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ORIGINAL PAPER

Lower Neurocognitive Functioning Disrupts the Effective Use of Internet-Based Health Resources in HIV Disease: The Mediating Effects of General Health Literacy Capacity

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Abstract
HIV-associated neurocognitive impairment is an independent predictor of low general health literacy, which can be associated with poor disease outcomes (e.g., viremia). Given the increasing frequency with which health behaviors occur in an online environment (e.g., health information seeking, provider interactions), there is a specific need to understand the predictors of electronic health (eHealth) literacy of persons living with HIV disease. In this study, 90 HIV+ persons completed the eHealth Literacy Scale (eHEALS), which measures one's awareness, skills and evaluation of online health resources. Participants also completed a comprehensive battery of clinical neurocognitive tests and well-validated performance-based measures of general health literacy capacity (e.g., knowledge, numeracy). Results showed that, independent of education, lower neurocognitive function was moderately related to lower eHEALS scores, particularly in the domains of learning and motor skills. Of particular note, general health literacy capacity emerged as a significant mediator of the relationship between neurocognition and eHealth literacy. Thus, the adverse effects of neurocognition on health literacy capacity carries a downstream adverse influence on HIV+ persons' awareness, skills, and evaluation of health-related resources in the online environment.

Keywords World Wide Web · Neuropsychological assessment · Internet navigation skills · AIDS dementia complex · Health behaviors

Introduction

Over the past few decades, the Internet has changed the way that people with HIV disease and other chronic illnesses manage their personal health. About half of HIV+ persons use the Internet for health-related activities (e.g., [1, 2]), such as searching for information on HIV (e.g., symptoms, treatments), engaging in health-related social activities (e.g., discussions), managing their healthcare (e.g., making appointments, accessing personal electronic medical records), participating in clinical research (e.g., prevention and adherence), and receiving direct healthcare services (e.g., [3]). Health-related Internet use is linked to many positive health outcomes and behaviors, including higher HIV testing rates (e.g., [4, 5]), greater healthcare engagement (e.g., [6]), higher adherence levels (e.g., [7, 8]), lower HIV viral loads (e.g., [9]), and better general health outcomes (e.g., [10, 11]).

Although the Internet has tremendous advantages as a healthcare delivery platform, there are also a number of potential barriers to its effective use in vulnerable populations such as HIV disease. Most notably these barriers include limited Internet access and low levels of eHealth literacy, which describes the knowledge, skills, and self-efficacy to use electronic resources for personal health management. Early studies estimate that 20–33% of HIV+ persons have low eHealth literacy [6, 12, 13], commonly experience anxiety related to technology (e.g., [9]), and often need help in using the Internet (e.g., [14]). For example, many HIV-infected persons report difficulty discriminating between high and low quality health websites [6], even after psychoeducation [13]. Thus it is important to identify potentially modifiable individual differences in eHealth literacy in the setting of HIV disease. Research to date suggests that lower health-related Internet use among HIV+ individuals is associated with older age and lower

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levels of education, income, and general health literacy (e.g., [8]).

Neurocognitive deficits may play a fundamental role in the eHealth functioning of HIV+ persons. At face value, it is easy to appreciate how difficulties with motor skills (e.g., using a keyboard and mouse), memory (e.g., forgetting passwords), attention (e.g., being distracted by alerts), and executive functions (e.g., problem-solving technical difficulties or non-intuitive websites) could affect Internet use and navigation. Studies from aging, traumatic brain injury, and multiple sclerosis suggest that Internet search and navigation skills are strongly related to neurocognitive abilities, particular memory and executive functions (see [15]), as well as their underlying brain networks (e.g., [16]). HIV disease is a major risk factor for impairment in the neurocognitive domains that support Internet navigation, as approximately 30–50% of infected persons meeting criteria for HIV-associated neurocognitive disorders (HAND; [17]). A study from our group shows that persons with HAND show large deficits on performance-based measures of Internet navigation skills, including household tasks such as shopping and financial management [18]. Of even more direct relevance to this study, persons with HAND show sizeable deficits on online measures of health-related Internet skills, including navigating pharmacy refills and electronic medical records [9]. HIV+ persons also have difficulty recalling websites they used for health-related information seeking (as cited in [19]).

We do not yet know the specific pathways by which neurocognitive functioning affects Internet-related health behaviors in HIV, but general health literacy is one potential mediating factor that is ostensibly worth examining. Health literacy is "the capacity to obtain, communicate, process, and understand basic health information and services to make appropriate health decisions" [20]. Low health literacy occurs in about one-quarter of HIV-infected persons [21] and adversely influences a variety of health behaviors, such as adherence (e.g., [22]), which can lead to poorer health outcomes, including higher viral loads (e.g., [23]). Emerging data show that lower neurocognitive functions may have downstream adverse effects on health literacy. In 2010, Waldrop-Valverde et al. [24] demonstrated that lower memory, attention, and complex visuomotor sequencing were independently associated with poorer health-related comprehension and numeracy in HIV. Subsequent research revealed that individuals with HAND are at risk for low health literacy, ranging from fundamental skills like numeracy [25] to higher-order capacities, such as medical decision-making [26] and engagement with healthcare providers [27]. Moreover, standard measures of health literacy relate to performance-based health-related Internet navigation skills among persons with HIV disease [9].

This study sought to examine the association between neurocognition and eHealth literacy among persons living with HIV disease. It was hypothesized that lower neurocognitive functioning in domains that have previously shown to be related to Internet navigation skills (i.e., executive functions, episodic memory, attention/working memory, psychomotor speed) would be associated with worse eHealth literacy, controlling for important co-factors (e.g., education). Moreover, we predicted that the relationship between neurocognition and eHealth literacy would be mediated by poorer general health literacy.

Methods

These data were drawn from a larger NIH-funded R21 study of 43 HIV- and 93 HIV+ persons that was approved by the human research review board at UC San Diego (UCSD) and whose primary outcomes have been reported elsewhere (see [9, 18]). Study participants were originally enrolled from various cohort studies at the UCSD HIV Neurobehavioral Research Program (HNRP), which recruits potential participants from the local community, HIV clinics, and community-based organizations. Informed consent was obtained from all individual participants included in the study. Exclusion criteria included severe psychiatric disorders (e.g., psychosis), neuromedical conditions that can affect neurocognitive functions (e.g., seizure disorders, head injury, and stroke), a positive Breathalyzer for alcohol or urine toxicology for illicit drugs, and use of the Internet < 5 times over the past 5 years (see [9, 18]). HIV serostatus was determined with Medmira rapid tests. In this investigation, we analyze the 90 HIV+ persons who completed the eHealth Literacy Scale (eHEALS; [28]). The demographic, psychiatric, and medical characteristics of these 90 HIV+ participants are shown in Table 1.

eHealth and Non-internet Health Literacy Scales

The primary outcome of interest in this study was the 8-item eHealth Literacy Scale (eHEALS; [28]). Participants used a 5-point Likert scale anchored by "Strongly Agree" and "Strongly Disagree" to respond to 8 statements about their use of the Internet as a health resource, which include issues of awareness (e.g., "I know what health resources are available"), skills (e.g., "I know how to find helpful health resources"), and evaluation (e.g., "I can tell high quality health resources from low quality health resources"). In an effort to enhance the practical relevance of the eHEALS, we scored each of the 8 items according to whether the participants endorsed "Agree" or "Strongly Agree" so that the range for each individual item was 0–1. This yielded an 8-item scale with a range of 0–8, with higher scores

Table 1 Demographic and clinical characteristics of the 90 HIV+ study participants

Variable	Study sample (N = 90)
Sociodemographic	
Age (years)	45.8 (10.1)
Education (years)	13.7 (2.3)
Sex (% women)	10.0
Ethnicity (%)	
Caucasian	54.4
Hispanic	20.0
Black	20.0
Other	5.6
Income (< $25,000/yr)	56.7
Psychiatric	
Major depression (%)[a]	61.8
Generalized anxiety (%)[a]	12.6
POMS total (of 200)	51.2 (36.7)
Substance use disorder (%)[a]	65.9
Medical[b]	
Hepatitis C (% seropositive)	10.3
AIDS (% with diagnoses)	54.0
Duration of HIV (years)	12.9 (9.2)
Nadir CD4 (cells/μL)	238.2 (220.0)
Current CD4 (cells/μL)	663.9 (336.1)
Antiretroviral therapy (ART, % prescribed)	89.7
Plasma HIV RNA (% detectable on ART)	9.1
Neurocognitive	
Global T-score	46.4 (7.0)
HIV-associated neurocognitive disorder (% yes)	51.1
Health literacy	
Expanded numeracy scale (of 7)	4.8 (2.1)
HIV knowledge questionnaire-18 (of 18)	15.4 (2.5)
Newest vital sign (of 6)	4.4 (1.6)
REALM (of 66)	63.5 (6.6)
Short assessment of health literacy (of 50)	47.9 (3.8)
TOFHLA (of 50)	44.1 (6.6)

POMS profile of mood states, *AIDS* acquired immune deficiency syndrome, *CD4* cluster of differentiation 4. *REALM* rapid estimate of adult literacy in medicine, *SAHL* short assessment of health literacy, *TOFHLA* test of functional health literacy in adults

[a]Denotes any lifetime disorder

[b]n = 87

reflecting better eHealth literacy. The Cronbach's alpha for this 8-item eHEALS was 0.954. In addition, the eHEALS includes 3 supplementary items that do not factor into its total score, which assess the use, usefulness, and importance of health resources on the Internet (see Table 2).

In order to anchor the specificity of the Internet-based health literacy findings, we also administered a parallel, non-Internet (ni) version of the eHEALS (niHEALS). The

Table 2 Computer and internet use characteristics of 90 HIV+ participants

Variable	Study sample (N = 90)
Basic computer and internet use	
Use computer at home (% yes)	84.4
Internet use frequency (% daily)	65.6
Difficulties using computers (% none)	81.1
Anxiety using computers (% none)	72.2
eHealth Literacy Scale (eHEALS)	
Standard eHEALS TOTAL (of 8)	6.1 (2.5)
eHEALS supplementary items	
Use internet as a source for health information[a]	3.8 (1.2)
Agree or strongly agree (%)	73.3
Internet is useful for health-related decisions[a]	3.9 (1.1)
Agree or strongly agree (%)	70.0
Internet is important for accessing health information[a]	4.0 (1.1)
Agree or strongly agree (%)	76.7
Non-internet health literacy scale (niHEALS)	
niHEALS total (of 8)	6.4 (2.2)
niHEALS supplementary item	
Use non-internet sources for health information[a]	3.7 (1.1)
Agree or strongly agree (%)	70.0

[a]Likert-scale anchored by 1 (strongly disagree) and 5 (strongly agree), with higher scores representing greater levels of agreement

item content, structure, order, and scoring of the niHEALS was identical to the eHEALS, with the exception that participants were asked to rate their level of agreement with statements about non-Internet based resources for health (e.g., books, social contacts). Total scores ranged from 0 to 8 with higher scores reflecting better non-Internet health literacy (see Table 2). The Cronbach's alpha for niHEALS was 0.922. Participants also answered questions about their basic computer and Internet use (Table 2).

Neuropsychological Functioning

Participants were administered a comprehensive neuropsychological test battery that was informed by the Frascati diagnostic criteria for HAND [29] and included the following eight domains: (1) Motor: dominant and non-dominant hands of the Grooved Pegboard Test [30, 31]; (2) Processing speed: WAIS-III Digit Symbol total [32] and Trailmaking Test Part A total time [31, 33]; (3) Response time: Detection (reaction time) and identification (reaction time) subtests of the CogState (www.cogstate.com); (4) Attention/Working Memory: PASAT-50 [34, 35] and the one-back (accuracy) and two-back (accuracy) subtests from the CogState; (5) Learning: Hopkins Verbal Learning Test-Revised (HVLT-R) Total 1–3 [36, 37], Brief Visuospatial Memory

Test-Revised (BVMT-R) Total 1–3 [37, 38], and CogState one-card learning (accuracy); (6) Delayed Memory: HVLT-R Delayed Recall, BVMT-R Delayed Recall, and CogState continuous paired associates (accuracy); (7) Verbal Fluency: animals and letter/FAS [31]; and (8) Executive Functions: Wisconsin Card Sorting Test (WCST-64; [37, 39] perseverative responses and Trailmaking Test Part B total time [31, 33]. A global score and eight individual domain scores were constructed using mean, demographically-adjusted T-scores (M = 50, SD = 10) based on the best available normative standards that considered age, education, sex, and ethnicity where possible and indicated.

Health Literacy

General health literacy capacity was measured by a comprehensive assessment that was comprised of well-validated measures of health knowledge, numeracy, and understanding, including: (1) Expanded Numeracy Scale [40]; (2) HIV Knowledge Questionnaire-18 (HIV-KQ-18; [41]); (3) Newest Vital Sign (NVS; [42]); (4) Rapid Estimate of Adult Literacy in Medicine (REALM; [43]); (5) Short Assessment of Health Literacy (SAHL; [44]); and (6) Test of Functional Health Literacy in Adults (TOFHLA; [45]). Raw scores on these health literacy variables are displayed in Table 1. In an effort to minimize Type I error, we created a continuous composite health literacy score using the mean of the sample-based raw total z-scores on these six measures.

Clinical Characterization

All participants underwent a neuromedical exam, history, and phlebotomy/labs, which provided information on HIV disease severity and comorbid conditions. Current mood was assessed by the Profile of Mood States (POMS; [46]). Lifetime mood and substance use disorders were operationalized by the Composite International Diagnostic Interview (Version 2.1) [47].

Results

The correlation between the eHEALS and niHEALS scales was 0.54 ($p < 0.001$), and the mean scores of two scales did not differ in magnitude ($p = 0.240$, $d = -0.13$). Lower eHEALS scores were associated with detectable plasma RNA among persons prescribed antiretroviral therapy (ART; $X^2 = 4.0$, $p = 0.046$, Cohen's $d = -0.80$) and with lower current CD4 count ($r_s = 0.221$, $p = 0.040$), but not with estimated duration of HIV infection, AIDS status, nadir CD4 count, or ART status (all $ps > 0.10$). Lower niHEALS showed a trend-level, but large association with detectable plasma RNA among persons prescribed ART ($X^2 = 3.2$, $p = 0.076$, Cohen's $d = -0.84$), but was not associated with any other HIV disease variable (all $ps > 0.10$)

Neuropsychological Functioning

Two separate multiple regression models were constructed, predicting the eHEALS and niHEALS from global neuropsychological T-score. Covariates for these two models were selected in a data-driven fashion by identifying the sociodemographic, psychiatric, and medical variables listed in Table 1 that were associated with both the global neuropsychological T-score and the HEALS scales (using a critical alpha of 0.10). Only education met those criteria and was therefore used as a covariate in both models. For the eHEALS, the overall regression model was significant ($F(2,87) = 8.8$, Adj $R^2 = 0.15$, $p = 0.0003$), with global neuropsychological T-score (B = 0.10, SE = 0.04, $p = 0.0099$) and education (B = 0.28, SE = 0.11, $p = 0.013$) both emerging as significant contributors. Specifically, higher eHEALS scores were associated with higher levels of education ($r_s = 0.27$, $p = 0.01$) and higher global neuropsychological T-scores ($r_s = 0.30$, $p = 0.004$; Fig. 1). Exploratory analyses of the 8 individual neuropsychological domains revealed that eHEALS was significantly associated with learning ($r_s = 0.22$, $p = 0.038$) and motor skills ($r_s = 0.27$, $p = 0.013$), but not with any other neuropsychological domain (all $ps > 0.10$).

For the niHEALS, the overall regression model was not significant ($F(2,87) = 1.4$, Adj $R^2 = 0.01$, $p = 0.264$) and neither global neuropsychological T-score (B = 0.00, SE = 0.03, $p = 0.975$) nor education (B = 0.16, SE = 0.10, $p = 0.115$) were significant contributors. The simple univariate

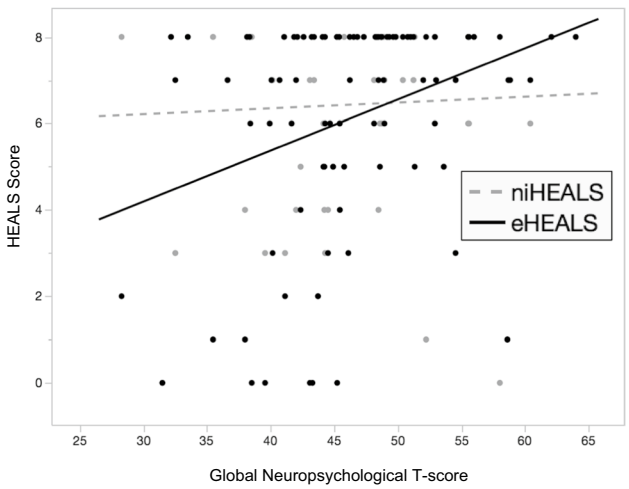

Fig. 1 Scatter plot showing the association between global neurocognitive functioning and the eHealth Literacy Scale (eHEALS) and the non-Internet Health Literacy Scale (niHEALS) in 90 persons living with HIV disease

correlation between niHEALS and global neuropsychological T-score was also non-significant ($r_s = 0.03$, $p = 0.806$; Fig. 1) and was significantly smaller than the correlation between eHEALS and global neuropsychological T-score ($z = 2.674$, $p = 0.004$).

Mediation Analyses

A mediation model was conducted in Mplus version 8 using maximum likelihood estimation and 95th percentile bootstrap confidence intervals. Health literacy significantly mediated the relationship between global neuropsychological T-score and eHEALS after controlling for education (Table 3, Fig. 2). The indirect effect of global neuropsychological T-score on eHEALS was significant, $b = 0.06$, 95% CI [0.01, 0.12], $p < 0.01$, while the direct effect of global neuropsychological T-score on eHEALS was no longer significant, $b = 0.04$, 95% CI [−0.05, 0.12], $p > 0.10$, when health literacy was used as a mediator. In other words, controlling for education level, a participant with a global neuropsychological T-score 10 points higher would be expected to score 0.6 points higher on eHEALS, via the influence of health literacy.

Table 3 Mediation model examining the associations between neurocognition, health literacy, and the eHealth Literacy Scale (eHEALS), adjusting for level of education (N = 90)

	Estimate	SE	Lower CI	Upper CI
Health literacy on				
Education	0.07**	0.02	0.03	0.12
Neurocognition	0.05**	0.13	0.02	0.07
eHEALS on				
Education	0.20	0.11	−0.02	0.42
Health literacy	1.18*	0.47	0.14	2.04
Neurocognition	0.04	0.04	−0.05	0.12
Intercepts				
eHEALS	1.57	2.48	−3.24	6.47
Health literacy	−3.22**	0.66	−4.56	−1.97
Residual variances				
eHEALS	4.86**	0.76	3.18	6.15
Health literacy	0.30**	0.07	0.16	0.42

SE standard error, *CI* 95% bootstrap confidence interval

*$p < 0.05$; **$p < 0.01$

Discussion

Persons with HIV and other chronic medical conditions commonly struggle to use the Internet for health-related purposes (e.g., [6]). Mild neurocognitive disorders are common in HIV (e.g., [17]) and can adversely affect real-world (e.g., [48]) and online health behaviors [9], as well as general health literacy (e.g., [24]). Consistent with our a priori hypotheses, this study demonstrated that HIV-associated neurocognitive deficits are also associated with lower eHealth literacy. In this case, eHealth literacy was measured by participants' perceptions of their own: (1) awareness of online health resources; (2) skills to locate and use online health resources; and (3) ability to evaluate the reliability and usefulness of online health resources. The relationship between neurocognition and eHealth literacy was accompanied by a medium effect size (per [49]) and was independent of sociodemographic (i.e., education) factors. Speaking to the clinical relevance of our measurement of eHealth literacy, eHEALS was significantly associated with viremia and lower immune function in this sample; nevertheless, the post hoc inclusion of those HIV disease factors in a multiple regression predicting eHEALS did not change the significance or strength of the association between eHealth literacy and neurocognition.

Interestingly, the association between eHealth literacy and neurocognition cannot be attributed solely to participant self-report of difficulties navigating health resources in general. Indeed, there was a statistically null and small association between neurocognition and participants' awareness, skills, and evaluation of health resources that were not Internet-based (e.g., books, social contacts). Nevertheless, the non-Internet health literacy scale showed good internal

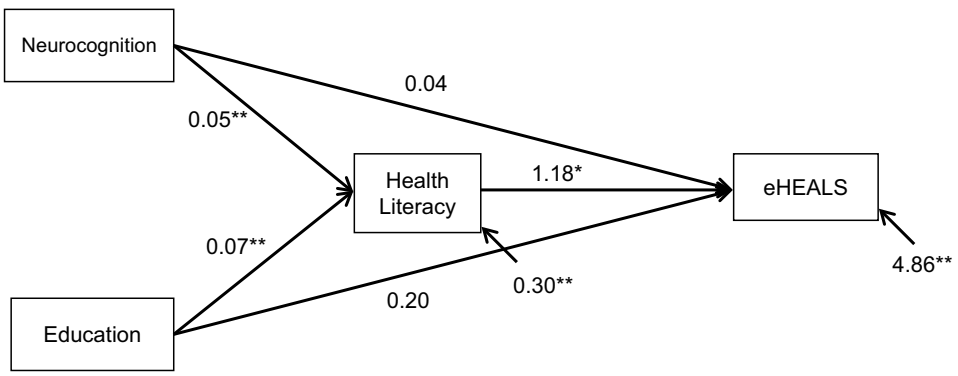

Fig. 2 Mediation model showing the pathways linking neurocognition, health literacy, and the eHealth Literacy Scale (eHEALS), adjusting for education (N = 90). Coefficients represent unstandardized bootstrap estimates. *$p < 0.05$; **$p < 0.01$

consistency, a trend-level association with viremia, and a large and positive correlation with eHEALS; in fact, there were no differences in the percentage of participants who agreed that both online and off-line resources were useful for health-related information. Thus, one interpretation of these findings is that the online environment has special demands that map onto neurocognition or are exacerbated by anxiety related to computer and Internet use.

At the domain level, measures of episodic memory (e.g., list and figure learning) and fine-motor skills demonstrated the strongest associations with eHealth literacy in this sample. These findings are consistent with a recent structured review from our laboratory [15] showing that tests of Internet navigation skill are sensitive to mild neurocognitive disorders (e.g., [50]) and correlate with clinical tests of neuropsychological functioning, particularly in the domain of episodic learning and memory for which medium-to-large effect sizes are observed (e.g., [9, 18, 51]). Likewise, two of three prior studies that examined the association between Internet navigation skills and basic motor functioning observed smaller, but significant associations (e.g., [18]). Not surprisingly, deficits in episodic memory and motor functions are among the most sensitive to HIV-associated neurocognitive disorders (e.g., [52, 53]) and are reliably associated with declines in other aspects of everyday functioning (see [54] for a review). Future studies may wish to examine the component mechanisms of these associations; for example, whether it is the strategic aspects of encoding and retrieval that drive the relationship between eHealth literacy and episodic memory impairment (e.g., [55]). Moreover, the extent to which theoretically-based approaches to enhancing learning and memory in HIV (e.g., [56, 57]) may be applied to health-related activities on the Internet deserves exploration.

A major finding from this study is that health literacy capacity appears to mediate the relationship between neurocognition and eHealth literacy in the setting of HIV disease. These data support the idea that health literacy capacity (viz., knowledge, numeracy, and understanding) is dependent in part on neurocognitive functioning (e.g., learning), as has been shown in prior studies from our group (e.g., [25–27]). Importantly, however, the relationship between neurocognition and perceived eHealth literacy is explained by health literacy capacity. In other words, the effects of lower neurocognition on general health literacy capacity as measured in the laboratory carries a downstream adverse influence on patients' awareness, skills, and evaluation of health resources in the online environment. The battery of health literacy capacity measures used in this study was comprised of well-validated and performance-based tests of health knowledge, numeracy, and understanding. Future studies may wish to investigate other aspects of health literacy capacity (see [58]) in this regard, including health-related decision-making (e.g., [26]). Findings suggest that enhancing health literacy capacity may also dampen the effects of neurocognition on eHealth literacy, although this remains to be determined by experimental work.

Several limitations to these findings deserve consideration. First, the sample included mostly Caucasian men with fairly high levels of education and low levels of frank health illiteracy, whose HIV disease was well-controlled on ART. As such, the external validity of these findings to more diverse samples with higher rates of health illiteracy and poorer disease control is not known. Second, the niHEALS was developed specifically for this study and although it demonstrated good psychometrics and convergent validity, many of its psychometric properties (e.g., test–retest reliability) and broader construct validity remain unknown at this time. Relatedly, while eHEALS is well-validated and widely used, it is a self-report measure and thus subject to bias. Performance-based measures of eHealth literacy, such as health-related search measures (e.g., [59]), may be of interest as this research moves forward. Finally, health literacy capacity is only one of several possible mediators of the relationship between neurocognition and eHealth literacy; future studies might examine other critical factors such as everyday functioning capacity (e.g., Internet navigation or search skill).

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in the study involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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