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Subjective Cognitive Impairment in 55-65-Year-Old Adults Is Associated with Negative Affective Symptoms, Neuroticism, and Poor Quality of Life

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Abstract. Although subjective cognitive impairment (SCI) is increasingly recognized clinically and in research as a risk factor for mild cognitive impairment and dementia (particularly Alzheimer’s disease), it is etiologically heterogeneous and potentially treatable. Compared to mild cognitive impairment and Alzheimer’s disease, SCI however remains poorly characterized with debate continuing regarding its clinical relevance. The primary aim of this study was to improve the characterization of SCI within the general public by investigating functions sometimes omitted clinically or in research, namely visual attention-related information processing speed (RT) and its intra-individual variability (IIV\textsubscript{RT}), general cognition, depression, anxiety, memory, quality of life (QOL), and neuroticism. Compared to individuals without SCI, those with SCI were more likely to reveal higher scores of anxiety, depression, and neuroticism and poorer perceived physical, psychological, and environmental QOL. Within-group analysis identified no significant relationships between any of the above variables for the non-SCI group whereas for the SCI group, poorer Cognitive Change Index scores were significantly correlated with slower RT, raised IIV\textsubscript{RT}, poorer memory, negative affective symptoms, higher neuroticism scores, and poorer QOL. This indicates perceived memory changes in SCI can also be associated with other characteristics, namely objectively measured detrimental change in other aspects of brain function and behavior. This outcome emphasizes the importance of a multi-function approach to characterizing and understanding SCI. Thus, although the effect of RT and IIV\textsubscript{RT} is not strong enough to differentiate SCI from non-SCI at group level, slowing and raised IIV\textsubscript{RT} do appear to characterize some people with SCI.

Keywords: Anxiety, dementia, depression, memory, neuroticism, quality of life, reaction time, subjective cognitive impairment, visual attention

INTRODUCTION

Subjective cognitive impairment (SCI) is defined clinically as perceived changes in memory and cognition that individuals report in the absence of objective evidence of abnormality [1]. SCI is increasingly recognized as a risk factor for mild cognitive impairment (MCI) and dementia (particularly Alzheimer’s disease [AD]) compared to demographically matched healthy adults free of SCI (hazard ratio 4.5; 95% CI 1.9–10.3) [2, 3]. Nevertheless, as in MCI, SCI appears etiologically heterogeneous. Although for some individuals, SCI may represent the outer limits of the normal aging process, or what is in fact normal aging...
individual with changes often considered to be ‘senior moments’ [4], a variety of risk and causal factors for SCI continue to be reported. These include age [5], low educational level [6], depression [9], chronic fatigue [10], whiplash [11], schizophrenia [12], bipolar disorder [13], obsessive compulsive disorder [14], epilepsy [16], stroke [17], fibromyalgia [19], medication side effects [20], and thyroid dysfunction [21]. Research has shown that MCI, vascular cognitive impairment (i.e., MCI and/or AD) and the prodromal stage) can be characterized by significant impairment, and AD (all of which may reveal SCI as a potentially treatable and may not be related to neurodegenerative disease [4, 22] and that the factors associated with SCI can detrimentally influence quality of life (QOL), self-perceived health [23, 24], perceived dementia and restrict social activities such as driving a car) [25]. Despite such familial associations and irrespective of etiology, SCI remains poorly characterized with respect to the integrity of a wide array of brain functions and with debate also continuing regarding the definition, SCI is characterized in research forums by the absence of objective measured aspects, and required support [25], factors such as age, gender, menopause [20], and thyroid dysfunction [21]. Such evidence indicates that some causes of SCI are potentially reversible causes or neurodegenerative diseases not specifically related to neurodegeneration, such as anxiety and mood and thus intervention for potentially reversible causes.

One of the aims of this study is to examine such function in SCI. Evidence of changes in such function in SCI can be expected to improve our understanding of factors contributing to the signs and symptoms of SCI.

A challenge when investigating SCI and the comparison of study outcome is the associated lack of consensus related to its concept and terminology [21]. However, subjective cognitive decline (SCD), related more specifically to the neurodegenerative decline associated with AD, is increasingly described clinically and in research [21]. SCI was examined in the present study in order to investigate the wider concept of perceived changes in a wide range of etiologies not specifically related to neurodegeneration, such as anxiety and mood and thus intervention for potentially reversible causes.

Furthermore, despite the fact that previous studies have tended to recruit people living with SCI with a formal diagnosis from memory services (i.e., received a clinical diagnosis of SCI), not everyone perceiving detrimental changes in cognitive function seeks medical attention and thus formal assessment [50, 51]. Such individuals may represent a sizeable proportion of community dwelling older adults [25, 50]. In order to redress this imbalance, SCI was investigated in those who had not been in contact with memory services. This study also extends previous work examining RT and IIVRT in relation to perceived memory changes in older adults [49, 52, 53].

SCI and anxiety, depression, quality of life, neuroticism, and memory
A. Jenkins et al. / Characterizing SCI

The current study was to further characterize SCI (in the general public) with respect to information processing speed (RT) and its IV_{RT}, visual and verbal memory function, and measured cognitive functioning, QOL, and neuroticism. We hypothesized the following: RT will be slower and IV_{RT} greater in individuals with compared to without SCI and that scores of general cognitive function, QOL, memory (visual and verbal) will be poorer, and scores of neuroticism, depression, and anxiety worse.

**METHODS**

**Participants**

An opportunity sample methodology was used. Males (N = 24) and females (N = 75) aged 55–65 years were recruited from the general public living in South Wales, UK (Number of participants [N] = 99; mean [M] age = 60.43 years, standard deviation [SD] = 2.96). Inclusion criteria: general public aged 55–65, and from a self-reported perspective, in good general medical and mental health. Exclusion criteria: a clinical diagnosis of MCI or dementia (self-report or diagnosis), self-report of decline in cognitive ability which can be explained by a psychiatric or neurological disease, previous head injury, medication (prescribed and non-prescribed use). A further exclusion factor was a visit to their general practitioner (GP) about memory concerns. Participants were recruited via advertisement on social media, group email (i.e., 50+ Network), posters, etc.

Older adults aged 55–65 years were recruited in order to represent the typical age-range through which SCI presents. This study was approved by Swansea University ethics review boards and written informed consent was obtained from all participants.

**Battery of measures**

Mean education level, ethnicity, employment status/level, and family history are presented in Table 1. The test battery comprised: Cognitive Change Index (Self report) (CCI-S) and the Cognitive Change Index (Informant report) (CCI-I) to measure SCI symptoms [71]; The World Health Organization Quality of Life (WHOQOL-BREF) (shortened version of the WHOQOL-100) [72]; Hospital Anxiety and Depression Scale (HADS) [73]; The Big Five Inventory (BFI) to measure neuroticism [74]; Montreal Cognitive Assessment (MoCA) [29]; The Rey Osterrieth Complex Figure (ROCF) to measure visual memory [75]; The Hopkins Verbal Learning Test (HVLT) to measure verbal memory [76]; The National Adult Reading Test (NART) to measure predicted IQ [77]; Trails A (TMT A) and Trails B (TMT B) [52]; and the adapted Multi-Item Localization task (MILO) [53].

Figure 1 is a schematic example of a trial from the tablet-based implementation of MILO which was employed in the current study [78]. The participants needed to touch each virtual pool ball from one to eight in ascending order as quickly, but as accurately as possible. The advantages of computer-based test presentation in comparison to paper-and-pencil tests include the recording of reaction times for each item, rather than basic completion overall such as that in the TMT (e.g., see [79]), and the capacity to investigate spatial patterns of search organization (e.g., see [80]). Additionally, the MILO task makes it possible to easily manipulate the sequence type (e.g., digits, letters, or both) and sequence behavior (e.g., items vanishing or remaining, sequence position remaining fixed or shuffling between responses), in order to investigate the temporal context of visual search [53]. Therefore, a task such as this could potentially be employed in a clinical situation, providing information about RT speed and variability and attention processing, and additional features of higher level, cognitive processing. For this study, a fixed sequence of the digits one to eight was used, and the display was configured so that items vanished when touched. The additional sequences (i.e., shuffling) were not used because only a simple measure of information processing time (RT) and IV_{RT} that did not take too long to complete was required, thus mimicking the limited time a clinician would have to use such a test in real life.

The sample was split based on their CCI-S scores (CCI-S) (i.e., the SCI group and the non-SCI group) in order to determine any between-group differences (i.e., between SCI and non-SCI) or within-group relationships. The CCI measure has one set of cut-off values to use as a method of grouping, which are the ones used within the well-established Alzheimer’s Disease Neuroimaging Initiative (ADNI) study [81].
Table 1
Participant characteristics in both the SCI and the non-SCI group

| SCI                      | Non-SCI                  | Pearson Chi Square Test results of the corresponding categories within the SCI and non-SCI group | Mann-Whitney Test results of the corresponding categories within the SCI and non-SCI group |
|--------------------------|--------------------------|-----------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|
| Total N                  | 47                       | –                                                                                             | NS                                                                                       |
| Age mean (SD)            | 60.34 (2.71)             | –                                                                                             | –                                                                                       |
| Gender                   | 35 (74.5) Female; 12 (25.5) Male | NS                                                                                             | –                                                                                       |
| Ethnicity group          | Welsh – 31 (66)          | Welsh – 35 (67.3)                                                                             | NS                                                                                       |
|                         | English – 8 (17)         | English – 6 (11.5)                                                                            | –                                                                                       |
|                         | British/other – 8 (17)   | British/other – 11 (21.2)                                                                     | –                                                                                       |
| Employment status        | Retired or unemployed – 23 (49) | NS                                                                                             | –                                                                                       |
|                         | Employed or self-employed (full time) – 15 (32) | –                                                                                             | –                                                                                       |
|                         | Employed or self-employed (part time) – 9 (19.1) | –                                                                                             | –                                                                                       |
| Employment level         | Supervisor – 12 (25.5)   | Supervisor – 11 (21.2)                                                                        | NS                                                                                       |
|                         | Manager – 19 (40.4)      | Manager – 27 (51.9)                                                                           | –                                                                                       |
|                         | None – 16 (34.0)         | None – 14 (26.9)                                                                              | –                                                                                       |
| Family history of cognitive impairment | Yes (maternal) – 18 (38.3) | Yes (maternal) – 20 (38.5)                                                                    | NS                                                                                       |
|                         | Yes (paternal) – 1 (2.1) | Yes (paternal) – 6 (11.5)                                                                      | –                                                                                       |
|                         | None – 28 (59.6)         | None – 26 (50.0)                                                                              | –                                                                                       |
| CCI-S mean (SD)          | 27.62 (7.45)             | –                                                                                             | –                                                                                       |
|                         | 15.04 (2.17)             | –                                                                                             | –                                                                                       |
| Cohen's effect size:     | –0.86 Large              | –                                                                                             | –                                                                                       |
|                         | –0.45 Medium             | –                                                                                             | –                                                                                       |
| NART errors mean (SD)    | 11.55 (7.82)             | –                                                                                             | –                                                                                       |
|                         | 9.31 (6.84)              | –                                                                                             | –                                                                                       |

∗NS, not significant.
They are the only validated cut-off values, but analysis using the full-scale scores yielded the same pattern of results. These cut-offs are based on the first 12 CCI items (out of 20) which relate to perceived memory concerns. Therefore, individuals are believed to be experiencing memory concerns if they score 20 or above on the first 12 items of the CCI-S.

Statistical analysis

MILO generates data-rich results due to its multiple-trial format, thus individual RT values can be provided for each item. MILO can for instance provide data relating to the time taken to touch the first virtual pool ball (RT1), also the cumulative time to touch the second pool ball (RT2) and so on, until all eight virtual pool balls have been touched (overall time is RT8). Within the current study, the measure of how quickly an individual touches all eight balls and completes the trial (RT8) was employed within the statistical analysis. As mentioned earlier, in this study, there were 30 trials in the MILO test. Therefore, the median value of RT8 was calculated for the statistical analysis of between-group differences and within-group correlations. The IIVRT in relation to these 30 trials was also calculated and statistically analyzed as interquartile range (IQR).

Overall, based on Kolmogorov-Smirnov analysis the data (i.e., on the CCI, TMT A, TMT B, MILO, MoCA, HVLT, ROCF, WHOQOL-BREF, HADS, and the BFI) were not normally distributed despite score transformations, therefore non-parametric analysis was applied. This lack of normality can be typical of such studies and therefore the use of non-parametric tests is common (e.g., see [31, 32]). To determine group differences (between the SCI and non-SCI group), the Mann-Whitney test was employed for continuous data and the Chi Square test was employed for categorical data. Furthermore, correlations (within-group relationships) between all test battery scores were analyzed using non-parametric Spearman’s correlation coefficient. Due to the multiple comparisons being investigated in some of the correlational analyses, the Bonferroni correction method was used in order to control for the possibility of type-one errors.

RESULTS

Hypothesized a priori predictions were made and therefore one-tailed analyses were run and reported below. For completeness the analysis at a two-tailed level was also carried out, but there were only scant and minor differences between these two sets of analyses.

As can be seen in (Table 1), no significant participant characteristic group differences (i.e., age and years in education) were identified apart from for the CCI scores (which was the means by which the groups were divided [CCI-S]) [71]. Figure 2 (non-SCI group) shows the distribution of scores on the CCI-S measure from 10 (lowest possible score) to 19 (highest possible score before the SCI group cut-off score of 20). Figure 3 (SCI group) shows the distribution of scores on the CCI-S measure from 20 (lowest possible score cut-off value) to 60 (highest possible score on the CCI-S measure).
Within-group relationships

There were no significant within-group correlations between CCI-S scores, RT, and IIVRT in the non-SCI group (all \( p \) values >0.05) (see Supplementary Table 2 for details). Within the SCI group, however, the time taken to perform TMT B was significantly positively correlated to CCI-S score, i.e., the higher the CCI-S score (indicating worse perceived cognitive functioning), the slower the RT (\( r_s = 0.35, p \) (1-tailed) <0.01) (Fig. 4). Furthermore, within the SCI group, a significant positive correlation between CCI-S scores and MILO IIVRT (\( r_s = 0.34, p \) (1-tailed) <0.01) was revealed (i.e., worse perceived cognitive functioning was related to greater RT variability) (Fig. 5). This remained significant after Bonferroni correction (\( p = 0.010 \)). Figures 4 and 5 also reveal that a proportion of individuals showed disproportional slowing (RT) and greater variability (IIVRT) only in the SCI group. This is shown by the outliers in RT and IIVRT, which appear in the SCI group only.

Subjective cognitive impairment, general cognitive functioning, depression, anxiety, QOL, memory, and neuroticism

Between-group differences

There were no significant differences in performance on general cognitive functioning, visual...
Within-group relationships

No within-group correlations in the SCI group were found between CCI-S scores and any of the individual variability of reaction time (IIVRT), general cognitive functioning, memory, depression, and neuroticism. For the SCI group, there were within-group differences on CCI-S scores and performance (visual RT: TMT B, worse levels of anxiety, or the social relationship QOL (all moderate, p < 0.01), psychological depression (U = 806.00 (Z = –2.809), Cohen’s effect size: –0.39 moderate), anxiety (U = 670.50 (Z = –3.881), Cohen’s effect size: –0.45 moderate), and neuroticism (U = 822.00 (Z = –3.093), Cohen’s effect size: –0.37 moderate). There were also significant differences on anxiety (U = 764.50 (Z = –3.26), p < 0.01), and neuroticism (U = 728.50 (Z = –3.51), p < 0.01) memory, psychological QOL, anxiety, and neuroticism. However, in the SCI group, there were within-group differences in anxiety and neuroticism (U = 709.00 (Z = –3.63), p < 0.01) and verbal memory; poorer physical, psychological, and environmental QOL; poorer perceived physical, psychological, and environmental QOL; worse anxiety and depression; and higher scores on neuroticism. However, after Bonferroni correction on the QOL sub-scales, the only measure of information processing speed (RT) that was significantly correlated with CCI-S scores in the SCI group. Therefore, further analyses were run to investigate whether TMT B and IIVRT performance was significantly related to anxiety and depression.

Statistical analysis revealed that IIVRT was not significantly related to anxiety ($r_s = 0.20, p > 0.05$) or depression ($r_s = 0.04, p > 0.05$) scores. In relation to RT, a significant positive correlation was identified between higher scores on anxiety and poorer TMT B score (higher score, i.e., slower information processing speed) ($r_s = 0.34, p$ (1-tailed) <0.01) in those with SCI. This suggests that worse anxiety symptoms are associated with slower information processing with respect to TMT B test performance and worse scores on the CCI-S measure (i.e., slowing associated with greater perceived feelings of poor cognitive functioning). After Bonferroni correction (α level 0.05/2 = 0.025), this remained significant ($p = 0.010$). In addition, statistical analysis revealed that there was no significant correlation between TMT B and depression ($r_s = 0.15, p$ (1-tailed) >0.05).

**DISCUSSION**

The aim of this study was to examine visual attention-related processing speed (RT), the intra-individual variability of reaction time (IIVRT), general cognitive functioning, memory, depression, anxiety, quality of life, and neuroticism in SCI in order to improve knowledge of its characteristics and thus of its potential signs and symptoms.

Contrary to our prediction that individuals with SCI would show greater slowing in information processing speed (RT) and greater IIVRT variability compared to those without SCI, there was no significant difference in mean RT or IIVRT between the SCI and non-SCI groups (see Supplementary Table 3 for details). However, there were significant differences between these two groups regarding physical (Z = –2.947), psychological (Z = –2.947), and environmental QOL; poorer scores on anxiety and depression. However, after Bonferroni correction the only significant within-group correlation to remain statistically significant (1-tailed) <0.05). Thus, within the SCI group, poorer scores in the SCI group was TMT B. Also, in relation to variability, IIVRT was significantly correlated (with CCI-S scores) in the SCI group. Therefore, further analyses were run to investigate whether TMT B and IIVRT performance was significantly related to anxiety and depression.

Statistical analysis revealed that IIVRT was not significantly related to anxiety ($r_s = 0.20, p > 0.05$) or depression ($r_s = 0.04, p > 0.05$) scores. In relation to RT, a significant positive correlation was identified between higher scores on anxiety and poorer TMT B score (higher score, i.e., slower information processing speed) ($r_s = 0.34, p$ (1-tailed) <0.01) in those with SCI. This suggests that worse anxiety symptoms are associated with slower information processing with respect to TMT B test performance and worse scores on the CCI-S measure (i.e., slowing associated with greater perceived feelings of poor cognitive functioning). After Bonferroni correction (α level 0.05/2 = 0.025), this remained significant ($p = 0.010$). In addition, statistical analysis revealed that there was no significant correlation between TMT B and depression ($r_s = 0.15, p$ (1-tailed) >0.05).
Such a pattern of results indicates that although slowing (with respect to certain brain processes recruited) may represent a predictor of further decline as slowed RT and increased IIVRT can be characteristics of MCI and AD [31–40]. However, the cross-sectional design of the current study precludes such analysis.

As predicted, levels of anxiety, depression, and neuroticism were significantly greater in the SCI compared to the non-SCI group, and QOL (all forms) was significantly poorer in the SCI group. Again, in the non-SCI group, CCI-S scores were correlated with visual and verbal memory, physical, environmental, and psychological QOL.

This suggests that some individuals with SCI can be disproportionately slowed and variable in their responses indicating that individuals with SCI should be investigated beyond the findings of general objective outcome in currently used psychological tests. These results further highlight the need for a stratified and person-centered approach to SCI, rather than simply comparing effects at group level particularly given the possibly detrimental influence upon daily life and its potential to represent early neurodegenerative disease.

Memory

As predicted, in the non-SCI group there were no significant correlations between CCI-S, HVLT (verbal), and ROCF (visual) scores. In the SCI group, however, both the HVLT and ROCF scores were significantly negatively correlated with CCI-S scores. The correlation between ROCF and CCI-S scores was stronger and had a greater effect size than that between HVLT and CCI-S scores. These results suggest that within the SCI group greater degrees of subjective impairment are associated with poorer visual/non-verbal memory and verbal recognition. This finding provides support for past research (i.e., see [83–85]) indicating that impairments in episodic memory are characteristic of SCI, although there are also inconsistencies in such research findings [86].

Neuroticism

Neuroticism was significantly greater in the SCI compared to the non-SCI group. Furthermore, within the SCI, but not the non-SCI group, neuroticism was significantly correlated with CCI-S score. These results are in alignment with those of Ausen et al. [66] in that a high level of neuroticism may represent a risk factor for experiencing cognitive impairment and for further decline [54, 66, 69].

As expected, anxiety and depression (specifically sub-clinical depression, thus low mood) scores were significantly poorer for the SCI compared to the non-SCI groups. Within the SCI group only, CCI-S score (i.e., poorer SCI scores) was significantly correlated with both higher levels of anxiety and depression (sub-clinical) [8], although directional causality [25, 62, 88–92] could not be ascertained in the current study.
Further analyses were run on the significant relationship found between anxiety and TMT B performance. A significant positive correlation was found between TMT B performance and anxiety, thus slower RT was associated with greater levels of anxiety indicating that processing speed on the TMT B could be associated with anxiety for those in the SCI group. No significant correlation was found between TMT B performance and sub-clinical depression scores. Despite the commonly identified co-morbid relationship between anxiety and depression [60], these results indicate that anxiety may have more impact on RT compared to depression.

The identified increase in negative affective symptoms and related slowing in the SCI group supports the recommendation by Jessen et al. [21] to not dismiss such sub-threshold symptoms, to ensure they are considered when assessing for cognitive decline (specifically SCD).

Quality of life

After Bonferroni correction, only psychological QOL was significantly correlated with CCI-S scores within the SCI group, thus indicating that SCI may be particularly associated with psychological factors, again of course causality cannot be determined here. Our finding of significantly higher levels of anxiety in the SCI group is in agreement with a study by Strine and colleagues [93] who found that individuals with higher levels of self-reported anxiety were more likely to have poorer health-related QOL. Therefore, there may be an association between poor SCI, poor anxiety, and poor QOL.

Despite the inability to determine causality and loss of post correction significance, what the current study does highlight is that a characteristic of SCI is a diminished sense of psychological wellbeing. To conclude, a number of variables measured appeared to characterize SCI in comparison to those without SCI. At group level, individuals with SCI were more likely to have higher scores on anxiety, depression (specifically low mood), neuroticism, and QOL.

Study limitations and future research

It is questionable whether a larger sample would have produced similar or different results. The sample size was determined based on past research studies of attention related RT tests, in MCI and AD, with typical numbers approximately between 20 and 30 participants. Since the relationship between SCI and RT (in the general public) has not been investigated using such studies and because the effects in SCI may be smaller than in MCI and AD, the number of participants in the present study was increased in each group to 50.

The fundamental aim of this study was to highlight potential SCI characteristics in a normal population and irrespective of etiology, and its cross-sectional design thus rendered it impossible to determine causal relationships and any relationship between the findings and the development of MCI or dementia, or the successful treatment of SCI. These are areas for further and longitudinal investigation; factors beyond the scope of the present study [23, 94].

This study has provided a valuable contribution to research regarding the characterization of SCI in the general population. It is clear that despite the sample having a low level of cognitive impairment, they were still reporting poorer scores in relation to anxiety, depression, and QOL. Regardless of whether the SCI symptoms are a cause or consequence of such distress, their cognitive concerns should not be dismissed as benign. Thus, appropriate SCI management might enable potentially reversible symptoms to be treated (e.g., psychological difficulties), therefore not only possibly alleviating SCI symptoms but also decreasing the risk of further cognitive decline [60].

DISCLOSURE STATEMENT

Authors' disclosures available online (https://www.j-alz.com/manuscript-disclosures/18-0810r3).

SUPPLEMENTARY MATERIAL

The supplementary material is available in the electronic version of this article: http://dx.doi.org/10.3233/JAD-180810.
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