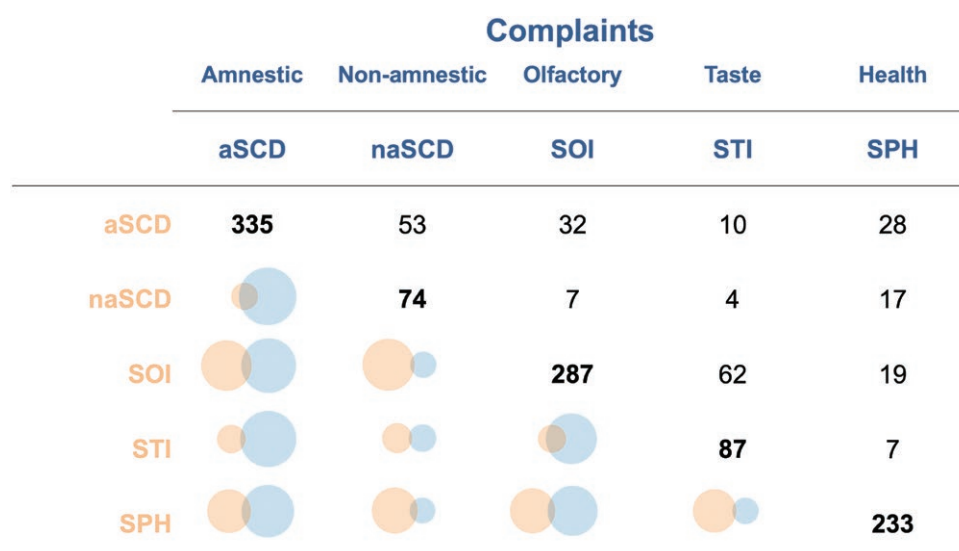


Fig. 1. Proportion of the different self-reported impairments and their overlap at baseline. Amnestic-SCD: Amnestic subjective cognitive decline; non-amnestic SCD: non-amnestic subjective cognitive decline; SOI: subjective olfactory impairment; STI: subjective taste impairment; SPH: Self-reported poorer health.

Predictors of incidence of Parkinson's disease dementia

A logistic regression model was used to identify predictors of PD dementia incidence at a 2-year follow-up. The following predictors were considered including the interaction terms between self-reported measures: amnestic SCD, non-amnestic SCD, SOI, STI, SPH, age, gender, education, and ethnicity.

Using the backward conditional variable inclusion method, two significant predictors remained significant in the model at step 17, with an $R^2 = 10.5\%$ and an adequate goodness-of-fit based on the Hosmer-Lemeshow test ($\chi^2_{(8)} = 6.53$; $P = 0.58$) (Fig. 2). Additionally, the overall predictive capacity of the model was examined through the omnibus test of model coefficients, yielding a $\chi^2_{(3)} = 21.17$ ($P < 0.001$) and a $-2\log$ likelihood = 184.78. SOI showed a strong association with PD dementia ($OR = 7.440$; $P < 0.001$), indicating that individuals reporting SOI at baseline were substantially more likely to progress to PD dementia. Age also exhibited a significantly increased risk ($OR = 1.065$, $P = 0.048$), with each incremental year associated with a higher likelihood of developing PD dementia. Gender remained a non-significant predictor in the final model ($OR = 0.330$, $P = 0.061$). The rest of the variables were excluded from the equation.

Predictors of incidence of any-other-cause dementia

A logistic regression model was used to identify predictors of any-other-cause dementia (i.e. not AD or PD dementia) incidence at 2-year follow-up. The following predictors were considered including the interaction terms between self-reported measures: amnestic SCD, non-amnestic SCD, SOI, STI, SPH, age, gender, education, and ethnicity.

Using the backward conditional variable inclusion method, three individual predictors and an interaction term remained significant in the model at step 15, with an $R^2 = 23.3\%$ and an adequate goodness-of-fit based on the Hosmer-Lemeshow test ($\chi^2_{(8)} = 15.03$; $P = 0.058$) (Fig. 2). Additionally, the overall predictive capacity of the model was examined through the omnibus test of model coefficients, yielding a $\chi^2_{(5)} = 93.14$

($P < 0.001$) and a $-2\log$ likelihood = 317.91. The presence of amnestic SCD ($OR = 6.824$; $P = 0.001$), non-amnestic SCD ($Exp(B) = 43.631$; $P = 0.002$) and their interaction term ($Exp(B) = 0.046$; $P = 0.004$) were significant. These results indicated that individuals reporting either of the SCD complaints at baseline were substantially more likely to progress to dementia, while those reporting both complaints showed a decreased risk of progression ($OR < 1$). Age also exhibited a significantly increased risk ($OR = 1.139$; $P = 0.001$), with each incremental year associated with a higher likelihood of developing dementia.

Discussion

Clinical dementia is often preceded by self-reported complaints in cognitive abilities. These complaints may reflect a sub-clinical, but progressive deterioration. Understanding the prognostic value of different types of complaints may facilitate early detection of those at risk of cognitive impairment. The current study aimed to investigate the potential prognostic value of different self-reported complaints as predictors of dementia. Using a population-based cohort of older adults from England, we found that different types of complaints are associated with different dementia outcomes. The progression to AD dementia was associated with self-reported subjective memory complaints (i.e. amnestic SCD), whereas the joint presence of complaints in memory and other cognitive abilities (i.e. amnestic + non-amnestic SCD) was associated with progression to dementia of any other cause. The presence of self-reported olfactory impairment, SOI, was strongly associated with progression to PD dementia. These findings highlight the relevance of self-reported complaints in the aging population when screening individuals at risk of neurodegenerative diseases and that the different types of complaints may reflect diverse underlying pathologies.

The value of SCD as a preclinical symptom of underlying neuropathological process was extensively documented in the last decade, especially in the context of preclinical AD (Jessen et al. 2014, 2020). SCD individuals have increased amyloid

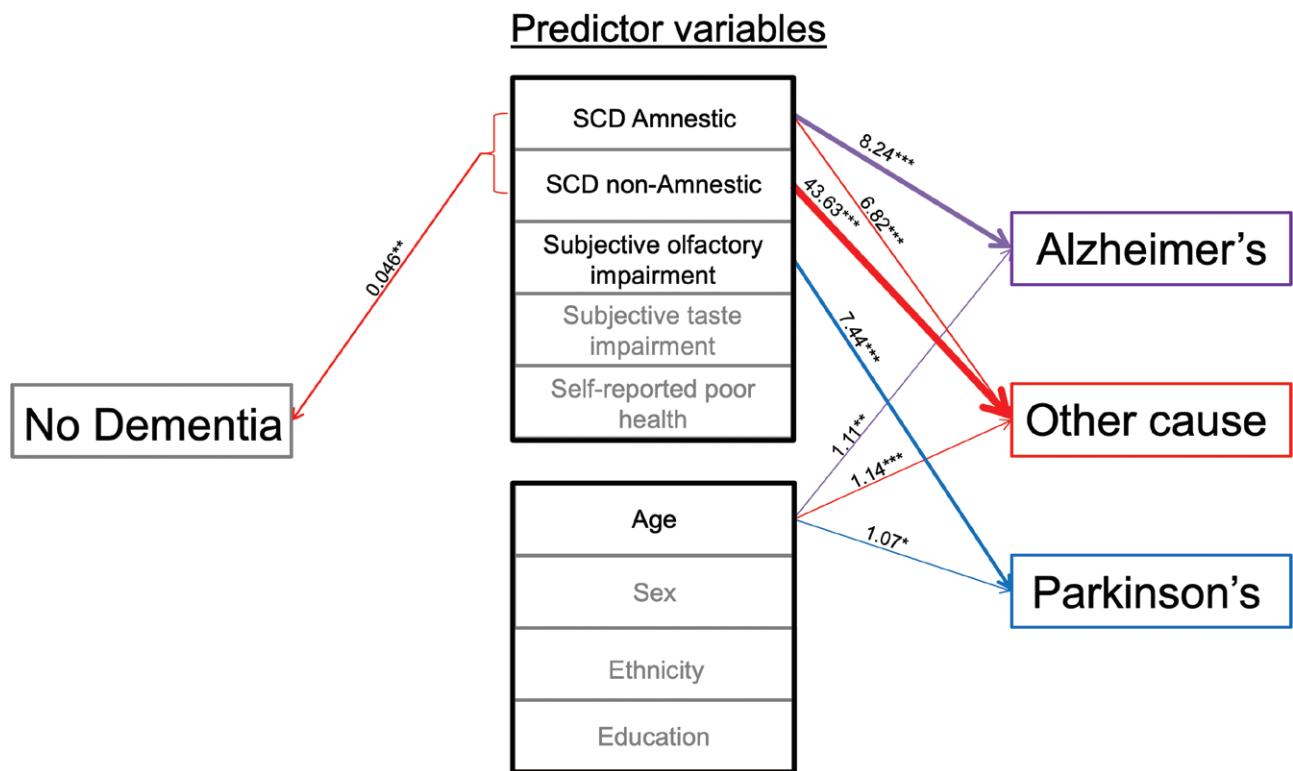


Fig. 2. Predictive logistic regression models for the different dementia outcomes. Amnestic-SCD: Amnestic subjective cognitive decline; non-amnestic SCD: non-amnestic subjective cognitive decline; SOI: subjective olfactory impairment; STI: subjective taste impairment. Color-specific arrows represent exp(B) size for each dementia outcome. Non-significant predictors are colored in gray ink. * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

and tau levels (Perrotin et al. 2017; Buckley et al. 2019), as well as cortical thinning and reduced white matter integrity (Cedres et al. 2021; Nemy et al. 2023), in the absence of any objective cognitive impairment. Nevertheless, little is known regarding the unique contribution of different complaints. A recent study using multiple operationalization approaches for SCD showed that different SCD phenotypes were associated with different patterns of neurodegeneration (Diaz-Galvan et al. 2021). While the single presence of amnestic SCD was associated with a typical AD-like brain atrophy pattern, the joint presence of memory complaints with complaints in other cognitive domains (i.e. amnestic + non-amnestic SCD) and the single presence of non-amnestic complaint was associated with increased cerebrovascular lesions (Diaz-Galvan et al. 2021). Similarly, using a longitudinal perspective in our study, we found that the presence of amnestic SCD was associated with an increased risk of progression to AD dementia and the presence of either non-amnestic SCD or amnestic SCD increased the risk of transitioning to non-AD-non-PD dementias. Although we lack specific information regarding the different types of “non-AD, non-PD” dementia patients in this cohort, vascular dementia is likely highly prevalent, being the second most common cause of dementia in older adults (Kalaria et al. 2008). Furthermore, as shown in a recent systematic review and meta-analysis, increased underlying cerebrovascular pathology is prevalent in SCD (Pitti et al. 2022). These findings highlight the relevance of cognitive complaints specificity and unique contribution to the risk of progression to different neurodegenerative diseases and dementia. On the other hand, the joint presence of amnestic and non-amnestic SCD decreased the risk of transitioning to non-AD-non-PD

dementia at follow-up. An increased number of subjective cognitive complaints has previously been associated with increased levels of depressive symptomatology (Cedres et al. 2019; Diaz-Galvan et al. 2021; Zöllinger et al. 2023; Zapater-Fajari et al. 2024). Thus, the joint presence of both complaints could be associated with other factors, such as the risk of depression, rather than underlying dementia.

On the other hand, the value of self-reported subjective olfactory loss is emerging as an early indicator of dementia and death (Stanciu et al. 2014; Cedres et al. 2023). Objective odor identification impairment is frequent in AD (Duff et al. 2002; Motomura and Tomota 2006) and PD (Doty 2012). In a previous study, we demonstrated that although individuals reporting SOI had similar odor identification performance as controls, the SOI individuals showed a steeper decline in odor identification at a 5-year follow-up, and a distinct emerging correlative pattern between odor identification performance and various cognitive measures (Cedres et al. 2023). Our current findings suggest SOI as a specific complaint associated with an increased risk of developing PD dementia in two years, even when other risk factors for PD are taken into account, such as age (Hindle 2010). Although subjective cognitive complaints were previously identified as a risk factor for cognitive impairment in PD patients (Galtier et al. 2019), we did not find significant associations between SCD at baseline and PD dementia progression when considering also the SOI effect. In the absence of objective measures of olfaction, we cannot definitively conclude that baseline SOI was reflecting subtle olfactory changes in these PD patients, but we believe this is highly likely since these individuals do not have cognitive impairments that could interfere with their

olfactory self-assessment (Ekström et al. 2019). Olfactory impairments in the preclinical stages of PD are profound (Rahayel et al. 2012) as a consequence of pathology-driven neurodegeneration in the olfactory bulb which prevents olfactory processing (Del Tredici et al. 2002; Iravani et al. 2021). These individuals are mostly cognitively intact in this stage so that their olfactory impairment is likely to be accurately reported. In AD and Lewy body dementia, in contrast, accumulation of Tau protein accumulates in olfactory circuits and adjacent medial-temporal areas, (Tsuboi et al. 2003; Attems and Jellinger 2006; Diez et al. 2024). This may contribute to a joint olfactory and episodic memory decline such that olfactory deficits are not noticed or remembered (Dintica et al. 2021). Future studies assessing the association between SOI and objective olfaction, as well as underlying pathology biomarkers, are needed.

Regarding the other types of self-reported measures, we did not find significant associations between STI or SPH and the dementia outcomes studied. Although SOI was a significant symptom, STI might be less prevalent and/or a less sensitive indicator of neurodegeneration. When objectively impaired, previous studies have shown that olfactory dysfunction is more prevalent than taste dysfunction in AD and PD patients (Doty 2017). These findings align with the frequencies for subjective olfaction and taste in the current study, with SOI being more prevalent. Furthermore, in 71% of the participants with STI complaints, SOI was also reported. Thus, although we did not find a specific contribution of STI to the dementia outcomes, future studies focused on the characterization of STI in the absence of SOI are needed. It is well known that self-reported poorer health is a risk factor for various disease outcomes and increased mortality risk (Strawbridge and Wallhagen 1999). Our results indicate that SCD and SOI assessments provide more specific prognostic utility than subjective health reports.

Some limitations of the current study should be considered when interpreting the results. Although our results are based on a large population-based, ELSA cohort is a focus only on the older English population with little ethnic variability (i.e. over 95% white people). The use of this single cohort may limit the generalization of our findings to other population groups. Future studies should replicate our findings using more diverse populations in terms of ethnicity and a wider age range. In addition, the current follow-up period was relatively short (i.e. 2 years follow-up), limiting the incidence of dementia and thus showing weaker results. Additionally, although dementia is frequently operationalized based on self-reported new diagnoses in large longitudinal population-based cohorts such as ELSA (Kimchi et al. 2017), this operationalization is not optimal. Furthermore, whether the reported dementia diagnosis was established by a neurology specialist, or a general practitioner, which could lead to potential misdiagnosis, is unknown. Future studies including clinical settings defining dementia diagnosis by a specialist and in concordance with the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINDS-ADRDA) criteria or (Mckhann et al. 2011) the International Working Group (IWG-2) (Dubois et al. 2014) criteria are needed. Nevertheless, even within this brief period, we found relevant findings regarding dementia incidence, SCD, and SOI. Our self-reported measures were based on single-item questions, which may not capture the complexity and multidimensionality of these complaints. Future studies should use more

comprehensive and validated questionnaires when assessing the subjective measures.

In sum, we found that different types of subjective reports, including the amnesic SCD, non-amnesic SCD, and olfactory domains, are specifically associated with the incidence of different dementia outcomes. Furthermore, we demonstrate that different types of subjective complaints show specificity when predicting different types of dementia and thus they may be reflecting different underlying pathologies. Our study demonstrates that self-reported complaints provide a useful and accessible tool when screening individuals at risk of dementia in the general population. Thus, it is important to include and monitor self-reported measures during routine assessments in clinical practice and in longitudinal research settings. Future studies should aim to deeply characterize the underlying pathologies corresponding to SOI and different SCD subtypes, as well as their association with other specific dementia outcomes such as vascular dementia. Also, it is important to test the efficacy and feasibility of interventions based on these subjective measures in order to prevent or delay cognitive decline and disease progression.

Funding

This work was supported by the Knut and Alice Wallenberg Foundation (KAW 2016:0229) and the Swedish Research Council (2020-00266) to J. K. Olofsson. The current study was not pre-registered.

Conflict of interest

The authors have no conflict of interest.

Ethical approval

Ethical approval for all the ELSA waves was granted from the National Research and Ethics Committee (<http://www.hra.nhs.uk/>).

Data availability

The data underlying this article were provided by www.elsa-project.ac.uk with permission. Data will be shared on request to the www.elsa-project.ac.uk through <https://portal.dementiasplatform.uk/Apply/ApplicationProcess>.

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