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ive Cognitive Impairment 5-Year-Old Adults Is Associated egative Affective Symptoms, icism, and Poor Quality of Life

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subjective cognitive impairment (SCI) is increasingly recognized clinically and in research as a risk itive impairment and dementia (particularly Alzheimer's disease), it is etiologically heterogeneous able. Compared to mild cognitive impairment and Alzheimer's disease, SCI however remains poorly ebate continuing regarding its clinical relevance. The primary aim of this study was to improve the CI within the general public by investigating functions sometimes omitted clinically or in research, namely ed information processing speed (RT) and its intra-individual variability (IIV_{RT}), general cognition, memory, quality of life (QOL), and neuroticism. Compared to individuals without SCI, those with SCI eveal higher scores of anxiety, depression, and neuroticism and poorer perceived physical, psychological, OL. Within-group analysis identified no significant relationships between any of the above variables for hereas for the SCI group, poorer Cognitive Change Index scores were significantly correlated with slower orer memory, negative affective symptoms, higher neuroticism scores, and poorer QOL. This indicates ived memory changes in SCI can also be associated with other characteristics, namely objectively l change in other aspects of brain function and behavior. This outcome emphasizes the importance of roach to characterizing and understanding SCI. Thus, although the effect of RT and IIV_{RT} is not strong

ividual with changes often consid-
moments' [4], a variety of risk and
SCI continue to be reported. These
ow educational level [6], depres-
[9], chronic fatigue [10], whiplash
zophrenia [12], bipolar disorder
mpulsive disorder [14], epilepsy
rosis [16], stroke [17], fibromyal-
nea [19], medication side effects
0], and thyroid dysfunction [21].
icates that some causes of SCI are
e and may not be related to neu-
ease [4, 22] and that the factors
may be more varied and complex
visaged. Furthermore, irrespective
detrimentally influence quality of
rceived health [23, 24], perceived
nance and restrict social activities
driving a car) [25]. Despite such
ental associations and irrespective
emains poorly characterized with
egrity of a wide array of brain
n debate also continuing regard-
esearch, and everyday relevance
herefore that further exploration to
haracteristics, consequences, pos-
and required support [25], factors
ially reversible causes or neurode-
, is imperative.

ssing speed and intra-individual

definition, SCI is characterized in
esearch forums by the *absence* of

are associated with brain white matter integrity [36], poorer daily activity levels and quality of life [43–49]. Therefore, 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 IIV_{RT} in relation to perceived memory changes in older adults [49, 52, 53].

SCI and anxiety, depression, quality of life, neuroticism, and memory

n the investigation of SCI in the

current study was to further char-
e general public) with respect to
sing speed (RT) and its $IIV_{RT,}$ and
ual and verbal memory function,
y measured cognitive function-
ssion, QOL, and neuroticism. We
ollowing: RT will be slower and
dividuals with compared to with-
ores of general cognitive function,
ual and verbal) will be poorer, and
sm, depression, and anxiety worse,

sample methodology was used.
d females (N = 75) aged 55–65
ted from the general public liv-
es, UK (Number of participants
] age = 60.43 years, standard devi-
Inclusion criteria: general public
om a self-reported perspective, in
cal and mental health. Exclusion
iagnosis of MCI or dementia (self-
iagnosis), self-report of decline in
hich can be explained by a psychi-
cal disease, previous head injury,
medication (prescribed and non-

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

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
	47	52	–	–
	60.34 (2.71)	60.52 (3.20)	–	NS
	35 (74.5) Female; 12 (25.5) Male	40 (76.9) Female; 12 (23.1) Male	NS	–
mean (SD)	14.26 (2.96)	15.15 (2.97)	–	NS
	Welsh – 31 (66)	Welsh – 35 (67.3)	NS	–
	English – 8 (17)	English – 6 (11.5)		–
	British/other – 8 (17)	British/other – 11 (21.2)		–
%)	Retired or unemployed – 23 (49)	Retired or unemployed – 22 (42.3)	NS	–
	Employed or self-employed (full time) – 15 (32)	Employed or self-employed (full time) – 18 (34.63)		–
	Employed or self-employed (part time) – 9 (19.1)	Employed or self-employed (part time) – 12 (23.08)		–

lti-Item Localization task (MILO).

validated cut-off values, but anal-
sing the full-scale scores yielded
f results. These cut-offs are based
items (out of 20) which relate to
concerns. Therefore, individuals
experiencing memory concerns if
bove on the first 12 items of the

es data-rich results due to its
at, thus individual RT values can
ach item. MILO can for instance
ng to the time taken to touch the
ll (RT1), also the cumulative time
the second pool ball (RT2) and
ght virtual pool balls have been
ime is RT8). Within the current
e of how quickly an individual

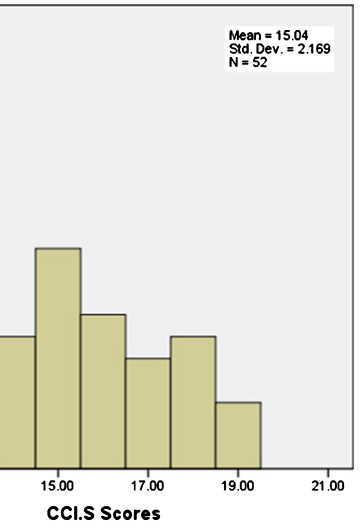
the use of non-parametric tests is common (e.g., see [31, 32]). To determine group differences (between the SCI and non-SCI group), the Mann-Whitney test was employed for continuous data and the Chi Square test was employed for categorical data. Furthermore, correlations (within-group relationships) 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

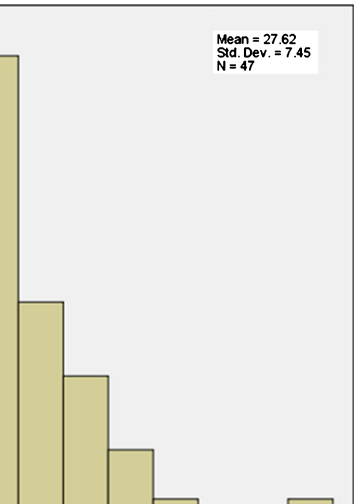
Hypothesized *a priori* predictions were made and therefore one-tailed analyses were run and reported below. For completeness the analysis at a two-tailed level was also carried out, but there were only scant and minor differences between these two sets of analyses.

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).



CCI-S scores within the non-SCI group.



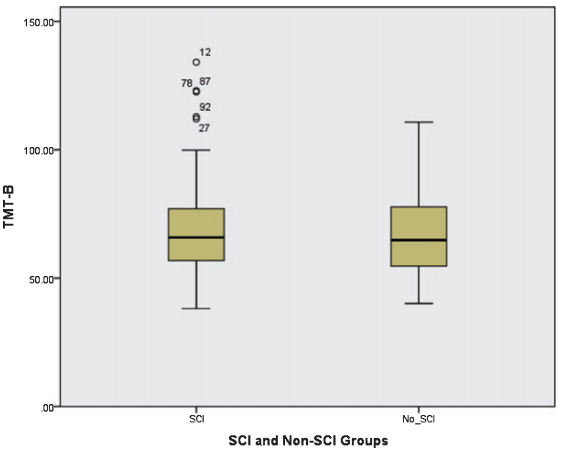


Fig. 4. Distribution of TMT B scores in the SCI and non-SCI group.

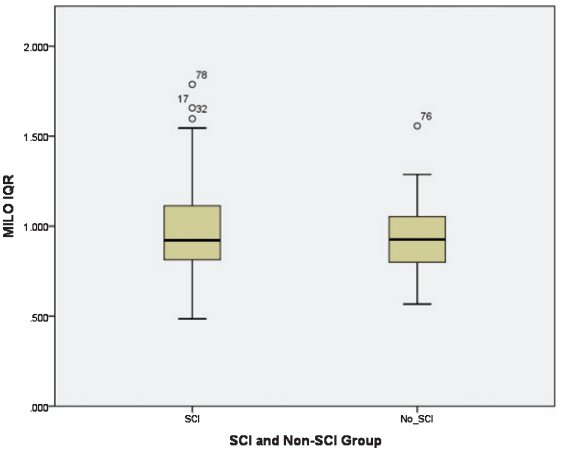


Fig. 5. Distribution of MILO IIV_{RT} scores in the SCI and non-SCI group.

CCI-S scores and MILO IIV_{RT} ($r_s = 0.34$, p (1-tailed)

y, or the social relationship QOL values >0.05) between the SCI ups (see Supplementary Table 3 ver, there were significant differ- se two groups regarding physical –3.63), $p < 0.01$), psychological 3.51), $p < 0.01$), and environmental 3.26), $p < 0.01$) QOL (all moderate were also significant differences on 0 ($Z = -3.881$), $p < 0.01$; Cohen's moderate), depression ($U = 806.00$ .01; Cohen's effect size: –0.30 roticism ($U = 822.00$ ($Z = -2.809$), , the SCI group demonstrated hysical, psychological, and envi- poorer scores on anxiety and gher levels of neuroticism respec- the non-SCI group.

ionships

within-group correlations in the ween CCI-S scores and any of the eral cognitive functioning, mem- y, depression, and neuroticism). CI group, there were within-group en CCI-S scores and performance 38, p (1-tailed) <0.01) and verbal tailed) <0.05) memory, physi- (1-tailed) <0.05), psychological ailed) <0.01), and environmen- (1-tailed) <0.05) QOL, anxiety ed) <0.01), depression ($r_s = 0.45$, , and neuroticism ($r_s = 0.26$, p (1- us, within the SCI group, poorer correlated with poorer visual and

ther analyses were run to investigate whether TMT B and IIV_{RT} performance was significantly related to anxiety and depression.

Statistical analysis revealed that IIV_{RT} 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 (IIV_{RT}), 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 IIV_{RT} variability compared to those without SCI, there was no sig-

. Such a pattern of results indi-
slowing (with respect to certain
e brain processes recruited) may
chological differences (e.g., anx-
represent a predictor of further
RT and increased IIV_{RT} can be
MCI and AD [31–40]. However, the
ign of the current study precludes

evels of anxiety, depression, and
significantly greater in the SCI
n-SCI group, and QOL (all forms)
oorer in the SCI group. Again, in
non-SCI group, CCI-S scores were
ated with visual and verbal mem-
sion, physical, environmental, and
.

at some individuals with SCI can
ely slowed and variable in their
g that individuals with SCI should
ond the findings of general objec-
urrently used psychological tests.
er highlight the need for a strati-
ntered approach to SCI, rather than
effects at group level particularly
ossibly detrimental influence upon
y life and its potential to represent
rative disease.

A score

population sample in the present
inical one but represented instead
the community who experience
ognition but do not approach mem-
eral practitioners about it. As can

nitive screening tools. This is further supported by the results of Reisberg et al. [2] which revealed that 54% of individuals with SCI declined to MCI or AD but that the average Mini-Mental State Examination [82] baseline scores for those who declined was 29 out of a maximum 30. In a clinical setting therefore, individuals with SCI, who would typically score normally on such measures, would most likely have been precluded from further investigation and follow up (see Jenkins et al. [28]).

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

s, RT and IIV$_{RT}$

es were run on the significant
l between anxiety and TMT B
gnificant positive correlation was
MT B performance and anxiety,
as associated with greater levels
ng that processing speed on the
associated with anxiety for those
. No significant correlation was
T B performance and sub-clinical
Despite the commonly identified
ship between anxiety and depres-
esults indicate that anxiety may
on RT compared to depression.
rease in negative affective symp-
lowing in the SCI group supports
on by Jessen et al. [21] to not dis-
eshold symptoms, to ensure they
en assessing for cognitive decline
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ni correction, only psychological
ntly correlated with CCI-S scores
up, thus indicating that SCI may
ociated with psychological factors,
usality cannot be determined here
finding of significantly higher lev-
e SCI group is in agreement with
es [93] who found that individuals
of self-reported anxiety were more
rer levels of health-related QOL
ere may be an association between
iety, and poor QOL.

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

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