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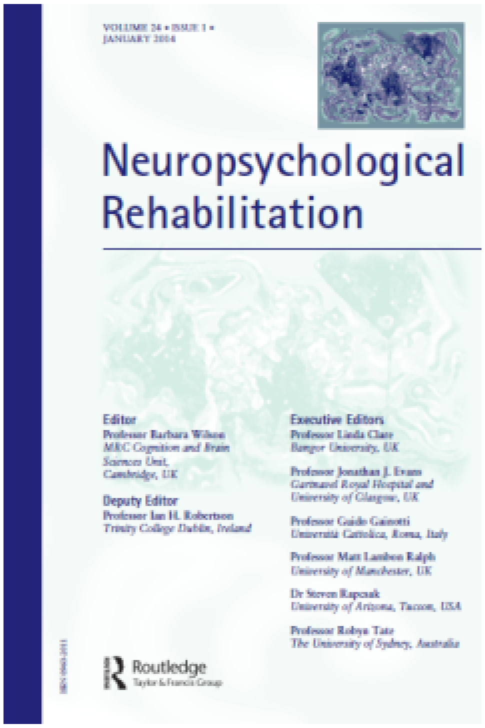

Social Isolation after Acquired Brain Injury: Exploring the Relationship Between Network Size, Functional Support, Loneliness and Mental Health.

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Social Isolation after Acquired Brain Injury: Exploring the Relationship Between Network Size, Functional Support, Loneliness and Mental Health.

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Abstract

Social isolation can be a consequence of acquired brain injury (ABI). Few studies have examined the relationship between social isolation and mental health after ABI. In this cross-sectional and case-control study we compared 51 ABI survivors and 51 matched healthy controls on measures of social isolation (network size, social support and loneliness) mental health and mental health problems. We explored the relationship between structural, functional and subjective components of social isolation and examined whether they were associated with mental health outcomes. No group differences were found on size of the network and perceived social support. The ABI group exhibited marginally higher levels of loneliness. The ABI group presented higher levels of depression, lower levels of quality of life and emotional wellbeing. In both groups, perception of social support was inversely related to subjective experience of loneliness. The relationship between network size and loneliness was only significant in the ABI group. Only loneliness significantly predicted quality of life, emotional wellbeing, depression and anxiety in people with brain injury. The relationship between social isolation variables in ABI is discussed, as well as the theoretical and clinical implications of focusing on loneliness to improve mental health after brain injury.

Brain Injury; Social Isolation, Loneliness, Social Network, Social Support, Mental Health

> It is in general very difficult for our patients to come into close contact with other people. They do not try to become intimate friends with other persons or to mingle in society; as a rule, they live in an isolated way.
>
> Kurt Goldstein (1940) *Human Nature in Light of Psychopathology p.57*

1. Introduction

Social isolation refers to the decreased *quantity* and inadequate *quality* of social relations with other people at the different levels where human interaction takes place - individual, group, community and the larger social environment (Zavaleta et al., 2014). In the last decade, social isolation has become a health and economic concern across the globe due to its association with mental health problems (Cacioppo et al., 2006; Heinrich & Gullone, 2006; Neeleman & Power, 1994), physical disease (Fox et al., 1994; Sorkin et al., 2002; Steptoe et al., 2004) and mortality risk (Holt-Lunstad et al., 2010). The high prevalence of social isolation in Europe, where 75 million people report meeting family or friends at most once a month, and 30 million report frequently feeling lonely (D'Hombres et al., 2018), has led governments to consider social isolation as a priority for social care and public health (Public Health England [PHE], 2014).

Social isolation can occur at all stages of the life course. However, particular individuals or groups may be more vulnerable than others (Durcan & Bell, 2015). Individuals with acquired brain injury appear to be especially vulnerable to social isolation due to motor, cognitive and socio-emotional impairments, which often limit social participation. Since the 1980s, several studies have reported a drastic decrease in the number of friends and frequency of social contact after brain injury (Aström et al., 1992; Dawson & Chipman, 1995; Elsass & Kinsella, 1987; Finset et al., 1995; Hoofien et al., 2001; Kinsella et al., 1989; Kozloff, 1987; Morton & Wehman, 1995; Mukherjee et al., 2003; Olver et al., 1996; Thomsen, 1984). In the last decade, a renewed interest in social isolation after brain injury has taken place in the field of neuropsychological rehabilitation. Such interest appears to be related to the so called 'relational turn', an epistemological shift that understands brain injury as something that occurs, and acquires meaning, 'in the space' between people (Bowen et al., 2018), often compromising survivors, relatives and friends' capacity to connect and sustain intimacy (Yeates, 2013; Yeates & Salas, 2020). Brain injury rehabilitation professionals have also become increasingly interested in the effects that social interaction has on identity reconstruction (social identity theory), health and well-being, thus incorporating group membership and social identities as key therapeutic ingredients of rehabilitation models (e.g., Haslam et al., 2012, 2018; Salas et al., 2020).

Research on social isolation after brain injury has presented, however, important conceptual and methodological challenges. One of the most significant ones is capturing the complexity of social isolation, in terms of both *quantity* and *quality* of social relations. In other words, compared to other fields, the discussion of what social isolation *is* and how best to *measure it*, has been relatively absent from the research agenda. Authors outside the field of neuropsychological rehabilitation (Zavaleta et al., 2014; Wang et al., 2017) have operationalized *quantity* as the **structural** characteristics of the social network, in terms of size, composition, frequency/length of contact and level of reciprocity. In contrast, the *quality* of social relations has been commonly defined as the instrumental value attached to those relationships, often described as perceived or objective **functional support** (e.g. emotional/information support, tangible support, affectionate support). Another key element that defines the quality of social relationships is the personal assessment of whether relations satisfy one person's expectations. This element refers to the **subjective experience of isolation**, commonly known as loneliness.

In general, researchers have tended to separately focus on these components when designing studies to explore social isolation after brain injury, emphasizing questions that address the structural and functional properties of the social network. The review by Northcott et al. (2015) exemplifies this point. The authors reported data from 22 qualitative and 48 quantitative studies, describing several trends in the literature on stroke and social isolation: a) a contraction in the size (structure) of the overall social network and non-kin network (friends); b) an inverse relationship between levels of functional support, depression and quality of life and c) the perception of social support as stable after the injury. The consideration of the subjective experience of social isolation (loneliness), and its relationship with structural and functional elements of the network, has been rarely addressed in the literature. An exception is a study by McLean et al. (2014) which described, in a sample of community-dwelling adults with moderate to severe TBI, that lower levels of loneliness were associated with higher levels of perceived social support and social integration. In another study, Rigon et al. (2018), reported that individuals with TBI, compared to healthy controls, exhibited higher levels of loneliness, but no differences in network size. Interestingly, these two variables were negatively associated only in the brain injury group. To our knowledge there are only two studies that have attempted to explore social isolation using structural, functional and subjective (loneliness) measures, though these studies have collected data from heterogeneous samples of people with chronic conditions -with brain injury survivors as one of them (Penninx et al., 1999; Tomaka et al., 2006). Unfortunately, only the study by Tomaka offered data regarding the relationship between social isolation variables, for the whole sample of chronic conditions. They reported that living alone was positively associated with levels of loneliness ($r = .46$) and negatively related with family support ($r = -.34$). Loneliness was negatively associated with family support ($r = -.37$).

There is robust evidence showing that, after brain injury, individuals can experience a decrease in wellbeing and quality of life (Haley et al., 2011; Hawthorne et al., 2009) and develop mental health problems, such as anxiety and depression (Aström et al., 1993; Coetzer, 2018; Hawthorne et al., 2009; Proctor & Best, 2019). However, existing knowledge on the relationship between structural, functional and subjective components of social isolation and brain injury survivors' mental health is limited, mainly due to a lack of studies considering all three components. For example, some studies have linked a reduction in the size of the overall social network (Cruice et al., 2003; Hilari & Northcott, 2006; Mackenzie & Chang, 2002), and satisfaction with functional support (Dayapoglu & Tan, 2010; King, 1996; Mackenzie & Chang, 2002) to health-related quality of life. Other reports have offered evidence relating a reduction in the size of the social network (Aström et al., 1993; Haley et al., 2011), and levels of perceived functional support (Cubis et al., 2019; Friedland & McColl, 1987; Hilari et al., 2010; King et al., 2002; Lewin et al., 2013; Morris et al., 1991; Taylor-Piliae et al., 2013; Townend et al., 2007; White et al., 2014), with depressive symptoms. Concerning subjective social isolation, to our knowledge, there is only one report describing loneliness as a relevant predictor of depression and anxiety (Hilari et al., 2010). The level of knowledge acquired in neuropsychological rehabilitation contrasts with research outside the field, where a robust set of data from neurotypical individuals has shown strong associations between social isolation, emotional wellbeing, quality of life and mental health problems (see reviews by Cacioppo et al., 2011; Leigh-Hunt et al., 2017; Wang et al., 2017).

In sum, there is robust evidence describing social isolation as a problem after brain injury, and a less developed literature exploring the association between social isolation and mental health. The study of social isolation in brain injury has, however, important theoretical and methodological limitations, compromising the understanding of how changes in structural, functional and subjective components of social isolation relate to mental health issues. This information is critical to understand how social isolation should be targeted therapeutically. The goal of this study is to address these theoretical and methodological gaps, using a cross-sectional and case-control design, thus answering three research questions: 1) Do individuals with acquired brain injury differ from matched healthy controls in measures of social isolation, wellbeing, quality of life anxiety and depression? 2) Do structural, functional and subjective components of social isolation relate to each other? 3) Which, if any, social isolation components predict quality of life, emotional wellbeing, depression and anxiety? In order to answer these questions, a sample of community dwelling individuals with acquired brain injury was compared to a group of matched healthy controls in structural, functional and subjective measures of social isolation, as well as measures of mental health (quality of life and well-being) and mental health problems (anxiety and depressive symptomatology).

2. Materials and Methods

2.1. Participants

The study recruited initially 56 community dwelling patients with acquired brain injury (ABI) and 81 healthy controls (HC), all residing in the Metropolitan Region (Chile). Participants passed through a selection process based on inclusion criteria and control-to-patient matching (See Figure 1A). For the acquired brain injury group, the following inclusion criteria were used: a) to have any form of acquired brain injury (e.g. stroke, TBI, tumor, hypoxia, etc); b) to be at least 18 years old; c) to be at least 12 months since injury. Exclusion criteria for this group were: a) to have a progressive neurological illness; b) severe language impairment that impedes understanding and completing questionnaires; c) the presence of a neurobehavioral disorder that impeded cooperation during assessment. Exclusion criteria for the control group were: a) an overall score below 81 in the Addenbrooke Cognitive Examination (ACE-R) suggesting cognitive decline; b) a percentage of functional change over 30% in the Activities of Daily Living Questionnaire (T-ADLQ) suggesting cognitive decline; c) cut-off score over 9 in the Patient Health Questionnaire (PHQ-9). Five individuals with ABI decided not to complete the study and 10 controls were excluded due low scores in the ACE-R and T-ADLQ.

We estimated a sample size of 51 ABI patients and 51 sex-, age- and education-matched HCs. The estimation was calculated with G * Power 3.1 software, using as criteria a one-tailed comparison between two independent groups, with a medium anticipated effect size (Cohen´s d 0.5), a type I error of 0.05 and statistical power of 0.8. In order to match both groups each participant was categorized in term of sex, age (18-45, 46-60, 61-75) and years of education (< 8, 8, <12, >12). Patients and controls were paired based on these criteria. When there was more than one control available for a pairing, one was chosen randomly.

Finally, ABI and HC groups were matched in terms of sex (Female n = 21; Males n = 30), age (ABI, M = 59.1; SD = 18.2; HC, M = 55.3; SD = 16.3; p = .26) and years of education (ABI, M = 12,7; SD = 4.3; HC, M = 13.37; SD = 4.6; p = .45). The ABI group was composed of 14 individuals with TBI (27.5%) and 37 with stroke (72.5%). At the time of the assessment the ABI group was 52.9 months post injury on average (SD = [Range: 12-240]) and had a significantly smaller proportion of employed individuals (ABI n = 16; HC, n = 33; p = .0001). Both groups lived with a similar number of people in their households (ABI, M = 3.6; SD = 1.7; HC, M = 3.7; SD = 1.9; p = .09). The proportion of participants that were single (ABI n = 14; HC n = 12) or married/with a partner (ABI n = 27; HC n = 26), was similar in both groups. There was no difference in the average number of children between groups (ABI, M = 2.3; SD = 1.8; HC, M = 2.34; SD = 1.4; p = .80).

2.2. Instruments

Two screening measures were used to assess participants' overall cognitive and functional level. The *Addenbrooke's Cognitive Examination Revised* (ACE-R, Mioshi et al., 2006; Muñoz-Neira et al., 2012) was employed as a proxy for overall cognitive performance. The ACE-R assesses five cognitive domains (Orientation and attention, memory, verbal fluency, visuo-spatial skills) and has a maximum overall score of 100 points. The *Activities of Daily Living Questionnaire* (T-ADLQ, Muñoz-Neira, López, et al., 2012) is a third-party report that explores the change in basic and instrumental activities of daily living. This questionnaire was developed to capture functional decline in people with dementia, however, it has also been used in people with acquired brain injury (Idiáquez et al., 2017). The T-ADLQ has 33 items that assess functionality in seven domains (Self-care, Household care, Shopping and Money, Employment and recreation, Travel, Communication, Technology). Each item is rated on a four-point scale from 0 (no problem) to 3 (no longer capable of performing the activity). A percentage of functional change can be calculated from the overall score. Two subscales -engagement in prosocial activities (SFS-PRO) and leisure (SFS-OCI)- of the Spanish version of the Social Functioning Scale (Torres & Olivares, 2005) were used to assess participants' level of involvement in community life. The Glasgow Outcome Scale Extended (GOSE, Wilson, Pettigrew & Teasdale, 1998) was used to measure the level of disability of each person in the ABI group. The GOSE is a global scale for functional outcomes that rates patient status in 8 levels and five broad categories (1 Death, 2 Vegetative State, 3-4 Severe Disability, 5-6 Moderate Disability, 7-8 Good Recovery).

Social network structure was captured using the *Social Network Map* (NETW; Subsecretaría de Redes Asistenciales, 2013). This instrument gathers information regarding the number of face-to-face contacts that an individual has had during the last 6 months. The map is divided in four quadrants that represent different social contexts (family, friends, work/education, community). This map offers a total score for the whole network and specific scores for each quadrant.

Social network functional support was assessed using the *Medical Outcome Study Social Support Survey* (MOSS, Sherbourne & Stewart, 1991). This is a 19-item self-report scale that measures functional support of the network. The survey explores how often four types of support are available when needed: emotional/information support, tangible support, affectionate support and positive social interaction. Each item has a five-response option, from 'none of the time' to 'all the time'. The MOSS has shown good internal consistency (α = .91 - .97), stability over time (r = .72 - .78) and validity (Sherbourne & Stewart, 1991). It has been used to explore social support in chronic conditions and in people with acquired brain injury (Hilari et al., 2003; Hilari & Northcott, 2006, 2017).

The subjective experience of social isolation was measured using the *Loneliness Scale* (UCLA, Russell et al., 1980). This is a 20 item self-report scale designed to measure the subjective feelings of loneliness and social isolation. Each item has a four-response option, from 'never' to 'often'. The UCLA scale has shown good internal consistency (α = .96) and stability over time (r = .73).

Two instruments were used to assess participants' mental health. Quality of life was explored using the *Quality of Life after Brain Injury* overall scale (QOLIBRI, von Steinbüchel et al., 2010). This scale captures people's level of satisfaction with different aspects of life after brain injury (e.g. physical condition, cognitive functioning, functionality, etc). This scale has six items that offer a four-response option, from 'Not at all' to 'Very'. The QOLIBRI scales meet standard psychometric criteria (internal consistency, = .81 to .91, test-retest reliability = .68 to .87) in a subgroup of participants with lower cognitive performance. The *Psychological Well-Being Scale* (Ryff, 1989; Véliz, 2012) was employed to assess levels of subjective well-being. This is a 39 item self-report scale with answers that offer six-response options, from 'totally agree' to 'totally disagree'. The scale has an overall score as well as specific scores for six sub-scales (Self-Acceptance, Positive Relationships, Environmental Mastery, Purpose in Life and Personal Growth). Higher scores suggest higher levels of well-being. The Ryff´s Scale has shown acceptable internal consistency (α = .54 - .79).

To explore mental health problems, two instruments were employed. The *Beck Anxiety Inventory* (BAI, Beck et al., 1988) was used to assess anxiety symptomatology. The BAI is a 21 item self-report scale, and each item has a four-response option, from 'Not at all' to 'Severely, it bothers me all the time'. The scale has shown good acceptability, internal consistency (α= 0.90) (de Beurs et al., 1997). Depressive symptoms were measured using the *Patient Health Questionnaire* (PHQ-9, Baader et al., 2012). This is a 9-item self-report scale that captures the presence of depressive symptoms during the last two weeks using DSM-IV criteria. Each item offers a four-response option, from 'Not at all' to 'Nearly every day'. PHQ-9 has shown a good sensitivity (88%) and a specificity (88%) for major depression (Kroenke, Spitzer and Williams, 2001).

2.3. Procedure

This study was approved by the Servicio de Salud Metropolitano Sur and the Diego Portales University Ethics Committees. Individuals with acquired brain injury were referred to participate in the study by rehabilitation professionals from outpatient clinics and community rehabilitation centers in Santiago, Chile. Data collection was carried out either at the Diego Portales University or in people's homes depending on their availability to travel, between March 2018 and December 2019. A team of six trained researchers assessed both patients and controls. The assessment was split into two sessions (2 hours each in a period of two weeks) for the brain injury group, in order to avoid fatigue. The control group carried out the assessment in one session. In the first session, the goal of the study was explained, and consent forms were signed. Demographic information as well as measures of structural and functional social isolation, were collected. The ACE-R and the ADDLQ-T were also administered during the first session. In the second session, participants completed loneliness and mental health questionnaires and were debriefed about the goals of the study.

2.4. Data Analysis

In order to answer question 1 (*Do individuals with acquired brain injury differ from matched healthy controls in measures of social isolation and mental health?*) differences and similarities between the HC and ABI groups were assessed in terms of size of the network (NETW total score); perceived functional support of the network (MOSS total score) and subjective experience of social isolation (UCLA total score). In relation to mental health, groups were compared in terms of quality of life (QOLIBRI total score), emotional well-being (RYFF total score), depressive (PHQ-9 total score) and anxiety symptoms (BAI total score). Three complementary statistical comparisons were carried to analyze data. Firstly, we aimed to compare the HC and ABI groups in each variable by assessing mean differences between groups, with a null model constructed by randomly permuting the HC-ABI pairs 10,000 times. For each permutation, and also for the non-permuted data, we computed the t-statistic associated with a two-sample t-test. The distribution of permuted t values corresponded to our null model, and we obtained a p-value by estimating the probability of obtaining the non-permuted t value, given our null distribution. Secondly, and complementing the first analysis, we estimated the effect size, computed as Hedges' g, a normalized difference of means, where $g = (m_{ABI} - m_{HC})/SD_{pooled}$. Using a bootstrap procedure of 10,000 iterations, we also estimated the 95% confidence intervals (CI_{bs}) of the estimated effect size (Hentschke & Stüttgen, 2011). Finally, we sought to estimate differences between the data distributions of each group, in some of the variables. For this purpose, we computed a two-sample Kolmogorov-Smirnov (KS) test, which uses a metric of probability distance between two empirical cumulative distribution functions (Pratt & Gibbons, 1981).

In order to answer question 2 (Do structural, functional and subjective components of social isolation relate to each other?), we estimated the relationship between our predictor variables (Fig. 1B NETW total score, MOSS total score and UCLA total score), by calculating the pairwise Spearman correlation coefficient matrix for them. We also tested for the significance of this measure and calculated an associated p-value.

In relation to question 3 (Which social isolation components predict mental health status and mental health problems?), we implemented multiple linear regressions using the following continuous regressors: NETW total score (structure), MOSS total score (functional support), and UCLA total score (subjective isolation/loneliness). In addition, we also used ABI/non ABI as a categorical regressor. We ran separate analyses for each target outcome variable (Fig. 1B): QOLIBRI and RYFF total scores for mental health and PHQ-9 and BAI total scores for mental health problems. For linear model calculations we used z-scored variables. We ran successive linear models in which we added, one by one, the variables we were interested in investigating their contribution to the outcomes. The sequence was: ABI, NETW, UCLA, MOSS. After introducing each predictor, we calculated a metric to assess how well the predictors accounted for the outcomes (i.e., goodness-of-fit). We used three different goodness-of-fit metrics (see Figure 3): the model's mean squared error (the difference between the model's prediction and the actual data), the model's Akaike information criterion (a measure of the difference between the number of estimated parameters in the model, and the maximum value of the likelihood function for the model), and the model's Coefficient of Determination (an estimate of the fraction of the outcome variance accounted for by the model). This provided us with a profile of the contribution of the introduction of each predictor to the complete linear model.

We ran diagnostic tests to check for collinearity in our predictors using procedures relying on the singular values of the predictors' matrix. These singular values are converted to 'condition indices', which are singular value ratios relative to the maximum singular value. The condition indices serve to estimate any dependencies between the columns of the predictors' matrix (Belsley et al., 1980). Using these diagnostics, we found no evidence of collinearity for the predictors' matrix X whose columns were NETW, UCLA, and MOSS.

To account for the potential sampling bias implied in our sample selection, we ran additional analyses using the entire set of control group data. This allowed us to assess how much larger or smaller the observed results might have been under various scenarios given by the selection of different control-group samples. We implemented a bootstrapping procedure of the total 80 control samples, randomly selecting, for each of 10,000 iterations, a subset of 51 samples to use as a match for the patients group. We thus obtained distributions of our statistical comparison measures (t-statistic, Kolmogorov-Smirnov statistic, Hedges' g), and compared them with the measures obtained from the matched control group. We found no significant differences between using the actual matched data group and selecting a different subset of control individuals, indicating that our findings are robust and not tied to specific features of the sample.

----------------------------------- insert here Fig. 1------------------------------

3. Results

3.1 Descriptive results

In general terms, compared to HC, individuals with ABI had significantly lower scores on measures of overall cognition.(ACE-R, ABI: *M* = 85; *SD* = 10.3; HC: *M* = 93.4; *SD* = 5; t(100) = 5.25; *p* < .001) and independence in activities of daily living (T-ADLQ, ABI, *M* = 28; *SD* = 18.1; HC, *M* = 6.2; *SD* = 8.36; t(100) = 8.17; *p* = <.001). They also exhibited lower levels of engagement in prosocial (SFS, ABI: *M* = 16.4; *SD* = 9.8; HC: *M* = 22.2; *SD* = 8.9; t(100) = 3.09; *p* = .003) and leisure activities(SFS, ABI: *M* = 13.5; *SD* = 5.3; HC: *M* = 19; *SD* = 5.5; t(100) = -5.00; *p* < .001) (See Figure 1C). Regarding the level of disability, most of the ABI sample (82%) was classified as moderate disability and good recovery (GOSE, *M* = 5.45; *SD* = 1,3; *min* = 3; *max* = 8; severe disability = 18%; moderate disability = 52%; good recovery = 30%).

3.2. Brain injury, social isolation and mental health results

In relation to question 1 (*Do individuals with ABI differ from matched healthy controls in measures of social isolation, wellbeing, quality of life and mental health problems?*), individuals with acquired brain injury did not differ from controls in terms of the total size of the network and functional support of the network. Marginally significant differences (*p* = .06, *g* = 0.38) were found in terms of loneliness (see Figure 2). As for mental health, people with acquired brain injury reported lower levels of overall quality of life, emotional wellbeing and higher levels of depressive symptomatology. No differences were found in relation to anxiety symptomatology (see Fig. 2 for participants' data from both groups and statistical comparisons among variable means and among distributions).

------------------------ insert here fig 2 -------------------

In relation to question 2 (*Do structural, functional and subjective components of social isolation relate to each other?*), we found that, for controls, there was a large inverse association between perception of social support (MOSS) and loneliness (UCLA) (see Table 1). A similar inverse association, of smaller size, was found in the ABI group. Interestingly, only in the ABI group a relationship (inverse) between size of the network and (NETW) and loneliness (UCLA) was found. The relationship between social support and network size did not appear significant for either group. Using a permutations test, we found no significant differences between the groups, regarding correlation coefficients (non-permuted t=-0.06; p=0.936; 10^4 permutations).

--------------insert here Table 1------------

Concerning question 3 (*Which social isolation components predict mental health status and mental health problems?*), we ran successive linear models in which we added, one by one, in the order suggested by our theoretical model (NETW, MOSS, UCLA), predictors we were interested in investigating their contribution to the observed outcome variables. To have a point of reference, we first ran the simplest model, usually called "constant", given by the mean of the outcome. After introducing each predictor, we calculated a metric assessing how well the predictors of the linear model account for outcome variables (see Figure 3). We performed this separately for each of the outcomes (QOLIBRI, PHQ, RYFF, BAI). This provided us with a 'goodness-of-fit' profile, for each outcome, of the contributions of each predictor to the complete linear model. In addition to the cumulative procedure depicted in Figure 3, in tables 2 to 5 we show the complete multivariate models for each of the four outcomes.

Using this procedure, we found that linear models explained between 10% to 40% of the variance of mental health (QOLIBRI and RYFF) and mental health problems (PHQ-9 and BAI) outcome variables in the ABI group (see Fig. 3). Interestingly, the same model explained a larger proportion of variance for all outcome variables in the healthy control group (18% to 58%). For the ABI group, the most important finding was that loneliness, or the subjective experience of social isolation (UCLA), was the only significant predictor for all mental health and mental health problems (see Table 2-5). Size of the network (NETW) and perceived social support (MOSS) did not contribute to explain the variance of outcome variables -with the exception of NETW for the RYFF. A similar trend is also evident for healthy controls, with loneliness (UCLA) as a predictor of quality of life, depressive and anxious symptomatology. Perceived social support (MOSS) was also a significant predictor of quality of life and emotional well-being in this group (see

Supplementary Materials). It is interesting to note that the predictive relationship between loneliness and quality of life is stronger for controls compared to brain injured participants, explaining 40% and 20% of the variance respectively. Finally, the total size of the network did not appear as a significant predictor of any of the mental health and mental health problems outcome variables in the ABI group or the healthy control group. These results were consistent across all goodness-of-fit metrics.

------------------------ insert here fig 3----------------------

Since brain injury was a categorical variable (i.e. we classified people into having a brain injury or not), we reasoned that perhaps this variable obscured functional heterogeneity amongst brain injury survivors, which could be relevant to explain mental health and mental health problems. Based on that assumption, we ran additional linear models, including level of functionality (T-ADLQ total score) as a predictor of the outcome variables. Results from this analysis did not support such an assumption, since the level of functionality did not significantly improve the models for any of the outcomes.

-------------insert here Tables 2 to 5------------

4. Discussion

The main goal of this study was to explore the relationship between structural, functional and subjective components of social isolation with mental health and mental health problems in a sample of chronic brain injury survivors. Data from this study shows that people with brain injury do not differ from matched healthy controls in terms of perceived social support and size of the network but exhibit marginally significant differences in levels of loneliness. In relation to mental health, brain injured survivors presented lower levels of emotional wellbeing and quality of life, as well as higher levels of depression. It was also found, both in controls and patients, that the perception of social support was inversely related to the subjective experience of loneliness. An inverse relationship between size of the network and loneliness was found significant in the ABI group. Surprisingly, only the subjective experience of social isolation predicted changes in quality of life, emotional well-being, depression and anxiety. For the control group, both loneliness and perceived social support predicted levels of mental health and mental health problems.

4.1 Mental Health after Brain Injury

Our data is consistent with studies that have described a high prevalence of depression (eg. Arwert et al., 2018; Burvill et al., 1995; Scholten et al., 2016), as well as lower levels of quality of life (Dijkers, 2004; Haley et al., 2011) and emotional well-being (eg.

Clarke, Marshall, Black & Colantonio; Paine et al., 2018), in ABI survivors during the chronic phase. However, this paper is the first to systematically explore the relationship between social isolation variables and mental health in the ABI population. The main finding -loneliness as a key predictor of mental health- is consistent with data from large studies with normotypical subjects which have described loneliness as a risk factor for mental health problems (e.g. Beutel et al., 2017; Cacioppo et al., 2006). There are two obvious clinical implications of these findings. The first one is the need to include loneliness as a variable that is explored during neuropsychological assessments. This will require developing a model of loneliness after brain injury, considering the particular characteristics and challenges of our population. In terms of therapeutics, targeting loneliness will require a paradigm shift for rehabilitation teams, moving from interventions that focus on the individual (e.g. decrease in symptomatology, optimizing positive emotions and strengths) towards interventions that focus on relations and social integration (e.g. relationship continuity, social identity continuity and sense of belonging).

4.2. A model of social isolation: similarities and differences between people with and without brain injury.

A main difficulty in building a model for social isolation after brain injury resides in the lack of studies directly exploring social isolation components. This problem has been stressed in the review by Northcott and colleagues (2015), where authors report no studies using social support, network size or loneliness as dependent variables, as well as no evidence of associations between these variables. Results from our second research question contribute directly to this gap, suggesting that the relationship between social isolation components considered in our model presents commonalities and differences between people with and without brain injury.

A common finding across groups was that individuals who scored higher in perceived social support reported lower levels of loneliness. This finding is consistent with data from a large study (*n* = 755) exploring social isolation in people with chronic conditions, where also a negative association between loneliness and family support was reported (-.37) (Tomaka et al., 2006). In a study with community dwelling TBI survivors McLean and colleagues (2014) reported a similar pattern, with lower levels of loneliness associated with higher levels of perceived social support. There is one study, however, with a contrasting finding. Hagger & Riley (2017), in a sample of 65 individuals with ABI, reported no association between loneliness (measured by the UCLA-LS) and social support (ESSQ, Hagger & Riley, 2017). However, the social support scale used by the authors was not a validated instrument. It is interesting to note that in our sample the association between social support and loneliness was smaller for the ABI group compared to healthy controls. Future studies should look for variables that may moderate this relationship and explain differences between people with and without brain injury in the strength of the relationship between social support and loneliness.

Another relevant finding, also observed across groups, is the lack of association between size of the network and perceived social support. In our study, individuals with ABI and controls did not differ in measures of social support and size of the network, suggesting that these variables do not change after the injury. Evidence regarding changes in network size after brain injury is inconclusive, with studies suggesting both a decrease in the number of contacts (Northcott et al., 2015; Northcott et al., 2016; Temkin et al., 2009) as well as a maintenance of them (e.g. Rigon et al., 2018). In terms of social support, studies have reported that after a stroke, survivors perceive themselves as well supported and that such perception is stable over time (Hilari and Northcott, 2006; Hilari et al., 2003; 2010; King, 1996; Knapp & Hewison, 1998; Tsouna-Hadjis et al., 2000; King et al., 2002). We are aware of one study that has reported an association between size of the network and social support (.23) in a sample of individuals with chronic aphasia (Hilari & Northcott, 2006).

Finally, a significant inverse relationship between size of the network and loneliness was observed only in the ABI group, suggesting that brain injury survivors with smaller networks reported higher levels of loneliness. These data are consistent with evidence from a study by Rigon and colleagues (2018), who also reported a large negative association (-.53) between size of the network (National Social Life Health and Aging Project Social Network Module) and loneliness (UCLA) in a sample of 24 TBI survivors. Interestingly, and similar to our data, such association was not found in the HC group. The authors pointed at evidence from other studies with similar findings (Stokes, 1985), and interpreted their data in terms of how ABI survivors are forced to relate to a smaller social network, even though that may not be their choice. In contrast, HCs with smaller social networks may voluntarily choose them and don't attach any negative meaning to them. Many interventions, aiming at increasing the size of the social network after brain injury, appear to be based on this negative relationship (see below for a discussion on this point).

4.3. We need a theory of loneliness after brain injury in order to develop therapeutic interventions.

A main clinical implication of this study is that neuropsychological rehabilitation efforts should aim at reducing loneliness, in order to improve mental health in brain injured survivors (Cruice et al, 2003). In the ABI group loneliness was a significant predictor of quality of life, emotional wellbeing, depression and anxiety. However, loneliness is rarely addressed as a problem in rehabilitation -compared to other commonly reported issues, such as cognitive or emotional impairments. If we look, for example, into the International Handbook in Neuropsychological Rehabilitation (Wilson, Winegardener, Van Heughten & Ownsworth, 2017), the word loneliness only appears six times and never as a topic on its own. This clearly reveals a paradox. We know that loneliness is a common problem after brain injury, particularly during the chronic phase. However, we rarely measure it when initiating a rehabilitation process, and the number of interventions specifically developed to target loneliness is scarce (see below).

This gap in the literature, and practice, means that future studies should focus on developing a model of loneliness after brain injury. To our knowledge there are three complementary hypotheses suggesting cognitive, socio-emotional and interpersonal factors relevant to understand loneliness after brain damage. However, they have not been systematically tested yet. It has been proposed that certain cognitive abilities (particularly executive skills) may be relevant to perceive loneliness (Cristofori et al., 2019). Other authors have gathered data suggesting that the tendency to experience negative affect after brain injury influences how survivors interpret social situations (Rigon et al., 2018). Finally, it has also been proposed that loneliness is associated with the concealment of information about the injury during interpersonal exchanges, in order to avoid anticipatory and internalized stigma (Hagger & Riley, 2017).

It will be useful as well to consider and adapt theoretical models of loneliness from outside the field of Neuropsychology, such as the Re-affiliation Motive (RAM, Qualter et al., 2015). This model is based on the Evolutionary Theory of Loneliness (Cacioppo & Patrick, 2008) and describes the sub-processes involved in searching for social connection when feeling lonely -also known as the re-affiliation process (perception of social isolation, behavioral activation, cognitive assessment of a social situation and behavior regulation). It is likely that people with diverse profiles of cognitive, socio-emotional and behavioral difficulties will be differentially compromised in some of these sub-processes, thus struggling to reconnect with others. Finally, and in order to develop a model of loneliness after brain injury, a mixed methods approach will be needed, using both quantitative and qualitative sources of information, including data from the brain injured survivor, caregivers, friends and extended network members (see Network Mapping Approach; Leonard, Horsfall & Noonan, 2015).

As noted above, there is also an important gap in the literature regarding *formal* interventions that directly address loneliness after brain injury. We stress this point since loneliness has traditionally been targeted by *informal* rehabilitation - drop-in groups, or peer support groups. However, there is little research on this matter (see Salas et al., 2020). There is some evidence suggesting that enlarging the social network via group interventions can contribute to decreasing loneliness/social isolation (Northcott et al., 2016; Rowlands, 2002; Vickers, 2010; Wade, 2003). In fact, our data shows that network size is inversely associated with levels of loneliness, thus, supporting this line of intervention. This idea has, nevertheless, been debated by some authors, who propose that enlarging the social network is not enough since survivors may need support in learning to see their social network positively. For example, the study by Rigon and colleagues (2018) reported that, in a sample of people with TBI, neuroticism (the tendency to experience negative affect) moderated the inverse relationship between size of the network and loneliness. In other words, brain injury survivors that tend to experience feelings of anxiety, worry, fear or anger may still feel lonely despite having a large social network. This view is consistent with studies that have found evidence relating high positive affect and low negative affect to the frequency of social participation and satisfaction with social participation (Juengst et al., 2014).

Other authors have stressed the need to visibilize and target interpersonal factors that contribute to social isolation (eg. stigma, concealment). As noted by studies exploring the Stress Buffering Hypothesis, in order to be beneficial to mental health, social interaction must match the individual's needs (Swift & Wright, 2000).That is not always the case after brain injury. There is a growing awareness in neuropsychological rehabilitation that social encounters can also be a source of stress, compromising identity reconstruction and emotional well-being (e.g. Hagger and Riley, 2017; Nochi, 1998). In conclusion, interventions that target social isolation should not only focus on expanding the social network, but also addressing individual difficulties in positively perceiving social interaction as well as educating the general public to modify misconceptions about brain injury. The consideration of these elements is a promising starting point in developing theoretically driven interventions to reduce loneliness and social isolation.

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Table 1. Correlation Table of Social Isolation Variables in Acquired Brain Injury and Control Groups

Variable	Control Group			ABI Group		
	NETW	UCLA	MOSS	NETW	UCLA	MOSS
1. NETW	--	-0.19	0.19	--	-0.28*	0.25
2. UCLA		--	-0.49**		--	-0.38**
3. MOSS			--			--

*p < .05. **p < .01.

Table 2. Results of multivariate linear model for predicting QOLIBRI in the ABI group (n=51)

	β	SE β	t	p
(Intercept)	-0.438	0.123	-3.567	0.001
NETW	-0.020	0.120	-0.164	0.871
UCLA	-0.437	0.129	-3.396	0.001
MOSS	0.054	0.119	0.456	0.650

Root Mean Squared Error: 0.861

R-squared: 0.25, Adjusted R-Squared: 0.202

F-statistic vs. constant model: 5.23, p-value = 0.00339

Abbreviations: β: Linear model coefficient; SE: Standard Error; t: value of the t-statistic; p:p-value; NETW: Social Network Map; UCLA: Loneliness Scale; MOSS: Medical Outcome Study Social Support Survey

Table 3. Results of multivariate linear model for predicting RYFF in the ABI group (n=51)

	β	SE β	t	p
(Intercept)	-0.239	0.109	-2.180	0.034
NETW	0.126	0.107	1.179	0.244
UCLA	-0.582	0.115	-5.070	<0.001
MOSS	0.046	0.106	0.439	0.662

Root Mean Squared Error: 0.767

R-squared: 0.46, Adjusted R-Squared: 0.425

F-statistic vs. constant model: 13.3, p-value < 0.01

Abbreviations: β: Linear model coefficient; SE: Standard Error; t: value of the t-statistic; p:p-value; NETW: Social Network Map; UCLA: Loneliness Scale; MOSS: Medical Outcome Study Social Support Survey

Table 4. Results of multivariate linear model for predicting PHQ-9 in the ABI group (n=51)

	β	SE β	t	p
(Intercept)	0.193	0.120	1.613	0.114
NETW	-0.006	0.117	-0.050	0.960
UCLA	0.637	0.125	5.078	<0.01
MOSS	-0.163	0.116	-1.406	0.166

Root Mean Squared Error: 0.839

R-squared: 0.468, Adjusted R-Squared: 0.434

F-statistic vs. constant model: 13.8, p-value <0.001

Abbreviations: β: Linear model coefficient; SE: Standard Error; t: value of the t-statistic; p:p-value; NETW: Social Network Map; UCLA: Loneliness Scale; MOSS: Medical Outcome Study Social Support Survey

Table 5. Results of multivariate linear models for predicting BAI in the ABI group (n=51)

	β	SE β	t	p
(Intercept)	0.109	0.145	0.748	0.458
NETW	0.210	0.142	1.479	0.146
UCLA	0.320	0.152	2.103	0.041
MOSS	-0.151	0.140	-1.074	0.288

Root Mean Squared Error: 1.02

R-squared: 0.155, Adjusted R-Squared: 0.101

F-statistic vs. constant model: 2.87, p-value = 0.046

Abbreviations: β: Linear model coefficient; SE: Standard Error; t: value of the t-statistic; p:p-value; NETW: Social Network Map; UCLA: Loneliness Scale; MOSS: Medical Outcome Study Social Support Survey

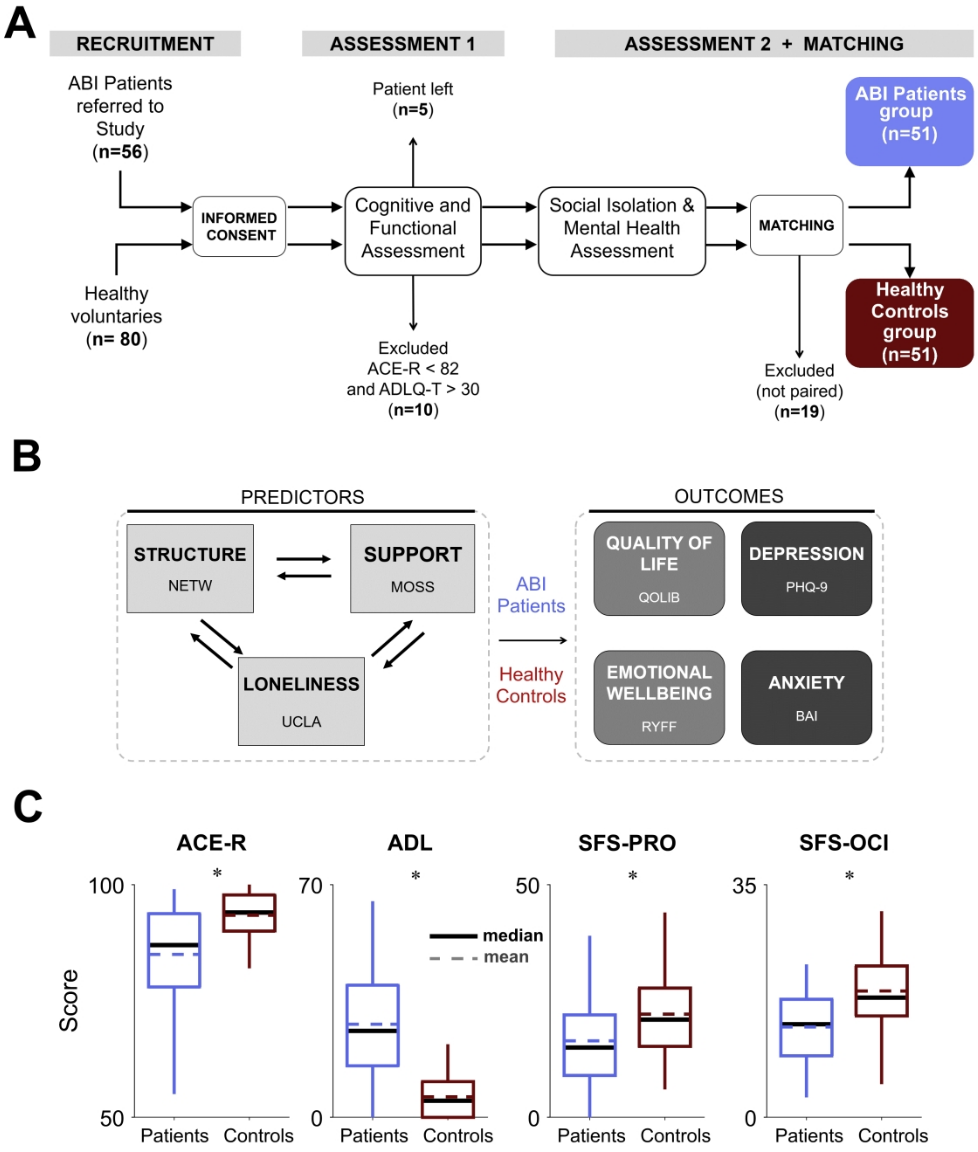

Figure 1. Overview of the study. A. Recruitment process, assessment of participants and matching between patients and controls. B. Conceptual map of predictors and outcomes of the study. The relationship between predictors was explored in question 2 and the relationship between predictors and outcomes in question 3. C.Comparison between patients and controls in terms of overall cognitive functioning (ACE-R), level of independence (ADLQ-T), engagement in pro-social (SFS-PRO) and leisure activities (SFS-OCI).

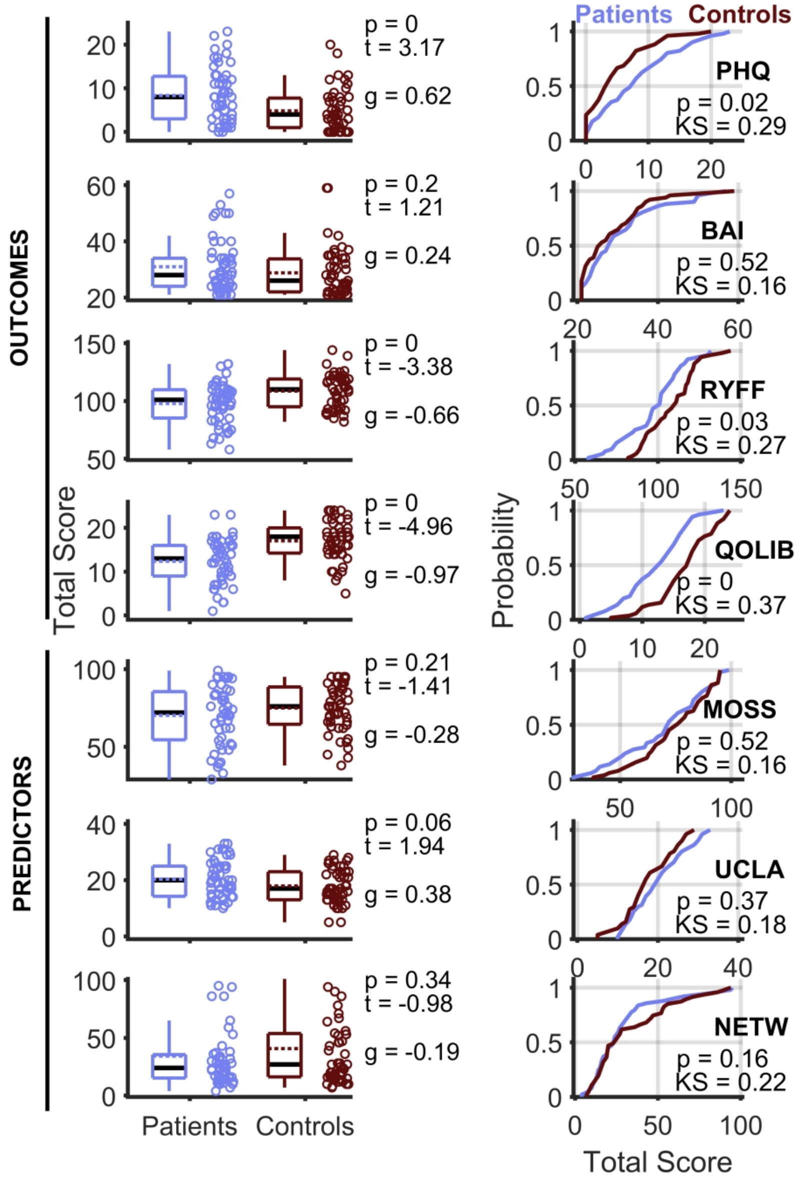

Figure 2. Comparisons among patients and control across the variables of the study. Each row of plots corresponds to the results from a given variable. Left-side plots present the distribution of the variable as boxplots and as a jittered scatterplot, where each dot corresponds to one participant. Patients are shown in blue and controls in red. Right side plots present the data as the empirical cumulative distribution of each variable, for both patients and controls. For example, for RYFF, the point at which the y-axis equals 0.5, in the patients' curve this corresponds to a score of 100. This indicates that 50% of patients have a score of 100 or less, while 50% of controls have a score of 120 or less.

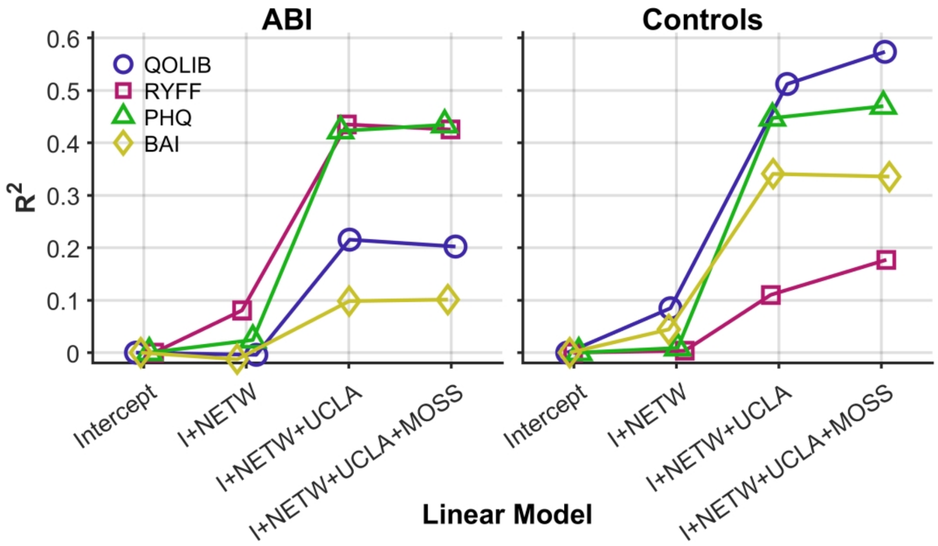

Figure 3. Goodness-of-fit (R2) profiles of Linear Models (cumulative). The plots show the R2 obtained as a function of the summative inclusion of each predictor in the model. R2 is an estimate of the proportion of total variance in the outcome variable accounted for by the inclusion of predictors. The value for the right-most predictor (MOSS) corresponds to the value obtained by including all predictors or the total model. Left: results for the ABI group. Right: results for the healthy control group.

SUPPLEMENTARY MATERIAL

Table 1. Results of multivariate linear model for predicting QOLIBRI Healthy Control Group (n=51)

	β	SE β	t	p
(Intercept)	0.206	0.081	2.535	0.014
NETW	0.142	0.076	1.874	0.067
UCLA	-0.484	0.093	-5.198	< 0.001
MOSS	0.277	0.098	2.811	0.007

Root Mean Squared Error: 0.562

R-squared: 0.599, Adjusted R-Squared: 0.574

F-statistic vs. constant model: 23.4, p < 0.001

Table. Results of multivariate linear model for predicting RYFF Healthy Control Group (n=51)

	β	SE β	t	p
(Intercept)	0.156	0.109	1.425	0.161
NETW	0.047	0.102	0.458	0.649
UCLA	-0.19	0.126	-1.513	0.137
MOSS	0.294	0.133	2.214	0.032

Root Mean Squared Error: 0.758

R-squared: 0.226, Adjusted R-Squared: 0.177

F-statistic vs. constant model: 4.59, p = 0.007

Table. Results of multivariate linear model for predicting PHQ-9 Healthy Control Group (n=51)

	β	SE β	t	p
(Intercept)	-0.150	0.089	-1.676	0.100
NETW	-0.026	0.083	-0.313	0.755
UCLA	0.520	0.102	5.074	< 0.001
MOSS	-0.189	0.108	-1.748	0.087

Root Mean Squared Error: 0.618

R-squared: 0.502, Adjusted R-Squared: 0.47

F-statistic vs. constant model: 15.8, p < 0.001

Table. Results of multivariate linear model for predicting BAI Healthy Control Group (n=51)

	β	SE β	t	p
(Intercept)	0.067	0.116	0.574	0.569
NETW	-0.134	0.109	-1.231	0.224
UCLA	0.531	0.133	3.981	< 0.001
MOSS	-0.111	0.141	-0.789	0.434

Root Mean Squared Error: 0.805

R-squared: 0.375, Adjusted R-Squared: 0.336

F-statistic vs. constant model: 9.42, p < 0.001