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REVIEW ARTICLE

Recent contributions to the field of subjective cognitive decline in aging: A literature review

Catherine E. Munro PhD[1] | Rory Boyle PhD[2] | Xi Chen PhD[3] | Gillian Coughlan PhD[2] | Christopher Gonzalez MS[4,5] | Roos J. Jutten PhD[2] | Jairo Martinez BS[5,6] | Irina Orlovsky MS[7] | Talia Robinson PhD[1] | Emma Weizenbaum PhD[5] | Celina F. Pluim MA[1,5,6] | Yakeel T. Quiroz-Gaviria PhD[2,5] | Jennifer R. Gatchel MD, PhD[5] | Patrizia Vannini PhD[1,2] | Rebecca Amariglio PhD[1]

[1]Brigham and Women's Hospital, Boston, Massachusetts, USA

[2]Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA

[3]Helen Wills Neuroscience Institute, University of California Berkeley, Berkeley, California, USA

[4]Department of Psychology, Illinois Institute of Technology, Chicago, Illinois, USA

[5]Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA

[6]Department of Psychological and Brain Sciences, Boston University, Boston, Massachusetts, USA

[7]Department of Psychological and Brain Sciences, University of Massachusetts Amherst, Amherst, Massachusetts, USA

Correspondence
Catherine Munro, PhD, Brigham and Women's Hospital, 60 Fenwood Rd., Floor 9, Boston, MA, USA.
Email: cmunro@bwh.harvard.edu

Abstract

Subjective cognitive decline (SCD) is defined as self-experienced, persistent concerns of decline in cognitive capacity in the context of normal performance on objective cognitive measures. Although SCD was initially thought to represent the "worried well," these concerns can be linked to subtle brain changes prior to changes in objective cognitive performance and, therefore, in some individuals, SCD may represent the early stages of an underlying neurodegenerative disease process (e.g., Alzheimer's disease). The field of SCD research has expanded rapidly over the years, and this review aims to provide an update on new advances in, and contributions to, the field of SCD in key areas and themes identified by researchers in this field as particularly important and impactful. First, we highlight recent studies examining sociodemographic and genetic risk factors for SCD, including explorations of SCD across racial and ethnic minoritized groups, and examinations of sex and gender considerations. Next, we review new findings on relationships between SCD and in vivo markers of pathophysiology, utilizing neuroimaging and biofluid data, as well as associations between SCD and objective cognitive tests and neuropsychiatric measures. Finally, we summarize recent work on interventions for SCD and areas of future growth in the field of SCD.

KEYWORDS
Aging, Alzheimer's disease, subjective cognitive concerns, subjective cognitive decline, subjective cognitive impairment

1 | INTRODUCTION

Subjective cognitive decline (SCD) is defined as the self-experienced, persistent decline in cognitive capacity compared with a previous normal cognitive status and is unrelated to an acute event.[1,2] Standardized terminology and criteria for SCD were first published in 2014 by the Subjective Cognitive Decline Initiative (SCD-I) group and, since then, several groups have worked to refine these diagnostic criteria and provide diagnostic considerations for health care professionals.[1–3] Despite these definitions, the term SCD is often applied and measured differently across different studies. For example, many research groups will use the term SCD to refer to a preclinical phase on the Alzheimer's

disease (AD) continuum, although others will utilize the term SCD as a diagnostic representation of any self-reported cognitive decline, even if such decline is unrelated to an underlying neurodegenerative process. In addition, several different terms are used inconsistently across studies to refer to various aspects of SCD and the construct of SCD itself, such as "subjective cognitive concerns," "subjective cognitive complaints (SCC)," and "subjective cognitive impairment."

One of the challenges regarding consistent assessment of SCD as a diagnostic group involves the assessment tools that exist to measure SCD and SCC, as assessments may cover a variety of cognitive domains and span different timeframes of measurement and comparison (e.g., "over the last year" vs "over the last 10 years"; compared to participant baseline vs peers). Jessen and colleagues recently proposed that SCD measures should also assess for details including: (1) whether specific worries are associated with the perceived cognitive decline; (2) when the onset of the perceived cognitive decline occurred; (3) whether there is an association with any physical or mental conditions; and (4) whether there is an association with the use of medication, alcohol, or other substances.[2] Standardized methods of SCD assessment that have been validated with respect to objective outcome measures (e.g., biomarker data, objective cognitive performance, diagnostic progression, and so on) are needed in this field of research, particularly in the context of the large number of SCD measures available and the many potential underlying causes of SCD. Other factors that increase the heterogeneity of SCD may include sociodemographic and cultural differences in the understanding and expression of SCD among individuals (e.g., racial, ethnic, and gender diversity), various biological and environmental risk factors, as well as neuropsychiatric and genetic factors.

The overall goal of this review is to summarize novel research in the field of SCD and how this work continues or adds to prior findings across several different themes and subtopics. This review aims to discuss such underlying factors that impact overall reporting of SCD, as well as to provide a brief synopsis of recent literature relating SCD to objective outcome measures (e.g., biomarker data, objective cognitive performance) and how these findings align with prior research or how they have carried our knowledge of SCD forward. Finally, we discuss avenues of future research necessary for better increasing our understanding of SCD and its relationship to the AD continuum. To ensure clear interpretation and consistency of summarized studies, throughout this manuscript we will use "SCD" to refer to the diagnostic group of subjective cognitive decline (i.e., individuals who have concerns about their cognition), whereas "SCC" will be used to refer to reported cognitive concerns (i.e., the number of, rates of, or types of concerns reported by individuals with SCD).

RESEARCH IN CONTEXT

1. **Systematic Review**: The members of the SCD Professional Interest Area of the Alzheimer's Association International Society to Advance Alzheimer's Treatment were polled to assist with identifying key themes of particular impact to the field of subjective cognitive decline (SCD) in 2021 and critical studies within these themes. The authors then conducted a search via online scholarly repositories (e.g., PubMed) to review articles published over the last few years encompassing "subjective cognitive decline (SCD)," "subjective cognitive impairment," or "subjective cognitive concerns." Studies were prioritized if they fit within the predefined themes. Studies were only reviewed if they were published between 2021 and early 2022.
2. **Interpretation**: This review aims to summarize recent contributions to the literature on assessment, diagnosis, and prognosis of SCD, as well as to identify areas of future study that would benefit the field.
3. **Future Directions**: This review highlights that, although research on SCD has continued to rapidly expand over the past decade, further work is needed to refine diagnostic criteria and assessment methods, with consideration for the impact of culture and racial/ethnic diversity on diagnosis, as well as identify appropriate interventions for individuals with SCD.

2 | METHOD OF REVIEW

The primary focus of the literature review was centered on articles published between 2021 and early 2022, encompassing the terms of "subjective cognitive decline," "subjective cognitive impairment," or "subjective cognitive concerns." Some manuscripts published in earlier years were included for the sake of comparison to prior research or to provide relevant background information for specific themes or subtopics. All members of the SCD Professional Interest Area (PIA) of the Alzheimer's Association International Society to Advance Alzheimer's Treatment were polled via email in 2021 to identify important themes in current SCD research, as well as to nominate recent articles in the field of SCD that they found most impactful. The results of this poll were used to establish the themes and subtopics covered in this review, as well as to provide additional guidance as to the most important works to highlight in this review. Several of the pre-identified themes were condensed during preparation of the manuscript to improve clarity and cohesiveness. The authors additionally used scholarly search engines (e.g., the National Institutes of Health [NIH] National Library of Medicine National Center for Biotechnology Information's "PubMed;" https://pubmed.ncbi.nlm.nih.gov) to identify all articles in the specified time frame with the above search criteria.

Over 700 manuscripts that met the above search criteria were identified in 2021 alone. We subsequently prioritized the inclusion of articles in this review that fit within the themes pre-identified by the SCD PIA poll as particularly impactful for the field, as well as those that included SCD as a separate and distinct diagnostic group, or directly examined SCC as a primary outcome measure (i.e., not focusing on

articles in which SCD was merely a data point along the continuous AD spectrum and clear results related to SCD were not discussed). Although of course this article does not contain a summarization of every report published that included SCD or SCC in the specified timeframe, we aim for this review to provide a snapshot of current important areas of research in the field of SCD, as identified by members of the field, and how recently published work replicates prior findings and/or moves the field forward.

3 | COGNITION AND RISK FOR FUTURE COGNITIVE IMPAIRMENT IN SCD

Conflicting reports exist as to whether SCD serves as an early marker of objective cognitive decline, and thus proves to be an imperative avenue to further investigate. As has been demonstrated previously, recent cross-sectional studies have linked SCD to lower cognitive performance in various domains compared to older adults without SCD,[4,5] although results that have found no cognitive differences between individuals with and without SCD have also been reported.[6]

Recently, the focus has shifted to studying the longitudinal relationships between trajectories of SCD and future cognitive decline/impairment. One such study did not detect any cognitive changes over 6 years in 40 individuals with SCD,[7] although the use of a global cognitive screening tool as the primary outcome measure may have lacked the sensitivity to detect subtle cognitive changes that occur before the dementia stage. Sabatini and colleagues found that higher scores on an SCD questionnaire (i.e., greater levels of SCC) predicted 2-year decline on learning and memory tasks.[8] However, looking at changes in cognition retrospectively from current measurements of SCC appears to be less helpful in detecting future change in SCC levels;. Gustavson and colleagues report that objective prior cognitive change over 10 years accounts for little variance in SCC ratings in individuals who were still cognitively normal at the time of initial assessment.[9]

At present, there are still conflicting results on SCD and its association with retrospective cognition, future cognitive decline, and risk for dementia. This could be attributed to the use of different measures to operationalize both SCD (as a construct)/SCC (as a symptom) and "objective cognition," but also may suggest that examining SCD/SCC alone may neither be sufficient nor sensitive to predict objective functioning/declining. More work is needed to unpack and to explore the complex associations with other factors, such as sex,[10] neuropsychiatric symptoms[11–14] and AD biomarkers.[15] Recent research on relationships between SCD and these potential contributing factors will be discussed in subsequent subtopics.

4 | SOCIODEMOGRAPHIC FACTORS AND SCD

4.1 | Racial and ethnic diversity and SCD

Observational research studies and clinical trials have historically struggled to recruit ethnically and racially diverse samples,[16] which has limited our ability to understand the patterns of risk for SCD and future cognitive impairment in these individuals. New evidence suggests that racial and ethnic minority groups are at greater risk for AD and related dementias.[17,18] Recent investigations into the patterns of SCD across various sociocultural groups have sought to better understand how SCD presents across these historically marginalized populations. Such efforts may provide further insight into the early identification of pathological changes in neurodegenerative disorders among vulnerable populations and may enable us to observe unique risk factors for SCD among diverse populations.

The availability of data from large scale public health surveys, which include questions related to cognitive performance and functional status has allowed for evaluation of SCD across various demographic groups.[19–22] Recent data examining differences in SCD across diverse groups have been mixed. One study using the Behavioral Risk Factor Surveillance System (BRFSS) data, an extensive telephone survey of United States adults, to compare patterns of SCD in non-Hispanic White, non-Hispanic Black, and Hispanic adults 45 years of age and older found that non-Hispanic Black and Hispanic participants with SCD were more likely to be younger, have lower educational attainment, have lack access to health care, live alone, have more chronic medical conditions, and have greater SCD-related functional limitations compared to non-Hispanic White individuals with SCD.[19] It is concerning that rates of discussing SCD with a health care provider were lower in the minority groups in this study despite higher rates of SCD. Along these lines, a separate study using the same data set found that Native Hawaiian/Other Pacific Islander (NHOPI) individuals had higher rates of SCD and SCD-related functional difficulties compared to Asian and non-Hispanic White respondents.[20] Another study evaluating SCD across U.S. Latino subgroups not only showed a greater percentage of reported SCD among Latino individuals relative to non-Hispanic White respondents overall but also significant heterogeneity in rates of reported SCD among Latino subgroups, indicating potential differences in reporting rates of SCD across different cultural or national groups.[21] Zlatar and colleagues also reported significant variation in demographic characteristics and risk factors by background within a heterogeneous Hispanic sample with SCD (e.g., age, education, cardiovascular risk factors, anxiety, and depression).[23] Along these lines, recent data further suggest that not only are there differences between SCD reporting rates in Latinos/as/x compared to non-Hispanic White respondents, but there may be different relationships between SCC and objective cognitive performance between these groups.[24] On the other hand, another group demonstrated that associations between self-reported SCD and lower life satisfaction were similar across the various racial and ethnic groups studied.[22]

In summary, recent research suggests that minority groups today face greater SCD-related challenges (possibly influenced by external stressors, cultural factors, or health factors in these groups) which, concerningly, are seemingly not discussed as frequently with health care providers and which potentially could limit early intervention for future cognitive impairment. These new data signal the importance of recruitment in the community to continue to develop our understanding of the complexities of SCD, particularly with regard to individuals

from racially and ethnically diverse backgrounds, and to determine the most effective early intervention strategies for individuals from such backgrounds with SCD. In addition, more research is needed to understand relationships between race, ethnicity, and SCD in other countries, as many of the studies reviewed utilized samples based in the United States or other high-income countries. Recent work has shown that individuals in low- and middle-income countries are more at risk for higher levels of SCC if they have other chronic, comorbid medical conditions, including those that may cause reversible cognitive impairment.[25,26]

4.2 | Sexual orientation and gender identity considerations in SCD

Recent work has also highlighted differences in reporting rates of SCD in individuals of different sexual orientations and gender identities. Sex is defined as the biological differences that females and males have (e.g., chromosome, gonads, hormones, and reproductive functions). Gender, on the other hand, refers to the psychosocial frameworks in which individuals live and which can influence their subjective sexual identity.[27] Data regarding sex and gender differences in SCD have been mixed. A study by Brown and Patterson recently explored the moderation of gendered group status in the association with self-reported SCD and life satisfaction and found no differences across male- and female-gendered individuals.[22] On the other hand, another study demonstrated that women with SCD tended to have lower education, lower premorbid intelligence scores, and were younger compared to men with SCD.[28] Similarly, a separate group examining individuals with autosomal dominant AD showed that females who carry a genetic mutation for AD endorsed greater levels of SCC compared to male carriers.[10] It is also important to further understand differences in SCD among sexual and gender minorities, as a recent study showed that the prevalence of SCD was higher in individuals who identified as lesbian, gay, bisexual, and/or transgender or gender non-binary.[29] Similar to data from studies examining racial and ethnic diversity in individuals with SCD, this study also found similar rates of discussing SCD as a condition with health care providers between heterosexual cisgender adults and sexual and gender minority adults despite higher reporting rates of SCD in the latter group, as well as greater SCD-related functional limitations overall.

Overall, little had previously been known about rates of SCD in individuals of different sexual orientations and gender identity; however, recent research suggests that, similar to what has been observed in individuals from racially and ethnically diverse backgrounds, individuals who identify as sexual and gender minorities are more likely to report SCD, although may have lower rates of discussing their cognitive concerns with health care providers. This bourgeoning area of study is, therefore, important to not only ensure individuals who identify as a sexual and/or gender minority are adequately represented in our ongoing and future observational studies and clinical trials (particularly to study long-term outcomes in these individuals), but also to ensure that the best opportunities for screening, care, and treatment are being offered for these individuals at greater risk for reporting SCD.

4.3 | Education, cognitive reserve, and SCD

Education has a complex relationship with SCD that may be influenced by other sociocultural and socioeconomic factors, including socioeconomic status.[30] Although educational attainment was associated with a greater likelihood of self-reported SCD among older adults with diabetes,[31] this association was not independent of additional covariates, including marital and health insurance status, physical health status, and lifestyle factors.[32] In addition, one recent study suggested that higher education is associated with earlier onset of SCD in females, although higher verbal intelligence was associated with later onset of SCD.[28]

Education may also influence SCD by contributing to higher cognitive reserve, a term that refers to the differential susceptibility of cognitive abilities to aging, pathology, or brain insult across individuals through the adaptability of cognitive processes.[33] Although null associations have been reported,[34] higher education levels and higher levels of cognitive reserve have also been associated with reduced levels of SCC and lower risk for developing AD dementia later in life,[35,36] supporting previous findings from other cohorts.[37,38] There is also evidence that greater education levels may support cognitive performance in individuals in SCD,[39–41] and that this consistent association is independent of age, sex, and neurodegeneration.[42] Finally, recent work suggests that education may protect against the accumulation of AD pathology in individuals with SCD, as higher education was associated with a reduced prevalence of amyloid positivity across 20 separate cohort studies, after adjusting for age, study setting and apolipoprotein E (*APOE*) ε4 status.[43]

In sum, recent advances in the SCD literature, consistent with and building off prior findings, have indicated that although educational attainment has been associated with greater reporting rates of SCD or earlier onset of SCD, it is also associated with better outcomes in individuals with SCD, including lower levels of SCC, better objective cognitive performance, and lower amyloid burden. As most of the reviewed studies were cross-sectional, longitudinal work will be needed to establish firmer evidence of these protective effects in SCD and to better understand what mechanisms are underlying these complex relationships between education levels, cognitive reserve, and SCD.

5 | GENETIC RISK FACTORS FOR SCD

In addition to demographic factors, recent work has indicated that genetic factors may increase the risk of SCD. The *APOE* ε4 allele, most commonly associated with AD dementia via increased levels of cerebral amyloid beta (Aβ), has also continued to show associations with changes in cognition and pathophysiological levels of amyloid and tau proteins in individuals with SCD.[44] In addition to associations with

increased cerebral amyloid burden, recent data suggest that *APOE* ε4 allele carrier status in individuals with SCD may also be linked to other health factors associated with cognition and brain health, such as mean arterial pressure, number of white matter hyperintensities,[46] and functional brain network changes.[47] In *APOE* ε4 allele carriers and non-carriers with SCD, mild cognitive impairment (MCI), AD dementia, and a combination of vascular dementia and AD dementia, a dose–response pattern was observed across all groups, including the unimpaired SCD group, such that objective cognitive performance was incrementally worse as the number of ε4 alleles increased.[44] Another group found that, although SCC were associated with cognitive decline regardless of *APOE* ε4 carrier status, spouse-appraised memory functioning had stronger associations with objective cognitive decline in individuals who were ε4 carriers than non-carriers.[48]

APOE is not the only gene implicated as a risk factor for cognitive decline among older adults with SCD. A recent study by Bessi and colleagues exploring the roles of *CLOCK* T3111C and *PER2* C111G, polymorphisms involved in the sleep–wake cycle, found that the two individuals with SCD who eventually progressed to AD dementia were both *PER2* C111G carriers (of eight carriers with SCD in total), whereas none of the non-carriers with SCD ($n = 33$) were diagnosed with dementia at the study end point.[49] A recent study sought to replicate findings from a 2017 study that initially compared unimpaired presenilin-1 (*PSEN1*) E280A mutation carriers, associated with early-onset autosomal dominant Alzheimer's disease (ADAD), to non-carriers, and found that levels of self-reported SCC were greater in carriers than in non-carriers, and that higher levels of study partner-reported SCC in carriers were associated with older age and lower hippocampal volume.[50] The results of this later study examining a larger sample of the same cohort was unable to replicate the findings regarding increases in self-reported SCC in carriers compared to non-carriers.[51]

In sum, recent research has shown links between certain genetic factors (i.e., alleles or mutations of *APOE*, *CLOCK*, *PER2*, and *PSEN1*) and worse objective cognitive performance, clinical progression to AD dementia, and/or increased AD biomarker burden (i.e., amyloid and tau) in individuals with SCD. That said, additional follow-up studies and longitudinal studies are needed to examine long-term progression rates to dementia and incident cognitive decline in individuals with SCD who carry such genetic markers, as some follow-up studies were unable to replicate previous findings regarding the link between SCC and genetic factors over longer time periods.

6 | FLUID BIOMARKERS IN SCD

The study of fluid biomarkers has promise to identify additional tests and measures for the detection of pathophysiological proteins, inflammatory markers, and other indications of cerebral dysfunction that are less invasive and costly than traditional neuroimaging measures. Given that SCD is a preclinical phase of cognitive impairment, fluid biomarkers represent the possibility of useful, non-invasive, and low-cost methods to determine whether SCC are linked to underlying pathological changes prior to overt changes in cognition on objective assessments. Ideally, fluid biomarkers would be used as accessible and early diagnostic methods to determine which individuals with SCD are more likely to progress to stages of MCI or dementia.

As in the past, cerebrospinal fluid (CSF) measures of amyloid and tau have continued to be studied as markers of central nervous system pathophysiology, even in preclinical stages such as SCD, with consistent associations between AD-like profiles of CSF markers and progression from SCD to cognitive impairment, poorer cognitive performance, and reduced white matter integrity.[52–54]

Additional work is being performed to identify alternative CSF markers that may be sensitive to early pathophysiological changes. An initial study examining N-224 tau found elevated levels in individuals with AD dementia compared to those with SCD, although N-224 levels were similar between individuals with SCD and healthy controls.[55] One group demonstrated a relationship between SCD and CSF neurofilament light chain (NfL), an indirect measure of axonal damage, such that SCD individuals had greater NfL compared to controls without SCD.[56] This relationship was moderated by Aβ status and linked to structural brain changes, such that SCD individuals with higher levels of Aβ tended to have greater NfL and reduced hippocampal volume. A similar relationship was also seen in a longitudinal sample of 304 post-stroke patients with SCD, where CSF circulating NfL predicted subsequent objective cognitive decline.[57] Elevated levels of CSF ferritin, a protein associated with inflammatory changes, have also been shown to have a dose–response relationship with AD-like profiles of CSF Aβ and total tau (t-tau) (i.e., greater levels of ferritin as AD pathophysiology and cognitive impairment progresses) in a group of healthy controls, SCD, and MCI individuals.[58]

In addition, there has been substantial interest in AD plasma biomarkers in relation to SCD, given their accessibility and ease of collection compared to CSF. Some success has been seen in blood plasma measurements of phosphorylated tau (p-tau); for example, the clinic-based BioFINDER study demonstrated that plasma p-tau217 predicted AD dementia within 4 years with greater accuracy than clinical prediction by memory clinic physicians in a mixed group of individuals with SCD and MCI.[59] In addition, this group reported even greater accuracy after adding in other factors such as cognitive performance and genetic risk factors (i.e., *APOE* ε4 allele carrier status) and they further replicated these results in an Alzheimer's Disease Neuroimaging Initiative (ADNI) sample using plasma p-tau181. A separate group also found that elevated plasma p-tau217 levels were seen in individuals with SCD who had elevated Aβ levels on positron emission tomography (PET) scans.[60]

However, certain plasma and biofluid markers may be less sensitive at discriminating preclinical SCD individuals from healthy controls. Separate studies examining CSF and plasma inflammatory levels and neutrophil gelatinase-associated lipocalin levels across healthy controls and individuals with SCD, MCI, and AD dementia found that CSF measurements of these markers were consistently able to discriminate between controls, SCD ,and cognitively impaired individuals.[61,62] However, plasma inflammatory markers were only elevated in the AD dementia group and there were no differences seen in plasma

neutrophil gelatinase-associated lipocalin levels across diagnostic groups. Similarly, another study showed a dose–response relationship across SCD, MCI, and AD dementia groups using CSF measurements of t-tau, although t-tau levels measured using tear fluid in these individuals were only able to differentiate between SCD and AD dementia groups and were not sufficiently sensitive to detect changes between SCD and MCI individuals.[63]

In sum, literature on the utility of biofluid-based biomarkers in the detection of underlying pathophysiology associated with AD and related dementias in early, preclinical stages such as SCD appears to be mixed. CSF markers of Aβ and tau continue to be studied as sensitive markers of underlying pathophysiology, even in preclinical individuals with SCD, including new markers of tau fragments, which may assist with the delineation between different types of tauopathies. Certain blood plasma markers of hyper-phosphorylated tau have also shown promising results in SCD and MCI individuals, although other blood plasma markers (e.g., inflammatory markers and markers of kidney dysfunction) and tear fluid tau levels seem to be less sensitive in discriminating between early preclinical stages of the AD process. That said, plasma markers represent an innovative area of research and opportunity for future studies to identify plasma biomarkers correlated with underlying cerebral pathophysiology in order to acquire less-invasive and costly biomarkers that are more accessible overall than traditional lumbar punctures and PET scans.

7 | NEUROIMAGING IN SCD

SCD has been and continues to be linked to both structural and functional neuroimaging correlates. Compared to healthy controls, individuals with SCD show differences in both gray and white matter structure,[64] including reduced hippocampal and basal forebrain volume and cortical thinning in frontal, temporal regions,[65–69] as well as both local[70] and widespread differences in white matter.[65,71,72] These differences are related to subtle cognitive deficits in SCD.[46,68,69,73,74] Recent studies have also highlighted the heterogeneous relationship between brain structure and SCD, which may be influenced by factors such as the study setting (i.e., clinical vs community).[64,75] The disease stage may also be a key moderator; at early stages, greater levels of SCC were associated with lower gray matter volume and reduced glucose metabolism, whereas at later stages of the AD continuum when cognition is impaired and insight is lessened, lower levels of SCC were related to greater neurodegeneration.[75]

Functional abnormalities, as evident in task-free network connectivity and task-based neural activation studies, are also present in individuals with SCD. Higher SCC have been linked to decreased functional connectivity in the default mode network, as well as in the medial temporal and insular regions.[76–81] Recent findings have expanded the research and reported decreased functional connectivity in spatial navigation networks that included the right retrosplenial and right prefrontal cortices and the right retrosplenial cortex and right hippocampus,[82] cognitive reserve networks defined by global connectivity to left frontal cortex,[83] and hippocampal networks in regions involved in olfactory function.[84] Moreover, an increasing number of studies in the field of SCD have begun to explore changes in dynamic functional connectivity,[85] which better captures the temporal properties of the functional network organization. The results have been somewhat inconsistent, with some studies reporting different dynamic brain patterns in individuals with SCD versus normal controls,[66,86] another study finding no differences,[87] a third study demonstrating more stable networks in SCD,[88] and finally another study finding regional differences in network variability.[89]

Functional activation changes in SCD have also been linked to differences in cognition and physical functioning. When completing a memory task, people with greater SCC showed reduced hippocampal activity, even after adjusting for actual task performance,[90] and higher activation in the parahippocampal areas was found to predict better memory performance in individuals with SCD.[91] Individuals with SCD appear to perceive memory deficits related to subtle neural changes that are subjectively sensible but cannot be detected by standard cognitive measurement,[75,90] validating that the basis of SCD is, at least partly, subtle objective cognitive decline.[92] Meanwhile, cerebrovascular[93,94] and metabolic abnormalities[94–97] have also been noted in SCD and linked to increased functional signals observed in the frontal lobe in functional magnetic resonance imaging (fMRI) during N-back tasks.[94] Future studies may investigate the roles of different psychosocial and physiological factors that are related to increased and decreased functional activations in SCD.

On the AD continuum, SCD is characterized as the transition stage from normal to clinical AD. Accumulating evidence based on PET imaging studies confirms an association between higher Aβ and SCC.[90,98–101] Recent research efforts have explored the role of Aβ and tau in SCD-related neural changes[102,103] and found individuals with elevated Aβ and tau and SCD showed the greatest neurodegeneration. Taken together, these findings suggest that the presence of SCC in individuals with elevated Aβ may represent an early symptom related to incipient neurodegeneration.

There is also a rapidly growing and exciting literature on SCD involving the use of machine learning to best utilize multi-modal neuroimaging data in order to predict clinical diagnoses and disease progression in individuals with SCD.[104–109] In a large retrospective study, stroke history, lower education, lower score on the Montreal Cognitive Assessment cognitive screening measure, smaller left amygdala, and enlarged white matter at the banks of the right superior temporal sulcus were predictive of progression from SCD to MCI.[110]

Overall, although recent research on neuroimaging in individuals with SCD has continued to be consistent with prior findings, these new data have built off prior work to show the benefit of incorporating multi-modal imaging to detect relationships between SCD and sensitive measures of structural, functional, and pathophysiological changes in the brain. Leveraging multi-modal information including neuroimaging and clinical data has great potential to predict clinical progression and can benefit the field with more refinement and future research attention.

8 | NEUROPSYCHIATRIC SYMPTOMS IN SCD

Neuropsychiatric symptoms (NPS) are commonly seen in dementia syndromes and can include depression, anxiety, apathy, agitation, delusions, hallucinations, and sleep disorders, among other symptoms.[111] However, as indicated by a recent clinic-based study that found that 81.4% of individuals with SCD had symptoms in at least one of these NPS domains per report (54% meeting the criteria for clinically relevant symptoms), NPS can also occur in preclinical stages of cognitive impairment.[112] Common NPS reported in individuals with SCD include: increased apathy, irritability, depression, anxiety, agitation, changes in subjective sleep quality, and mental rigidity.[112–118] Minor hallucinations in cognitively unimpaired patients with Parkinson's disease (PD) have also been linked to an increased likelihood of SCC and increased rate of brain atrophy within 2 years of diagnosis.[119]

However, NPS in SCD may not be entirely explained by early pathophysiological changes, as one community-based study estimated that 24.9% of the variability in reported SCC was explained by psychological and psychosocial factors.[120] Along these lines, elevated and worsening reports of SCC and NPS, including increased depression, anxiety, loneliness, social isolation, and general emotional distress, were reported during the coronavirus disease 2019 (COVID-19) pandemic despite stable objective cognitive performance.[121,122] Another study found that 34% of the variance in SCC reported during the COVID-19 pandemic was explained by a combination of perceived stress, negative emotions, and poorer general physical health related to prolonged confinement or quarantine.[123] Certain medical conditions may also be associated with elevated reports of SCC and increased NPS, including migraines and cerebrovascular disease, although the study examining cerebrovascular disease found that NPS were more associated with perceived SCD than cerebrovascular disease itself.[124,125]

Data regarding the relationships between SCD, NPS, and cognition remain mixed. As stated previously, some studies found increases in SCC and NPS in the context of stable objective cognitive performance.[121,122] However, others have demonstrated that higher levels of anxiety, depression, and SCC are associated with lower performance on executive functioning and memory tasks.[8,11] In addition, one group showed that depressive symptoms partially mediated the relationship between SCD and objective memory performance, such that individuals with both depression and SCD were at risk for poor cognitive outcomes.[13] Another group utilizing a sample of cognitively normal older adults only found a link between higher levels of SCC and worse objective cognitive performance when controlling for depressive symptoms.[14] Differences in depressive symptom time of onset, duration, and severity among individuals across these studies may partially underlie these discordant findings.

The presence of SCD and NPS together has also been found to predict risk of future cognitive decline or dementia. A systematic review of studies examining NPS and cognitive decline demonstrated that individuals with SCD and anxiety, but not depression, were more at risk for future cognitive impairment.[126] Another group showed that comorbid depression and SCD had an additive effect on future risk of progressing to dementia, even when considering independent risks of these factors.[127] Over the past few years, research has also focused on a new diagnostic construct, mild behavioral impairment, to encompass functionally impairing, late-in-life-onset NPS across one or more domains of motivation, affect, impulse control, social appropriateness, and perception/thought content.[128] A recent study found that individuals with comorbid SCD and mild behavioral impairment were at greatest risk of incident cognitive decline over a 3-year period, compared to controls and those with either SCD or mild behavioral impairment alone.[129]

Regarding relationships between structural brain changes, NPS, and SCD, findings have been mixed and may be influenced by severity of SCC. For example, NPS have been associated with medial temporal lobe atrophy in a mixed cohort of both SCD and MCI individuals.[130] These relationships may also be impacted by cerebral amyloid burden, as shown by two studies that showed correlations between greater worry or anxiety related to SCD and higher cerebral amyloid levels and, in one study, lower gray matter volume.[100,102] However, NPS and SCD may also be linked independently of structural and pathophysiological brain changes, as demonstrated by a study that found no alterations in hippocampal subfield volumes across groups of healthy controls and individuals with SCD and with primary depressive disorders, compared to reduced hippocampal subfield volumes in AD.[131] Along these lines, a separate group demonstrated that elevated SCC levels were correlated consistently with higher levels of trait anxiety in a sample of 70-year-old individuals, and a cross-sectional relationship between higher SCC levels and Aβ positivity emerged only once anxiety was included in the model.[101] It is worth noting recent work that demonstrated differences in relationships between SCD, NPS, and levels of Aβ across clinical and research samples and may help to explain these mixed findings.[43] In addition, study-partner reports of cognitive decline may be helpful in delineating cognitive changes related to NPS and cognitive changes related to underlying pathophysiology. Indeed, one study demonstrated that longitudinal study-partner cognitive complaints were more closely associated with in vivo AD biomarker levels that were participant complaints and were also less vulnerable to participant-reported NPS.[132]

Overall, NPS may be present in preclinical stages of AD, such as SCD, and have been linked to structural and pathophysiological changes in the brain. However, the relationship between neurodegenerative disease and NPS is complex and difficult to disentangle, as data have shown that SCD and NPS can exist independently of any brain changes linked to neurodegeneration. Furthermore, the nature of the NPS themselves (e.g., depression vs anxiety) may differentially impact, mediate, and/or moderate relationships between SCD and structural, cognitive, and functional changes. Additional work is needed to improve our ability to discriminate between SCD associated with primary psychiatric syndromes in the absence of a progressive neurodegenerative process versus SCD and NPS co-occurring as early behavioral symptoms of neurodegeneration.

9 | INTERVENTIONS IN SCD

Because the stage of SCD is increasingly recognized and understood to be a risk factor for cognitive decline, more interventions have been targeted to individuals in this preclinical stage prior to the onset of objective cognitive impairment. Given the paucity of treatment for neurodegenerative disorders, intervention at the point of SCD may be one of the earliest points of action with the potential of influencing trajectory and rate of progression. A recent systematic review of randomized control trials (RCTs) for interventions at the stage of SCD found that, overall, education programs, compared to cognitive training, physical training, or mind–body interventions, were most effective in improving memory function.[133] Several of these interventions, designed to support socialization and brain health education, appeared to support quality of life and holistic functioning in individuals with SCD.[134,135] Multimodal educational and health programs, involving combinations of brain health education, mindfulness practice, music listening, and/or exercise, were generally associated with increased subjective cognitive functioning post-intervention or reductions in anxiety levels.[136,137] Another recent systematic review also found strong evidence for cognitive/mental/physical training on cognitive and non-cognitive outcomes in SCD individuals.[138]

There is mixed evidence supporting nutritional interventions in SCD, although stronger evidence for improved cognition and increased brain activity in individuals with SCD was seen in studies using shentai tea polyphenols, fermented dairy products (e.g., β-lactolin found in products such as yogurt), and combinations of nutrients, with less promising evidence for beneficial effects using other supplements such as vitamin D, specific proteins, and amino acids.[139–142]

In addition, other studies examining the effects of exercise in individuals with SCD demonstrated improvement in fitness and mobility, but not necessarily improvement in subjective cognitive performance. In a study of older adults with SCD and comorbid hypertension, moderate and high intensity exercise programs improved fitness but not global cognitive function.[143] In a large four-arm RCT of exercise and exercise education programs in older individuals with SCD, participants in all programs showed improved gait parameters.[144]

As various technologies have become ubiquitous, older adults are increasingly comfortable using a range of digital devices, opening the door to new treatment modalities that can result in improved cognitive functioning across various domains. Interventions for SCD using at-home digital devices and immersive virtual reality experiences have begun to be evaluated for feasibility and efficacy. Not only have these interventions been shown to be feasible, but evidence has shown that some computerized training programs can be associated with improved cognitive functioning in individuals with SCD.[145,146] Recent work has also demonstrated feasibility and enjoyability of an immersive virtual reality grocery store task to realistically measure general functioning in individuals with SCD.[147] In addition, an RCT examining biweekly virtual reality cognitive therapy reported positive increases in visuospatial function, apathy, affect, quality of life, and increased frontal-occipital functional connectivity in older people with SCD and MCI.[148]

Other studies have examined the use of direct neuromodulation as an intervention for SCD. An RCT measuring the effect of a combined transcranial direct current stimulation (tDCS) and mindfulness-based stress reduction in individuals with SCD found that although feasible and safe, there were no statistically significant effects on outcome measures (i.e., mindfulness, social functioning, mood, subjective cognition and objective cognitive performance) compared to combined sham tDCS with mindfulness-based stress reduction.[149] A double-blind tDCS versus sham study found that individuals with SCD who had greater structural and functional brain integrity (per MRI) had the greatest tDCS-induced memory consolidation effect, indicating these individuals may benefit most from this form of neuromodulation.[150] A study of repeated transcranial magnetic stimulation in older adults with SCD found evidence of enhanced visual working memory, and significantly improved attention and executive function when the left dorsolateral prefrontal cortex was stimulated.[151]

In sum, data on recent interventions in SCD have been mixed. Educational programs have been highlighted as particularly effective for improving memory function in individuals with SCD, with good evidence for multimodal programs that also include psychological practices (e.g., mindfulness) and physical exercise as well as brain health education. Evidence has also shown that these programs can be delivered effectively via digital devices or computerized programs. On the other hand, data on specific nutrition/dietary supplements and transcranial stimulation for decreasing SCC and improving cognitive function have been more mixed and may depend on the specific supplement or intervention administered. Future research is needed to examine the long-term effects of these interventions on individuals with SCD, specifically as to whether they have any preventative or slowing effects on potential future cognitive decline and/or progression to dementia.

10 | OPPORTUNITIES AND PRIORITIES FOR FUTURE RESEARCH IN SCD

Overall, there are numerous areas of opportunity for future research in the field of SCD, made evident through the work presented here and as highlighted by members of the Alzheimer's Association International Society to Advance Alzheimer's Research and Treatment SCD PIA. First, there has been a call for improved diagnostic processes for individuals with SCD for both clinical identification of individuals early in the disease process, as well as to serve as a potential outcome measure for clinical prevention trials. Several potential areas of improvement or future research in diagnostic processes have been identified, including the use of more universal and consistent assessments that capture cognitive decline across a variety of cognitive domains, more research on utilization of multimodal biomarker data in the diagnostic process (particularly for less invasive and costly biomarkers such as plasma tau measurements), and the utilization of both self- and study-partner reported data to accommodate diminished insight during the latter stages of AD. There are also other factors that need to be better understood to improve diagnostic accuracy of SCD, including SCD in cross-cultural settings, the impact of

cognitive reserve factors such as education on SCD, and the relationships between NPSs and SCD. Finally, there is also a need to continue identifying appropriate interventions for individuals with SCD beyond psychopharmaceutical approaches, including cognitive, behavioral, physical, and neuromodulatory approaches, as well as a need for studies examining long-term effects of interventions on individuals with SCD (e.g., with data on future rates of progression to cognitive impairment/dementia or cognitive decline).

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CONFLICT OF INTEREST STATEMENT

None of the authors (C.E.M, R.B., X.C., G.C., C.G., R.J.J., J.M., I.O., T.R., E.W., Y.T.Q., J.R.G., P.V., and R.A.) have any relevant disclosures or conflicts of interest. Author disclosures are available in the Supporting Information.

CONSENT STATEMENT

No human subjects were recruited for this review of previously published works, and, as such, additional consent was not necessary. Details of informed consent for each study included in this review can be found in the original publications.

ORCID

Catherine E. Munro PhD https://orcid.org/0000-0002-8707-1826

REFERENCES

1. Jessen F, Amariglio RE, van Boxtel M, et al. A conceptual framework for research on subjective cognitive decline in preclinical Alzheimer's disease. *Alzheimers Dement*. 2014;10(6):844-852. doi:10.1016/j.jalz.2014.01.001
2. Jessen F, Amariglio RE, Buckley RF, et al. The characterisation of subjective cognitive decline. *Lancet Neurol*. 2020;19(3):271-278. doi:10.1016/S1474-4422(19)30368-0
3. Jack CR, Bennett DA, Blennow K, et al. NIA-AA research framework: toward a biological definition of Alzheimer's disease. *Alzheimer's Dement*. 2018;14(4):535-562. doi:10.1016/j.jalz.2018.02.018
4. Zullo L, Clark C, Gholam M, et al. Factors associated with subjective cognitive decline in dementia-free older adults—a population-based study. *Int J Geriatr Psychiatry*. 2021;36(8):1188-1196. doi:10.1002/gps.5509
5. Tsatali M, Poptsi E, Moraitou D, et al. Discriminant validity of the WAIS-R digit symbol substitution test in subjective cognitive decline, mild cognitive impairment (Amnestic subtype) and Alzheimer's disease dementia (add) in Greece. *Brain Sci*. 2021;11(7):881. doi:10.3390/brainsci11070881
6. Rivera-Fernández C, Custodio N, Soto-Añari M. Neuropsychological profile in the preclinical stages of dementia: principal component analysis approach. *Dement Neuropsychol*. 2021;15(2):192-199. doi:10.1590/1980-57642021dn15-020006
7. Scharre DW, ing ChangS, Nagaraja HN, Wheeler NC, Kataki M. Self-administered Gerocognitive examination: longitudinal cohort testing for the early detection of dementia conversion. *Alzheimers Res Ther*. 2021;13(1):1-11. doi:10.1186/s13195-021-00930-4
8. Sabatini S, Woods RT, Ukoumunne OC, Ballard C, Collins R, Clare L. Associations of subjective cognitive and memory decline with depression, anxiety, and two-year change in objectively-assessed global cognition and memory. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn*. 2022;29(5):840-866. doi:10.1080/13825585.2021.1923634
9. Gustavson DE, Jak AJ, Elman JA, et al. How well does subjective cognitive decline correspond to objectively measured cognitive decline? *J Alzheimer's Dis*. 2021;83(1):291-304. Assessment of 10-12 Year Change.
10. Martinez JE, Pardilla-Delgado E, Guzmán-Vélez E, et al. Subjective cognitive decline and its relation to verbal memory and sex in cognitively unimpaired individuals from a Colombian cohort with autosomal-dominant Alzheimer's disease. *J Int Neuropsychol Soc*. 2022;28(6):541-549. doi:10.1017/S1355617721000801
11. Ahn S, Mathiason MA, Lindquist R, Yu F. Factors predicting episodic memory changes in older adults with subjective cognitive decline: a longitudinal observational study. *Geriatr Nurs (Minneap)*. 2021;42(1):268-275.
12. Ahn S, Mathiason MA, Yu F. Longitudinal cognitive profiles by anxiety and depressive symptoms in American older adults with subjective cognitive decline. *J Nurs Scholarsh*. 2021;53(6):698-708. doi:10.1111/jnu.12692
13. Hill NL, Bhargava S, Bratlee-Whitaker E, et al. Longitudinal relationships between subjective cognitive decline and objective memory: depressive symptoms mediate between-person associations. *J Alzheimer's Dis*. 2021;83(4):1623-1636. doi:10.3233/JAD-210230
14. Teles M, Shi D. Longitudinal association between subjective and objective memory in older adults: a study with the Virginia Cognitive Aging Project sample. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn*. 2022;30(2):231-255.
15. Zhao M, Chen G, Li T, Sheng C, Li Y, Han Y. The impact of study setting on clinical characteristics in older Chinese adults with subjective cognitive decline: baseline investigation of convenience and population-based samples. *Biomed Res Int*. 2021;2021:5538323. doi:10.1155/2021/5538323
16. Konkel L. Racial and ethnic disparities in research studies: the challenge of creating more diverse cohorts. *Env Heal Perspect*. 2015;123(12):A297-A302. doi:10.1289/2Fehp.123-A297
17. Bothongo PLK, Jitlal M, Parry E, et al. Dementia risk in a diverse population: a single-region nested case-control study in the East End of London. *Lancet Reg Heal—Eur*. 2022;15:100321. doi:10.1016/j.lanepe.2022.100321
18. Shiekh SI, Cadogan SL, Lin LY, Mathur R, Smeeth L, Warren-Gash C. Ethnic differences in dementia risk: a systematic review and meta-analysis. *J Alzheimers Dis*. 2021;80(1):337-355. doi:10.3233/JAD-201209
19. Gupta S. Racial and ethnic disparities in subjective cognitive decline: a closer look, United States, 2015-2018. *BMC Public Health*. 2021;21(1):1-12. doi:10.1186/s12889-021-11068-1
20. Ganbat U, Wu YY. Disparities of subjective cognitive decline among native Hawaiians/other pacific Islanders, Asian Americans, and White Americans in Hawai'i: behavioral risk factor surveillance system 2015 and 2017. *Asia-Pacific J Public Heal*. 2021;33(5):587-594. doi:10.1177/10105395211020902
21. Garcia MA, Warner DF, García C, Downer B, Raji M. Age patterns in self-reported cognitive impairment among older latino subgroups and non-latino Whites in the United States, 1997-2018: implications for public health policy. *Innov Aging*. 2021;5(4):1-15. doi:10.1093/geroni/igab039
22. Brown M, Patterson R. Gendered racial differences and similarities in subjective cognitive decline and life satisfaction: results from a population-based sample. *Aging Ment Heal*. 2021;25(9):1636-1641.
23. Zlatar ZZ, Tarraf W, González KA, et al. Subjective cognitive decline and objective cognition among diverse U.S. Hispanics/Latinos: results from the Study of Latinos-Investigation of Neurocognitive Aging (SOL-INCA). *Alzheimer's Dement*. 2021(April):1-10. doi:10.1002/alz.12381

24. Nakhla MZ, Cohen L, Salmon DP, et al. Self-reported subjective cognitive decline is associated with global cognition in a community sample of Latinos/as/x living in the United States. *J Clin Exp Neuropsychol*. 2021;43(7):663-676. doi:10.1080/13803395.2021.1989381
25. Pereira ML, De Vasconcelos THF, De Oliveira AAR, et al. Memory complaints at primary care in a middle-income country: clinical and neuropsychological characterization. *Dement e Neuropsychol*. 2021;15(1):88-97. doi:10.1590/1980-57642021dn15-010009
26. Koyanagi A, Smith L, Shin JI, et al. Multimorbidity and subjective cognitive complaints: findings from 48 Low- and Middle-Income countries of the world health survey. *J Alzheimers Dis*. 2021;81(4):1737-1747. doi:10.3233/JAD-201592
27. Reale C, Invernizzi F, Panteghini C, Garavaglia B. Genetics, sex, and gender. *J Neurosci Res*. 2023;101(5):553-562. doi:10.1002/jnr.24945
28. Giacomucci G, Mazzeo S, Padiglioni S, et al. Gender differences in cognitive reserve: implication for subjective cognitive decline in women. *Neurol Sci*. 2022;43(4):2499-2508. doi:10.1007/s10072-021-05644-x
29. Flatt JD, Cicero EC, Lambrou NH, et al. Subjective cognitive decline higher among sexual and gender minorities in the United States, 2015-2018. *Alzheimer's Dement Transl Res Clin Interv*. 2021;7(1):2-11. doi:10.1002/trc2.12197
30. Peterson RL, Carvajal SC, McGuire LC, Fain MJ, Bell ML. State inequality, socioeconomic position and subjective cognitive decline in the United States. *SSM—Popul Heal*. 2019;7:100357. doi:10.1016/j.ssmph.2019.100357
31. Roh M, Dan H, Kim O. Influencing factors of subjective cognitive impairment in middle-aged and older adults. *Int J Environ Res Public Health*. 2021;18(21):11488. doi:10.3390/ijerph182111488
32. Huang Y-C, Cuevas HE, Zuñiga JA, García AA. Predictors of subjective cognitive decline among people with diabetes: data from the behavioral risk factor surveillance system. *Sci Diabetes Self-Management Care*. 2021;47(3):207-215.
33. Stern Y, Arenaza-Urquijo EM, Bartrés-Faz D, et al. Whitepaper: defining and investigating cognitive reserve, brain reserve, and brain maintenance. *Alzheimer's Dement*. 2020;16(9):1305-1311. doi:10.1016/j.jalz.2018.07.219
34. Wen C, Hu H, Ou YN, et al. Risk factors for subjective cognitive decline: the CABLE study. *Transl Psychiatry*. 2021;11(1):1-9. doi:10.1038/s41398-021-01711-1
35. Lin LH, Bin WangS, Xu WQ, et al. Subjective cognitive decline symptoms and its association with socio-demographic characteristics and common chronic diseases in the southern Chinese older adults. *BMC Public Health*. 2022;22(1):1-9. doi:10.1186/s12889-022-12522-4
36. Jia F, Li Y, Li M, Cao F. Subjective cognitive decline, cognitive reserve indicators, and the incidence of dementia. *J Am Med Dir Assoc*. 2021;22(7):1449-1455. doi:10.1016/j.jamda.2020.08.005 e4
37. Hao L, Sun Y, Li Y, et al. Demographic characteristics and neuropsychological assessments of subjective cognitive decline (SCD) (plus). *Ann Clin Transl Neurol*. 2020;7(6):1002-1012. doi:10.1002/acn3.51068
38. Lee JH, Sung J, Choi MK. The factors associated with subjective cognitive decline and cognitive function among older adults. *J Adv Nurs*. 2020;76(2):555-565. doi:10.1111/jan.14261
39. Chen G, Zhao M, Yang K, et al. Education exerts different effects on cognition in individuals with subjective cognitive decline and cognitive impairment: a population-based study. *J Alzheimers Dis*. 2021;79(2):653-661. doi:10.3233/JAD-201170
40. Mondini S, Pucci V, Montemurro S, Rumiati RI. Protective factors for subjective cognitive decline individuals: trajectories and changes in a longitudinal study with Italian elderly. *Eur J Neurol*. 2022;29(3):691-697. doi:10.1111/ene.15183
41. Montemurro S, Mondini S, Arcara G. Heterogeneity of effects of cognitive reserve on performance in probable Alzheimer's Disease and in subjective cognitive decline. *Neuropsychology*. 2021;35(8):876-888. doi:10.1037/neu0000770
42. Jansen MG, Geerligs L, Claassen JAHR, et al. Positive effects of education on cognitive functioning depend on clinical status and neuropathological severity. *Front Hum Neurosci*. 2021;15:723728. doi:10.3389/fnhum.2021.723728
43. Janssen O, Parnetti L, Jansen WJ, et al. Characteristics of subjective cognitive decline associated with amyloid positivity. *Alzheimers Dement*. 2022;18(10):1832-1845. doi:10.1002/alz.12512
44. Hestad K, Engedal K, Horndalsveen P, Strand BH. Cognition in patients with memory difficulties and dementia relative to APOE e4 status. *Front Psychol*. 2021;12:686036. doi:10.3389/fpsyg.2021.686036
45. Saunders AM, Strittmatter WJ, Schmechel D, et al. Association of apolipoprotein E allele ε4 with late-onset sporadic Alzheimer's disease. *Neurology*. 1993;43:1467-1472. doi:10.1002/ajmg.1320540319
46. Jung Y, Viviano RP, Van Rooden S, Van Der Grond J, Rombouts SARB, Damoiseaux JS. White matter hyperintensities and apolipoprotein e affect the association between mean arterial pressure and objective and subjective cognitive functioning in older adults. *J Alzheimer's Dis*. 2021;84(3):1337-1350. doi:10.3233/JAD-210695
47. Deng S, Sun L, Chen W, Liu X, Chen S. Effect of APOEε4 on functional brain network in patients with subjective cognitive decline: a resting state functional MRI study. *Int J Gen Med*. 2021;14:9761-9771. doi:10.2147/ijgm.s342673
48. Bellaali Y, Woodard JL, Hanseeuw B, Ivanoiu A. Spouse-appraised memory functioning predicts memory decline better than subjective memory complaints in community dwelling older adults at genetic risk for Alzheimer's disease. *Front Psychiatry*. 2021;12:633102. doi:10.3389/fpsyt.2021.633102
49. Bessi V, Giacomucci G, Mazzeo S, et al. PER2 C111G polymorphism, cognitive reserve and cognition in subjective cognitive decline and mild cognitive impairment: a 10-year follow-up study. *Eur J Neurol*. 2021;28(1):56-65. doi:10.1111/ene.14518
50. Norton DJ, Amariglio R, Protas H, et al. Subjective memory complaints in preclinical autosomal dominant Alzheimer disease. *Neurology*. 2017;89(14):1464-1470. doi:10.1212/WNL.0000000000004533
51. Vannini P, Hanseeuw BJ, Gatchel JR, et al. Trajectory of unawareness of memory decline in individuals with autosomal dominant Alzheimer disease. *JAMA Netw Open*. 2020;3(12):1-14. doi:10.1001/jamanetworkopen.2020.27472
52. Scarth M, Rissanen I, Scholten RJPM, Geerlings MI. Biomarkers of Alzheimer's Disease and cerebrovascular lesions and clinical progression in patients with subjective cognitive decline: a systematic review. *J Alzheimer's Dis*. 2021;83(3):1089-1111. doi:10.3233/JAD-210218
53. Wang X, Zhao M, Lin L, Han Y. Plasma β-Amyloid levels associated with structural integrity based on diffusion tensor imaging in subjective cognitive decline: the SILCODE study. *Front Aging Neurosci*. 2021;12:592024. doi:10.3389/fnagi.2020.592024
54. Ma YH, Wang YY, Tan L, et al. Social networks and cerebrospinal fluid biomarkers of Alzheimer's disease pathology in cognitively intact older adults: the CABLE study. *J Alzheimer's Dis*. 2021;81(1):263-272. doi:10.3233/JAD-201426
55. Cicognola C, Hansson O, Scheltens P, et al. Cerebrospinal fluid N-224 tau helps discriminate Alzheimer's disease from subjective cognitive decline and other dementias. *Alzheimer's Res Ther*. 2021;13(1):1-12. doi:10.1186/s13195-020-00756-6
56. Sánchez-Benavides G, Suárez-Calvet M, Milà-Alomà M, et al. Amyloid-β positive individuals with subjective cognitive decline present increased CSF neurofilament light levels that relate to lower hippocampal volume. *Neurobiol Aging*. 2021;104:24-31. doi:10.1016/j.neurobiolaging.2021.02.026

57. Wang JH, Huang J, Guo FQ, et al. Circulating neurofilament light predicts cognitive decline in patients with post-stroke subjective cognitive impairment. *Front Aging Neurosci*. 2021;13:665981. doi:10.3389/fnagi.2021.665981
58. Ayton S, Janelidze S, Roberts B, et al. Acute phase markers in CSF reveal inflammatory changes in Alzheimer's disease that intersect with pathology, APOE ε4, sex and age. *Prog Neurobiol*. 2021;198(April 2020):101904. doi:10.1016/j.pneurobio.2020.101904
59. Palmqvist S, Tideman P, Cullen N, et al. Prediction of future Alzheimer's disease dementia using plasma phospho-tau combined with other accessible measures. *Nat Med*. 2021;27(6):1034-1042. doi:10.1038/s41591-021-01348-z
60. Janelidze S, Berron D, Smith R, et al. Associations of Plasma Phospho-Tau217 levels with tau positron emission tomography in early Alzheimer disease. *JAMA Neurol*. 2021;78(2):149-156. doi:10.1001/jamaneurol.2020.4201
61. Cullen NC, Mälarstig A, Stomrud E, Hansson O, Mattsson-Carlgren N. Accelerated inflammatory aging in Alzheimer's disease and its relation to amyloid, tau, and cognition. *Sci Rep*. 2021;11(1):1-9. doi:10.1038/s41598-021-81705-7
62. Naudé PJW, Ramakers IHGB, van der Flier WM, et al. Serum and cerebrospinal fluid Neutrophil gelatinase-associated lipocalin (NGAL) levels as biomarkers for the conversion from mild cognitive impairment to Alzheimer's disease dementia. *Neurobiol Aging*. 2021;107:1-10. doi:10.1016/j.neurobiolaging.2021.07.001
63. Gijs M, Ramakers IHGB, Visser PJ, et al. Association of tear fluid amyloid and tau levels with disease severity and neurodegeneration. *Sci Rep*. 2021;11(1):1-8. doi:10.1038/s41598-021-01993-x
64. Pini L, Wennberg AM. Structural imaging outcomes in subjective cognitive decline: community vs. clinical-based samples. *Exp Neurol*. 2021;145:111216.
65. Cedres N, Diaz-Galvan P, Diaz-Flores L, et al. The interplay between gray matter and white matter neurodegeneration in subjective cognitive decline. *Aging (Albany NY)*. 2021;13(16):19963-19977. doi:10.18632/aging.203467
66. Liang L, Yuan Y, Wei Y, et al. Recurrent and concurrent patterns of regional BOLD dynamics and functional connectivity dynamics in cognitive decline. *Alzheimer's Res Ther*. 2021;13(1):1-12. doi:10.1186/s13195-020-00764-6
67. Nellessen N, Onur OA, Richter N, et al. Differential neural structures, intrinsic functional connectivity, and episodic memory in subjective cognitive decline and healthy controls. *Neurobiol Aging*. 2021;105:159-173.
68. Chen Q, Wu S, Li X, et al. Basal forebrain atrophy is associated with allocentric navigation deficits in subjective cognitive decline. *Front Aging Neurosci*. 2021;13:596025. doi:10.3389/fnagi.2021.596025
69. Hong YJ, Park JW, Lee SB, et al. The influence of amyloid burden on cognitive decline over 2 years in older adults with subjective cognitive decline: a prospective cohort study. *Dement Geriatr Cogn Disord*. 2021;50(5):437-445. doi:10.1159/000519766
70. Tao W, Li H, Li X, et al. Progressive brain degeneration from subjective cognitive decline to amnestic mild cognitive impairment: evidence from large-scale anatomical connection classification analysis. *Front Aging Neurosci*. 2021;13(July):687530. doi:10.3389/fnagi.2021.687530
71. Archer DB, Moore EE, Pamidimukkala U, et al. The relationship between white matter microstructure and self-perceived cognitive decline. *NeuroImage Clin*. 2021;32(March):102794. doi:10.1016/j.nicl.2021.102794
72. Fogel H, Levy-Lamdan O, Zifman N, et al. Brain network integrity changes in subjective cognitive decline: a possible physiological biomarker of dementia. *Front Neurol*. 2021;12:699014. doi:10.3389/fneur.2021.699014
73. Wang S, Rao J, Yue Y, et al. Altered frequency-dependent brain activation and white matter integrity associated with cognition in characterizing preclinical Alzheimer's disease stages. *Front Hum Neurosci*. 2021;15(February):625232. doi:10.3389/fnhum.2021.625232
74. Wei YC, Hsu CCH, Huang WY, et al. White Matter integrity underlies the physical-cognitive correlations in subjective cognitive decline. *Front Aging Neurosci*. 2021;13(August):1-14. doi:10.3389/fnagi.2021.700764
75. Kuhn E, Perrotin A, Tomadesso C, et al. Subjective cognitive decline: opposite links to neurodegeneration across the Alzheimer's continuum. *Brain Commun*. 2021;3(3):1-15. doi:10.1093/braincomms/fcab199
76. Sharma N, Murari G, Vandermorris S, et al. Functional connectivity between the posterior default mode network and Parahippocampal Gyrus is disrupted in older adults with subjective cognitive decline and correlates with subjective memory ability. *J Alzheimer's Dis*. 2021;82(1):435-445. doi:10.3233/jad-201579
77. Viviano RP, Damoiseaux JS. Longitudinal change in hippocampal and dorsal anterior insulae functional connectivity in subjective cognitive decline. *Alzheimer's Res Ther*. 2021;13(1):1-15. doi:10.1186/s13195-021-00847-y
78. Wang S, Sun H, Hu G, et al. Altered insular subregional connectivity associated with cognitions for distinguishing the spectrum of pre-clinical Alzheimer's disease. *Front Aging Neurosci*. 2021;13(February):1-15. doi:10.3389/fnagi.2021.597455
79. Chen S, Song Y, Xu W, et al. Impaired memory awareness and loss integration in self-referential network across the progression of Alzheimer's disease spectrum. *J Alzheimer's Dis*. 2021;83(1):111-126. doi:10.3233/JAD-210541
80. Zhang Z, Cui L, Huang Y, Chen Y, Li Y, Guo Q. Changes of regional neural activity homogeneity in preclinical Alzheimer's disease: compensation and dysfunction. *Front Neurosci*. 2021;15(June):1-13. doi:10.3389/fnins.2021.646414
81. Xu W, Rao J, Song Y, et al. Altered functional connectivity of the basal nucleus of Meynert in subjective cognitive impairment, early mild cognitive impairment, and late mild cognitive impairment. *Front Aging Neurosci*. 2021;13(June):1-11. doi:10.3389/fnagi.2021.671351
82. Chen Q, Qing Z, Jin J, et al. Ego- and allo-network disconnection underlying spatial disorientation in subjective cognitive decline. *Cortex*. 2021;137:35-48. doi:10.1016/j.cortex.2020.12.022
83. Du W, Ding C, Jiang J, Han Y. Women exhibit lower global left frontal cortex connectivity among cognitively unimpaired elderly individuals: a pilot study from SILCODE. *J Alzheimer's Dis*. 2021;83(2):653-663. doi:10.3233/JAD-210376
84. Chen B, Wang Q, Zhong X, et al. Structural and functional abnormalities of olfactory-related regions in subjective cognitive decline, mild cognitive impairment and Alzheimer's disease. *Int J Neuropsychopharmacol*. 2022;25(5):361-374.
85. Hutchison RM, Womelsdorf T, Allen EA, et al. Dynamic functional connectivity: promise, issues, and interpretations. *Neuroimage*. 2013;80:360-378. doi:10.1016/j.neuroimage.2013.05.079
86. Chen Q, Lu J, Zhang X, et al. Alterations in dynamic functional connectivity in individuals with subjective cognitive decline. *Front Aging Neurosci*. 2021;13(February):646017. doi:10.3389/fnagi.2021.646017
87. Chumin EJ, Risacher SL, West JD, et al. Temporal stability of the ventral attention network and general cognition along the Alzheimer's disease spectrum. *NeuroImage Clin*. 2021;31:102726. doi:10.1016/j.nicl.2021.102726
88. Yang Y, Zha X, Zhang X, et al. Dynamics and concordance abnormalities among indices of intrinsic brain activity in individuals with subjective cognitive decline: a temporal dynamics resting-state functional magnetic resonance imaging analysis. *Front Aging Neurosci*. 2021;12(January):1-12. doi:10.3389/fnagi.2020.584863
89. Xue C, Qi W, Yuan Q, et al. Disrupted dynamic functional connectivity in distinguishing subjective cognitive decline and amnestic mild cognitive impairment based on the triple-network model. *Front*

Aging Neurosci. 2021;13(September):1-12. doi:10.3389/fnagi.2021.711009
90. Chen X, Farrell ME, Rundle MM, et al. The relationship of functional hippocampal activity, amyloid deposition, and longitudinal memory decline to memory complaints in cognitively healthy older adults. *Neurobiol Aging*. 2021;105:318-326. doi:10.1016/j.neurobiolaging.2021.04.020
91. Ruiz-Rizzo AL, Pruitt PJ, Finke K, Müller HJ, Damoiseaux JS. Lower-resolution retrieval of scenes in older adults with subjective cognitive decline. *Arch Clin Neuropsychol*. 2021;37:408-422. doi:10.1093/arclin/acab061
92. Chen X, Farrell ME, Moore W, Park DC. Actual memory as a mediator of the amyloid-subjective cognitive decline relationship. *Alzheimer's Dement Diagnosis, Assess Dis Monit*. 2019;11:151-160. doi:10.1016/j.dadm.2018.12.007
93. Yang Z, Rong Y, Cao Z, et al. Microstructural and cerebral blood flow abnormalities in subjective cognitive decline plus: diffusional kurtosis imaging and three-dimensional arterial spin labeling study. *Front Aging Neurosci*. 2021;13(625843):1-15. doi:10.3389/fnagi.2021.625843
94. Zhang Y, Du W, Yin Y, et al. Impaired cerebral vascular and metabolic responses to parametric N-back tasks in subjective cognitive decline. *J Cereb Blood Flow Metab*. 2021;41(10):2743-2755. doi:10.1177/0271678x211012153
95. Zhang Q, Wang Q, He C, et al. Altered regional cerebral blood flow and brain function across the alzheimer's disease spectrum: a potential biomarker. *Front Aging Neurosci*. 2021;13(February):630382. doi:10.3389/fnagi.2021.630382
96. Dong QY, Li TR, Jiang XY, Wang XN, Han Y, Jiang JH. Glucose metabolism in the right middle temporal gyrus could be a potential biomarker for subjective cognitive decline: a study of a Han population. *Alzheimer's Res Ther*. 2021;13(1):1-12. doi:10.1186/s13195-021-00811-w
97. Vannini P, Hanseeuw B, Munro CE, et al. Hippocampal hypometabolism in older adults with memory complaints and increased amyloid burden. *Neurology*. 2017;88(18):1759-1767. doi:10.1212/WNL.0000000000003889
98. Amariglio RE, Sikkes SAM, Marshall GA, et al. Item-Level investigation of participant and study partner report on the cognitive function index from the a4 study screening data. *J Prev Alzheimer's Dis*. 2021;8(3):257-262. doi:10.14283/jpad.2021.8
99. de Vries BM, Golla SSV, Ebenau J, et al. Classification of negative and positive 18F-florbetapir brain PET studies in subjective cognitive decline patients using a convolutional neural network. *Eur J Nucl Med Mol Imaging*. 2021;48(3):721-728. doi:10.1007/s00259-020-05006-3
100. Schwarz C, Lange C, Benson GS, et al. Severity of subjective cognitive complaints and worries in older adults are associated with cerebral amyloid-β load. *Front Aging Neurosci*. 2021;13(August):1-9. doi:10.3389/fnagi.2021.675583
101. Pavisic IM, Lu K, Keuss SE, et al. Subjective cognitive complaints at age 70: associations with amyloid and mental health. *J Neurol Neurosurg Psychiatry*. 2021;92(11):1215-1221. doi:10.1136/jnnp-2020-325620
102. Wang X, Wang M, Wang X, et al. Subjective cognitive decline-related worries modulate the relationship between global amyloid load and gray matter volume in preclinical Alzheimer's disease. *Brain Imaging Behav*. 2022;16(3):1088-1097. doi:10.1007/s11682-021-00558-w
103. Sanchez JS, Becker JA, Jacobs HIL, et al. The cortical origin and initial spread of medial temporal tauopathy in Alzheimer's disease assessed with positron emission tomography. *Sci Transl Med*. 2021;13(577):eabc0655. doi:10.1126/scitranslmed.abc0655
104. Wittens MMJ, Sima DM, Houbrechts R, et al. Diagnostic performance of automated MRI volumetry by icobrain dm for Alzheimer's disease in a clinical setting: a REMEMBER Study. *J Alzheimer's Dis*. 2021;83(2):623-639. doi:10.3233/JAD-210450
105. Chen H, Li W, Sheng X, et al. Machine learning based on the multimodal connectome can predict the preclinical stage of Alzheimer's disease: a preliminary study. *Eur Radiol*. 2021:448-459. doi:10.1007/s00330-021-08080-9
106. Liu Y, Yue L, Xiao S, Yang W, Shen D, Liu M. Assessing clinical progression from subjective cognitive decline to mild cognitive impairment with incomplete multi-modal neuroimages. *Med Image Anal*. 2022;75:102266. doi:10.1016/j.media.2021.102266
107. Huang W, Li X, Li X, Kang G, Han Y, Shu N. Combined support vector machine classifier and brain structural network features for the individual classification of amnestic mild cognitive impairment and subjective cognitive decline patients. *Front Aging Neurosci*. 2021;13(July):1-11. doi:10.3389/fnagi.2021.687927
108. Lei B, Cheng N, Frangi AF, et al. Auto-weighted centralised multitask learning via integrating functional and structural connectivity for subjective cognitive decline diagnosis. *Med Image Anal*. 2021;74:102248. doi:10.1016/j.media.2021.102248
109. Gouw AA, Hillebrand A, Schoonhoven DN, et al. Routine magnetoencephalography in memory clinic patients: a machine learning approach. *Alzheimer's Dement Diagnosis, Assess Dis Monit*. 2021;13(1):1-11. doi:10.1002/dad2.12227
110. Yue L, Hu D, Zhang H, et al. Prediction of 7-year's conversion from subjective cognitive decline to mild cognitive impairment. *Hum Brain Mapp*. 2021;42(1):192-203. doi:10.1002/hbm.25216
111. Finkel SI, Costa e Silva J, Cohen G, Miller S, Sartorius N. Behavioral and psychological signs and symptoms of dementia: a consensus statement on current knowledge and implications for research and treatment. *Int Psychogeriatr*. 1996;8(suppl 3):497-500.
112. Eikelboom WS, Van Den Berg E, Singleton EH, et al. Neuropsychiatric and cognitive symptoms across the Alzheimer disease clinical spectrum: cross-sectional and longitudinal associations. *Neurology*. 2021;97(13):e1276-e1287. doi:10.1212/WNL.0000000000012598
113. Jenkins A, Tree J, Tales A. Distinct profile differences in subjective cognitive decline in the general public are associated with metacognition, negative affective symptoms, neuroticism, stress, and poor quality of life. *J Alzheimer's Dis*. 2021;80(3):1231-1242. doi:10.3233/JAD-200882
114. Saari T, Smith EE, Ismail Z. Network analysis of impulse dyscontrol in mild cognitive impairment and subjective cognitive decline. *Int Psychogeriatrics*. 2022;34(6):553-562. doi:10.1017/S1041610220004123
115. Jiang HX, Xie X, Xu Y, Wang R, Lei X, Yu J. Older adults' subjective cognitive decline correlated with subjective but not objective sleep: a mediator role of depression. *Int J Aging Hum Dev*. 2022;95(1):42-56. doi:10.1177/00914150211024186
116. Xu WQ, Lin LH, Ding KR, et al. The role of depression and anxiety in the relationship between poor sleep quality and subjective cognitive decline in Chinese elderly: exploring parallel, serial, and moderated mediation. *J Affect Disord*. 2021;294(April):464-471. doi:10.1016/j.jad.2021.07.063
117. Nicolazzo J, Xu K, Lavale A, et al. Sleep symptomatology is associated with greater subjective cognitive concerns: findings from the community-based Healthy Brain Project. *Sleep*. 2021;44(9):1-9. doi:10.1093/sleep/zsab097
118. Smit D, Koerts J, Bangma DF, Fuermaier ABM, Tucha L, Tucha O. Look who is complaining: psychological factors predicting subjective cognitive complaints in a large community sample of older adults. *Appl Neuropsychol*. 2021;0(0):1-15. doi:10.1080/23279095.2021.2007387

119. Bejr-kasem H, Sampedro F, Marín-Lahoz J, Martínez-Horta S, Pagonabarraga J, Kulisevsky J. Minor hallucinations reflect early gray matter loss and predict subjective cognitive decline in Parkinson's disease. *Eur J Neurol*. 2021;28(2):438-447. doi:10.1111/ene.14576
120. Kim M, Lim K-C, Ko H. Factors influencing subjective cognitive function among community-dwelling older adults. *Geriatr Nurs (Minneap)*. 2021;42(5):1070-1076.
121. Nogueira J, Gerardo B, Silva AR, et al. Effects of restraining measures due to COVID-19: pre- and post-lockdown cognitive status and mental health. *Curr Psychol*. 2022;41(10):7383-7392. doi:10.1007/s12144-021-01747-y
122. Soldevila-Domenech N, Forcano L, Boronat A, et al. Effects of covid-19 home confinement on mental health in individuals with increased risk of Alzheimer's disease. *J Alzheimer's Dis*. 2021;79(3):1015-1021. doi:10.3233/JAD-201408
123. Podlesek A, Komidar L, Kavcic V. The relationship between perceived stress and subjective cognitive decline during the COVID-19 epidemic. *Front Psychol*. 2021;12(August):647971. doi:10.3389/fpsyg.2021.647971
124. Diaz-Galvan P, Cedres N, Figueroa N, Barroso J, Westman E, Ferreira D. Cerebrovascular disease and depressive symptomatology in individuals with subjective cognitive decline: a community-based study. *Front Aging Neurosci*. 2021;13(July):656990. doi:10.3389/fnagi.2021.656990
125. Esmael A, Abdelsalam M, Shoukri A, Elsherif M. Subjective cognitive impairment in patients with transformed migraine and the associated psychological and sleep disturbances. *Sleep Breath*. 2021;25(4):2119-2126. doi:10.1007/s11325-021-02308-0
126. Desai R, Whitfield T, Said G, et al. Affective symptoms and risk of progression to mild cognitive impairment or dementia in subjective cognitive decline: a systematic review and meta-analysis. *Ageing Res Rev*. 2021;71(May):101419. doi:10.1016/j.arr.2021.101419
127. Wang SM, Do HanK, Kim NY, et al. Late-life depression, subjective cognitive decline, and their additive risk in incidence of dementia: a nationwide longitudinal study. *PLoS One*. 2021;16(7 July):1-15. doi:10.1371/journal.pone.0254639
128. Ismail Z, Smith EE, Geda Y, et al. Neuropsychiatric symptoms as early manifestations of emergent dementia: provisional diagnostic criteria for mild behavioral impairment. *Alzheimer's Dement*. 2016;12(2):195-202. doi:10.1016/j.jalz.2015.05.017
129. Ismail Z, McGirr A, Gill S, Hu S, Forkert ND, Smith EE. Mild Behavioral impairment and subjective cognitive decline predict cognitive and functional decline. *J Alzheimer's Dis*. 2021;80(1):459-469. doi:10.3233/JAD-201184
130. Matuskova V, Ismail Z, Nikolai T, et al. Mild behavioral impairment is associated with atrophy of entorhinal cortex and hippocampus in a memory clinic cohort. *Front Aging Neurosci*. 2021;13(May):1-9. doi:10.3389/fnagi.2021.643271
131. Hansen N, Singh A, Bartels C, et al. Hippocampal and hippocampal-subfield volumes from early-onset major depression and bipolar disorder to cognitive decline. *Front Aging Neurosci*. 2021;13(April):626974. doi:10.3389/fnagi.2021.626974
132. Munro CE, Buckley R, Vannini P, et al. Longitudinal trajectories of participant- and study-partner-rated cognitive decline, in relation to Alzheimer's disease biomarkers and mood symptoms. *Front Aging Neurosci*. 2022;13(806432):1-11. doi:10.3389/fnagi.2021.806432
133. Roheger M, Hennersdorf X, Riemann S, Flöel A, Meinzer M. A systematic review and network meta-analysis of interventions for subjective cognitive decline. *Alzheimer's Dement Transl Res Clin Interv*. 2021;7(1):1-25. doi:10.1002/trc2.12180
134. Cooper C, Mansour H, Carter C, et al. Social connectedness and dementia prevention: pilot of the APPLE-Tree video-call intervention during the Covid-19 pandemic. *Dementia*. 2021;20(8):2779-2801. doi:10.1177/14713012211014382
135. Liou H, Stonnington CM, Shah AA, Buckner-Petty SA, Locke DEC. Compensatory and lifestyle-based brain health program for subjective cognitive decline: self-implementation versus coaching. *Brain Sci*. 2021;11(10):1306. doi:10.3390/brainsci11101306
136. Pang Y, Kim O. Effects of smartphone-based compensatory cognitive training and physical activity on cognition, depression, and self-esteem in women with subjective cognitive decline. *Brain Sci*. 2021;11(8):1029. doi:10.3390/brainsci11081029
137. Innes KE, Montgomery C, Selfe TK, Wen S, Khalsa DS, Flick M. Incorporating a usual care comparator into a study of meditation and music listening for older adults with subjective cognitive decline: a randomized feasibility trial. *J Alzheimer's Dis Reports*. 2021;5(1):187-206. doi:10.3233/ADR-200249
138. Brioschi Guevara A, Bieler M, Altomare D, et al. Protocols for cognitive enhancement. A user manual for brain health services—part 5 of 6. *Alzheimer's Res Ther*. 2021;13(1):1-13. doi:10.1186/s13195-021-00844-1
139. Kanatome A, Ano Y, Shinagawa K, Ide Y, Shibata M, Umeda S. β-Lactolin Enhances neural activity, indicated by event-related P300 amplitude, in healthy adults: a randomized controlled trial. *J Alzheimer's Dis*. 2021;81(2):787-796. doi:10.3233/jad-201413
140. Gutierrez L, Folch A, Rojas M, et al. Effects of nutrition on cognitive function in adults with or without cognitive impairment: a systematic review of randomized controlled clinical trials. *Nutrients*. 2021;13(11):3728. doi:10.3390/nu13113728
141. Forcano L, Fauria K, Soldevila-Domenech N, et al. Prevention of cognitive decline in subjective cognitive decline APOE ε4 carriers after EGCG and a multimodal intervention (PENSA): study design. *Alzheimer's Dement Transl Res Clin Interv*. 2021;7(1):1-10. doi:10.1002/trc2.12155
142. Ni L, Zhao M, Hu Z, et al. Neural mechanism of Shentai tea polyphenols on cognitive improvements for individuals with subjective cognitive decline: a functional near-infrared spectroscopy study. *J Alzheimer's Dis*. 2021;82(3):1137-1145.
143. Boa Sorte Silva NC, Petrella AFM, Christopher N, et al. The benefits of high-intensity interval training on cognition and blood pressure in older adults with hypertension and subjective cognitive decline: results from the heart & mind study. *Front Aging Neurosci*. 2021;13(April):1-17. doi:10.3389/fnagi.2021.643809
144. Fujita K, Umegaki H, Makino T, et al. Short- and long-term effects of different exercise programs on the gait performance of older adults with subjective cognitive decline: a randomized controlled trial. *Exp Gerontol*. 2021;156(September):111590. doi:10.1016/j.exger.2021.111590
145. Hu M, Wu X, Shu X, et al. Effects of computerised cognitive training on cognitive impairment: a meta-analysis. *J Neurol*. 2021;268(5):1680-1688. doi:10.1007/s00415-019-09522-7
146. Senczyszyn A, Wallner R, Szczesniak DM, Łuc M, Rymaszewska J. The effectiveness of computerized cognitive training combined with whole body cryotherapy in improving cognitive functions in older adults. A case control study. *Front Psychiatry*. 2021;12(June):1-13. doi:10.3389/fpsyt.2021.649066
147. Arlati S, Di Santo SG, Franchini F, et al. Acceptance and usability of immersive virtual reality in older adults with objective and subjective cognitive decline. *J Alzheimer's Dis*. 2021;80(3):1025-1038. doi:10.3233/JAD-201431
148. Kang JM, Kim N, Lee SY, et al. Effect of cognitive training in fully immersive virtual reality on visuospatial function and frontal-occipital functional connectivity in predementia: randomized controlled trial. *J Med Internet Res*. 2021;23(5):e24526. doi:10.2196/24526

149. Brooks H, Oughli HA, Kamel L, et al. Enhancing cognition in older persons with depression or anxiety with a combination of mindfulness-based stress reduction (MBSR) and transcranial direct current stimulation (tDCS): results of a pilot randomized clinical trial. *Mindfulness (N Y)*. 2021;12(12):3047-3059. doi:10.1007/s12671-021-01764-9
150. Vaqué-Alcázar L, Mulet-Pons L, Abellaneda-Pérez K, et al. tDCS-induced memory reconsolidation effects and its associations with structural and functional MRI substrates in subjective cognitive decline. *Front Aging Neurosci*. 2021;13(July):1-11. doi:10.3389/fnagi.2021.695232
151. Liu M, Nie ZY, Li RR, et al. Neural mechanism of repeated transcranial magnetic stimulation to enhance visual working memory in elderly individuals with subjective cognitive decline. *Front Neurol*. 2021;12(July):665218. doi:10.3389/fneur.2021.665218

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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