Routledge
Taylor & Francis Group

Journal of Clinical and Experimental Neuropsychology

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ncen20

Depression symptoms in neurological patients: A survey of a large cohort of patients with focal brain lesions

Emma M. Brandt, Nicholas T. Trapp, Aaron D. Boes & Daniel Tranel

To cite this article: Emma M. Brandt, Nicholas T. Trapp, Aaron D. Boes & Daniel Tranel (2022) Depression symptoms in neurological patients: A survey of a large cohort of patients with focal brain lesions, Journal of Clinical and Experimental Neuropsychology, 44:7, 499-513, DOI: 10.1080/13803395.2022.2123896

To link to this article: https://doi.org/10.1080/13803395.2022.2123896

JOURNAL OF CLINICAL AND EXPERIMENTAL NEUROPSYCHOLOGY
2022, VOL. 44, NO. 7, 499–513
https://doi.org/10.1080/13803395.2022.2123896

Depression symptoms in neurological patients: A survey of a large cohort of patients with focal brain lesions

Emma M. Brandt[a], Nicholas T. Trapp[b], Aaron D. Boes[c] and Daniel Tranel[a,c]

[a]Department of Psychological and Brain Sciences, University of Iowa, Iowa City, Iowa, USA; [b]Department of Psychiatry, University of Iowa, Iowa City, Iowa, USA; [c]Department of Neurology, University of Iowa, Iowa City, Iowa, USA

ABSTRACT

Introduction: Examining depression following neurological injury is useful for understanding post-lesion depression and depression more generally. The extant literature shows variability in the incidence and severity of depression post-lesion, likely due to heterogeneity in study methodology, patient samples, measures of depression, and time of assessment. Here, we aim to characterize depression symptoms and their demographic correlates in a large sample of individuals in the chronic epoch following a focal brain lesion.

Method: We sampled 492 individuals who had focal, stable brain lesions and were in the chronic epoch (≥3 months post-onset). Demographic (gender, years of education), temporal (age at lesion onset, time since lesion onset), and lesion (lesion laterality, lesion etiology, lesion volume) factors were used to predict depression symptoms measured by the Beck Depression Inventory (BDI).

Results: We found that on average, neurological patients exhibited elevated levels of depression symptoms (although not clinically significant) relative to a community sample, and the neurological patients showed higher rates of mild and moderate depression symptoms than are typical in a community sample. Gender and lesion etiology were predictive of depression symptoms, whereby women and patients with ischemic stroke had higher levels of depression symptoms.

Conclusions: Our results suggest that depression symptom severity may be elevated following a focal brain lesion. Moreover, some individuals may be more likely to develop depression symptoms post-lesion than others. This may be mediated by individual factors such as gender and lesion etiology. The findings have important implications for the diagnosis, prognosis, and treatment of depression in neurological patients.

ARTICLE HISTORY
Received 24 February 2022
Accepted 7 September 2022

KEYWORDS
Depression; lesion; BDI; poststroke depression; neurological outcomes

It would not be surprising for someone to develop elevated depression symptoms after suffering a major neurological event that led to permanent brain injury. However, the extant literature reports a wide range of incidence rates for depression post-lesion, likely due to variability in study design (Espárrago Llorca et al., 2015). Additionally, although there is an extensive body of literature examining poststroke depression (PSD), there is less research on depression symptoms following other neurological events leading to focal brain lesions (such as tumor resection and focal contusion). Understanding the incidence of depression symptoms and identifying individual factors that predict elevated depression symptoms post-lesion could aid in the diagnosis, prognosis, and treatment of depression in neurological patients. Thus, the current research aims to survey depression symptoms in neurological patients with focal, stable brain lesions in the chronic epoch (≥ 3 months post-lesion onset) and examine the individual characteristics that predict the severity of depression symptoms in these patients.

Of note, a distinction is often made between depression symptoms and a formal diagnosis of a depressive disorder under conventional diagnostic rubrics, such as Major Depressive Disorder as outlined in the Diagnostic and Statistical Manual of Mental Disorders (DSM; American Psychiatric Association, 2013). Depression symptoms are typically measured by self-report measures whereas depressive disorders are assessed via structured or semi-structured interviews to ensure that formal diagnostic criteria are met. Individuals who endorse symptoms of depression on a self-report measure may or may not meet diagnostic criteria for a depressive disorder. In our review of the literature, we use PSD to refer to both depression symptoms and diagnoses, and we specify what assessment techniques were used where applicable. That said, we want to be clear that the focus of the present study is on depression

CONTACT Emma M. Brandt emma-brandt@uiowa.edu Department of Psychological and Brain Sciences, University of Iowa, G60 PBSB, 340 Iowa Ave, Iowa City, IA 52242, USA

symptoms, and we did not include any assessment of formal diagnostic criteria for depressive disorders.

Incidence of depression following brain lesion

Depression following focal brain lesion has been most widely studied in patients with stroke. However, the incidence of PSD varies substantially from study to study. One meta-analysis of PSD found the incidence of minor depression to range from 9% in community-based settings to 23.9% in outpatient samples and the incidence of major depression to range from 14% in community-based settings to 24% in outpatient samples using DSM-IV diagnostic criteria (Robinson & Spalletta, 2010). Another meta-analysis found the incidence of PSD to be 31% in a pool of studies including patients with various stroke etiologies measuring depression in both the acute and chronic epochs using different interview and self-report measures of depression (Hackett & Pickles, 2014). In this meta-analysis, the lowest estimate of PSD incidence was 5% in a sample of patients with ischemic or hemorrhagic stroke evaluated for depression two to 5 days post-stroke using the Hospital Anxiety Depression Scale (Townend et al., 2007). The highest estimate of PSD incidence was 84% in a sample of patients 3 months post-ischemic stroke evaluated using the Patient Health Questionnaire – 9-Item Version (Bar et al., 2009). The variability in incidence of PSD is likely due to methodological differences in studies, such as diagnostic criteria for depression, scales used to measure depression, inclusion criteria for patients, and the setting in which patients are examined (Espárrago Llorca et al., 2015). This variability could also be explained by the fact that rates of PSD may increase during the first year poststroke and then decrease after the first year, but longitudinal research on PSD is sparse and does not show consistent findings (Ayerbe et al., 2013).

Similar to studies of stroke, there has not been a clear association between brain tumor resection and the onset of depression or its severity (Keng et al., 2020). Estimates for the rates of depression following tumor resection are around 16–18% for both acute and chronic epochs, although few data are available for the incidence of depression between one-month and one-year post-surgery (Keng et al., 2020).

Although there is an extensive body of literature looking at depression symptoms following traumatic brain injury, previous work has not focused on the incidence of depression following focal contusion (i.e., brain injury isolated to one part of the brain as opposed to more diffuse, non-focal damage). Thus, our work adds to the literature on this etiology of focal brain lesion (focal contusion).

Predictors of depression following brain lesion

Knowing what factors are associated with higher rates of depression following focal brain lesion could aid in early diagnosis, treatment, and possibly even prevention of these symptoms. However, the extant literature is equivocal as to what factors are potential predictors of depression. Many studies have found women to have higher levels of depression symptoms post-brain lesion than men (Haghgoo et al., 2013; Keng et al., 2020; Nazarinasab et al., 2018; Robinson & Jorge, 2016; White et al., 2011). However, other studies have failed to find any association between post-lesion depression symptoms and gender (Przewoźnik et al., 2015; Robinson & Jorge, 2016). Years of education has not been found to be associated with PSD (Angeleri et al., 1997; Nazarinasab et al., 2018; Przewoźnik et al., 2015), but there is some evidence that lower education is associated with higher prevalence of depression following tumor resection (Keng et al., 2020). Studies have generally not found age to be associated with PSD (Nazarinasab et al., 2018; Przewoźnik et al., 2015; Robinson & Jorge, 2016); however, one study did find older age to be associated with lower rates of PSD (White et al., 2011) and some studies have found longer time since stroke to be associated with higher incidence of PSD (Eastwood et al., 1989) and greater depression symptom severity (Nazarinasab et al., 2018).

Studies of lesion laterality and depression are mixed with some evidence for an association between left lateralized stroke and worse depression symptoms (Nazarinasab et al., 2018; Robinson & Jorge, 2016), some evidence for an association between right lateralized lesion and worse depression symptoms (Tranel et al., 2002), and other studies failing to find an association between depression and lesion laterality (Angeleri et al., 1997; Irle et al., 1994; Przewoźnik et al., 2015). Some studies have suggested that lesion volume may influence the onset of PSD with larger lesions being more strongly associated with depression than smaller lesions (Norrving, 2003; Sharpe et al., 1990, 1994). Likewise, some research on mood changes following tumor resection surgery shows a positive association between negative mood and lesion size (Irle et al., 1994). To our knowledge, no previous studies have looked at the effect of lesion etiology on depression symptoms. However, examining this could help us broaden our understanding of depression symptoms following a neurological event.

Present study

In the current study, we aimed to broaden understanding of depression symptoms in neurological patients by characterizing depression symptom severity in a large sample of individuals in the chronic epoch (≥ 3 months post-lesion onset) following varied neurological events leading to a focal brain lesion. Given that previous literature on poststroke depression and depression following tumor resection suggests that gender, years of education, age at lesion onset, time since lesion onset, lesion laterality, and lesion volume may be predictive of depression symptoms post-lesion, we also examined whether these factors were predictive of depression symptoms in our sample. Additionally, we examined the predictive power of lesion etiology as our sample had more heterogeneous lesion etiologies than previous studies of post-lesion depression.

We report Beck Depression Inventory (BDI) data on 492 neurological patients with focal, stable brain lesions. The BDI data were from the chronic epoch (≥ 3 months post onset). We compared our findings to the findings from a survey of a large community sample with similar demographics to the sample reported here (Segal et al., 2008). Segal et al. (2008) examined psychometric properties of the BDI in older and younger adults recruited from the community. Thus, their study provided helpful information on BDI scores in a normative sample, to which we could compare our results. This was utilized purely to provide context for the results reported here, and we did not have any a priori predictions about how our results would compare to those found in the Segal et al. (2008) study. We also examined several individual characteristics as predictors of depression symptoms following neurological event. The study was designed as a survey, and not as a hypothesis-driven investigation.

Materials and methods

Participants

Participants were 492 individuals from the Patient Registry of the Division of Neuropsychology and Cognitive Neuroscience at the University of Iowa Department of Neurology. All participants were adults with stable, focal brain lesions and were studied in the chronic epoch (≥ 3 months post-lesion onset). Patients are considered to be in the chronic (as opposed to acute) epoch following lesion onset when they reach the point at which the majority of recovery has occurred, generally agreed to be around 3 months following lesion onset (Wade et al., 1985). Although some participants had pediatric-onset brain lesions, all depression symptom data were collected from participants over the age of 18. Exclusion criteria included a history of significant alcohol or substance abuse as substance abuse history can cause cognitive and behavioral changes prior to lesion onset, which would make it more difficult to interpret cognitive and behavioral changes due to acquired focal lesion. Exclusion criteria also included significant psychiatric disorder prior to the brain lesion. Importantly, none of the patients had a diagnosis of Major Depressive Disorder or Persistent Depressive Disorder prior to lesion onset, which was determined by review of patient medical records. Finally, individuals with another neurologic disorder unrelated to the lesion were excluded as it is difficult to interpret lesion–deficit relationships if there are multiple lesions. We did not include patients from our Patient Registry who had undergone resection surgery for epilepsy to avoid confounding effects of the "lesion" in such patients being a positive intervention designed to improve the patients' primary neurological disorder (epilepsy), and previous work has demonstrated that mood disorders are highly comorbid with epilepsy (Kanner, 2003). Demographic and lesion information for participants is presented in Table 1. All participants completed informed consent and all procedures were approved by the University of Iowa Institutional Review Board.

Measures

Participants completed the Beck Depression Inventory (BDI) as part of the standard neuropsychological testing protocol of the Benton Neuropsychology Laboratory (Tranel, 2019). The BDI is a 21-item self-report measure designed to assess recent depression symptoms (A. T. Beck et al., 1996a). Scores range from 0 to 63. According to the BDI manual, scores of 0 to 13 indicate "minimal" depression symptoms, scores of 14 to 19 indicate "mild" depression symptoms, scores of 20 to 28 indicate "moderate" depression symptoms, and scores of 29 to 63 indicate "severe" depression symptoms. The BDI is designed to assess emotional, cognitive, and somatic symptoms of depression and has been shown to be highly reliable and valid (Wang & Gorenstein, 2013). In our study, some participants completed the original version, BDI-I (n = 156) and some participants completed the second version, BDI-II (n = 336). A.T. Beck et al. (1996b) have shown that total scores on the two versions are highly correlated (r = .93); however, scores on the BDI-II tend to be significantly (albeit numerically only slightly) higher than scores on the BDI-I. To facilitate comparison across different versions of the BDI, items were analyzed for consistency. In total, three items were identified as inconsistent across versions (Table 2). For each of these three items, the mean item score for

Table 1. Demographic and lesion information.

Women	245 (49.8%)		
Men	247 (50.2%)		
Ischemic stroke	217 (44.1%)		
Hemorrhagic stroke	77 (15.7%)		
Subarachnoid hemorrhage	25 (5.1%)		
Benign tumor resection	61 (12.4%)		
Other resection	27 (5.5%)		
Focal contusion	17 (3.5%)		
Other etiology	13 (2.6%)		
Multiple etiologies	55 (11.2%)		
Right lateralized lesion	195 (39.6%)		
Left lateralized lesion	210 (42.7%)		
Bilateral lesion	87 (17.7%)		
	M	SD	range
Years of Education	13.50	2.47	8–20
Current age	51.00	15.00	18–93
Age at lesion onset	47.00	17.00	0–79
Time since lesion onset (years)	3.73	6.82	0.25–50.63
Lesion Volume (mm^3)	43,042	70,615	110–772,186

Values represent n (%) for gender, lesion etiology, and lesion laterality. Means (M), standard deviations (SD), and ranges are provided for years of education, age at lesion onset, time since lesion onset, and lesion volume. Lesion etiologies for individuals in "Other" category are as follows: Herpes simplex encephalitis (n = 8), limbic encephalitis (n = 2), Urbach-Wiethe disease (n = 1), cyst (n = 1), cryptogenic frontal lesion (n = 1).

participants who completed the BDI-II was calculated. We then replaced the corresponding item scores with each of the mean scores for participants who completed the BDI-I. Analyses were also conducted on the different versions of the BDI separately. Note that for purposes of exposition, we will use "BDI" to refer to the Beck instrument generally, and we will specify which version (I or II) when necessary. Additionally, some individuals completed the BDI more than once in the chronic epoch. For these patients, we used the first BDI score available in the chronic epoch in our main analyses. We also conducted an exploratory analysis examining BDI scores at two different time points in the subset of patients who had more than one chronic BDI score available.

Procedures

Each participant completed a research-quality structural imaging scan including T1 and T2 sequences on MRI. For research MRIs acquired after year 2000 (n = 331), T1 and T2-weighted sequences were acquired on a 3.0 T GE Discovery 750 W MRI Scanner with a 32 channel head coil. A set of 242 slices were acquired in the coronal plane at 1 mm isotropic resolution using the following protocol: Cor-FSPGR BRAVO, TE maximum, TR 3200, echo train length 140, FOV 25.6 cm, 256 × 256 mm matrix with interleaved slice order. Older scans from 2000 and prior (n = 161) were described previously (Fiez et al., 2000; Tranel et al., 1988). We included lesion volume and laterality as potential predictors of depression symptom severity. Lesion volume was derived from a manually segmented lesion mask, which is a three-dimensional representation of the lesion location in MNI152 space. Lesion laterality was ascertained by determining whether the lesion mask overlapped with the left or right hemisphere, or both. Lesion tracing methods are described in more detail elsewhere (see Bowren et al., 2020).

Statistical analysis

Statistical analyses were performed using SPSS version 27. Hierarchical multiple linear regression was used to predict BDI score from demographic variables (gender and years of education), temporal variables (age at lesion onset and time since lesion onset), and lesion variables (lesion etiology, lesion laterality, and lesion volume). The effects of each set were examined while controlling for the other two sets. Within each set (demographic, temporal, and lesion), we examined all two-way interaction effects (gender x years of education, age at lesion onset x time since lesion onset, lesion etiology x lesion laterality, lesion etiology x lesion volume, lesion laterality x lesion volume). A repeated-measures ANOVA was used to determine whether there was any significant change in BDI score over time. Because patients had varied intervals of time between testing sessions (M = 3.89 years, SD = 3.93; median = 2.38 years; range = 0.13–17.50 years), we controlled for time between administrations of the BDI in our analyses.

Table 2. BDI-I and BDI-II item reconciliation.

BDI-I Item Number	BDI-II Item Number	Assessment of Similarity	Adjustment Made
1 – Sadness	1 – Sadness	Identical	Included
2 – Pessimism	2 – Pessimism	Similar	Included
3 – Past Failure	3 – Past Failure	Almost Identical	Included
4 – Loss of Pleasure	4 – Loss of Pleasure	Similar	Included
5 – Guilty Feelings	5 – Guilty Feelings	Almost Identical	Included
6 – Punishment Feelings	6 – Punishment Feelings	Identical	Included
7 – Self-Dislike	7 – Self-Dislike	Similar	Included
8 – Self-Criticalness	8 – Self-Criticalness	Similar	Included
9 – Suicidal Thoughts/Wishes	9 – Suicidal Thoughts/Wishes	Identical	Included
10 – Crying	10 – Crying	Similar	Included
11 – Irritability	17 – Irritability	Similar except "2" and "3" values	If "3" value on BDI-I, changed to "0," and if "2" value on BDI-I, changed to "3" to align with BDI-II
12 – Loss of Interest	12 – Loss of Interest	Similar	Included
13 – Indecisiveness	13 – Indecisiveness	Almost Identical	Included
14 – Appearance	*14 – Worthlessness*	*Different*	*Mean BDI-II item score imputed*
15 – Loss of Energy	15 – Loss of Energy	Similar	Included
16 – Changes in Sleep Pattern	16 – Changes in Sleep Pattern	Similar	Included
17 – Tiredness or Fatigue	20 – Tiredness or Fatigue	Similar	Included
18 – Changes in Appetite	18 – Changes in Appetite	Similar	Included
19 – Weight Loss	*19 – Concentration Difficulty*	*Different*	*Mean BDI-II item score imputed*
20 – Somatic Worry	*11 – Agitation*	*Different*	*Mean BDI-II item score imputed*
21 – Loss of Interest in Sex	21 – Loss of Interest in Sex	Identical	Included

BDI items from each version of the scale were collapsed as described in the table. For items unique to the BDI-I, mean item scores were calculated for the corresponding BDI-II item and imputed for individuals who completed the BDI-I. Then total BDI scores were calculated by summing across items.

Results

Demographic data are presented in Table 1. BDI information for the entire sample (N = 492) is provided in Table 3. The overall mean BDI score in our sample was 10.97 (median = 9.00). Both the mean and median scores fall in the "minimal depression" range according to the BDI-II manual (A. T. Beck et al., 1996a). In terms of severity level, 342 (69.5%) patients reported "minimal-range" depression symptoms, 73 (14.8%) reported "mild-range" depression symptoms, 61 (12.4%) reported "moderate-range" depression symptoms, and 16 (3.3%) reported "severe-range" depression symptoms (Table 3).

For context, we used z tests for equality of percentages using independent samples to compare the rates of minimal, mild, moderate, and severe depression symptoms in our sample to those of a large community sample (Segal et al., 2008; Figure 1). The community sample was demographically similar to ours in terms of

Table 3. *BDI scores* (n = 492).

Severity					
Minimal (0–13)	342 (69.5%)				
Mild (14–19)	73 (14.8%)				
Moderate (20–28)	61 (12.4%)				
Severe (29–63)	16 (3.3%)				
	M	SD	MED	IQR	range
Overall	10.97	7.91	9.00	5.00–15.00	0.00–42.00
Women	11.97	7.91	10.00	6.00–16.00	0.00–38.00
Men	9.99	7.79	8.67	4.00–13.67	0.00–42.00
Ischemic stroke	12.24	8.38	10.00	6.00–16.00	0.00–42.00
Hemorrhagic stroke	9.30	6.99	8.00	4.00–13.00	0.00–31.00
Subarachnoid hemorrhage	10.59	5.52	10.67	7.00–14.00	0.00–23.00
Benign tumor resection	9.63	6.95	8.00	3.67–14.00	0.00–30.00
Other resection	11.63	8.27	10.00	5.34–16.50	0.00–30.67
Focal contusion	11.84	9.10	11.00	4.67–19.00	0.00–27.00
Other etiology	11.69	9.07	8.00	5.00–13.67	2.00–27.00
Multiple etiologies	9.25	7.71	8.00	3.00–14.00	0.00–30.00
Right lateralizaed lesion	11.03	8.17	9.00	8.84–15.00	0.00–38.00
Left lateralized lesion	10.65	8.08	8.84	4.67–15.00	0.00–42.00
Bilateral lesion	11.63	6.86	10.67	6.34–16.34	0.00–28.67

Values are n (%) for severity. Means (M), standard deviations (SD), medians (MED), interquartile ranges (IQR), and ranges are provided for BDI scores overall and by gender, etiology, and laterality.

age, years of education, and race and also used the BDI-II to measure depression symptoms. Of note, the participants in the Segal et al. (2008) study were not excluded for a history of neurological injury. However, because this was a community-based sample, we would expect the rates of neurological injury in this sample to be similar to the typical prevalence rates of stroke and other neurological disorders and very low overall. The overall mean BDI score in our patient sample (10.97) was elevated compared to this community sample, which found a mean BDI-II score of 8.59. Also, for several ranges of depression symptom severity, the rates in our sample were significantly different from those reported by Segal et al. (2008; Figure 1). Segal et al. found that 81.9% of people reported minimal depression symptoms. This was significantly higher than our sample, which found that 69.5% of patients reported minimal depression symptoms (diff = −12.4%, $p < .001$). In the "mild" and "moderate" ranges, the percentages in Segal et al.'s sample were significantly lower than in our sample. Nine percent of the Segal et al. sample (compared to 14.8% in our sample) reported mild depression symptoms (diff = 5.8%, $p = .010$) and 6.4% of the Segal et al. sample (compared to 12.4% in our sample) reported moderate depression symptoms (diff = 6.0%, $p = .003$). For the "severe" range, 2.7% of the Segal et al. sample reported severe depression symptoms. This did not differ significantly from our sample, which found that 3.3% of patients reported severe depression symptoms (diff = 0.6%, $p = .612$; Figure 1).

Visualization of a histogram and boxplot of BDI scores suggested some deviation from normality, and a Shapiro–Wilk test of normality of the residuals was statistically significant ($p < .001$). We calculated the square root of BDI scores, and the square root values were normally distributed with a non-significant Shapiro–Wilk test of normality of the residuals ($p = .102$). Thus, the following analyses were performed on the square root of BDI scores.

The final regression model of all variables predicting level of depression was statistically significant ($F(39, 452) = 1.73$, $p = .005$). When controlling for temporal and lesion factors, the demographic variables were a significant predictor of BDI scores ($R^2 = .03$, $F(2, 477) = 6.67$, $p = .001$). Gender was a significant predictor of BDI score, whereby women reported higher BDI scores on average than men (Beta = .13, $t = 2.99$, $p = .003$, $sr = .13$). Years of education was not a significant predictor of BDI score (Beta = −.09, $t = -1.90$, $p = .058$, $sr = -.08$). Adding the interaction between gender and years of education to the regression model was not significant ($R^2 < .01$, $F(1, 476) = 0.18$, $p = .676$).

When controlling for demographic and lesion factors, the temporal variables were not a significant predictor of BDI score ($R^2 = .01$, $F(2, 477) = 2.98$, $p = .052$), so the individual effects of age at lesion onset and time since lesion onset were not examined, nor was their interaction.

When controlling for demographic and temporal factors, the lesion variables were a significant predictor of BDI score ($R^2 = .04$, $F(10, 477) = 2.05$, $p = .027$). Lesion etiology was a significant predictor of BDI score, whereby individuals with ischemic stroke had higher BDI scores than those with other lesion etiologies (Beta = .12, $t = 2.45$, $p = .015$, $sr = .11$) and those with

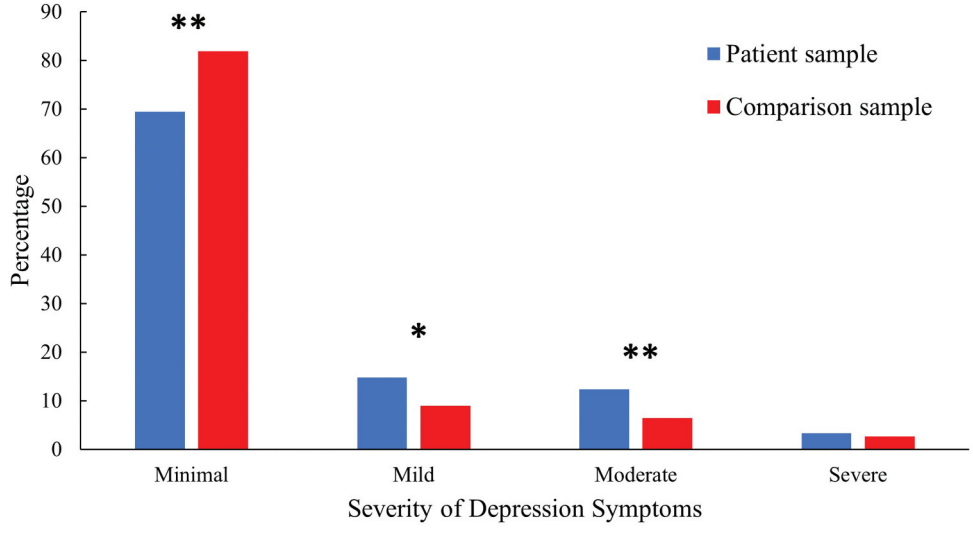

Figure 1. BDI score by severity level. Note. Comparison sample values were taken from a large study of community-dwelling adults examining the psychometric properties of the Beck Depression Inventory (Segal et al., 2008). * indicates $p < .05$, ** indicates $p < .01$.

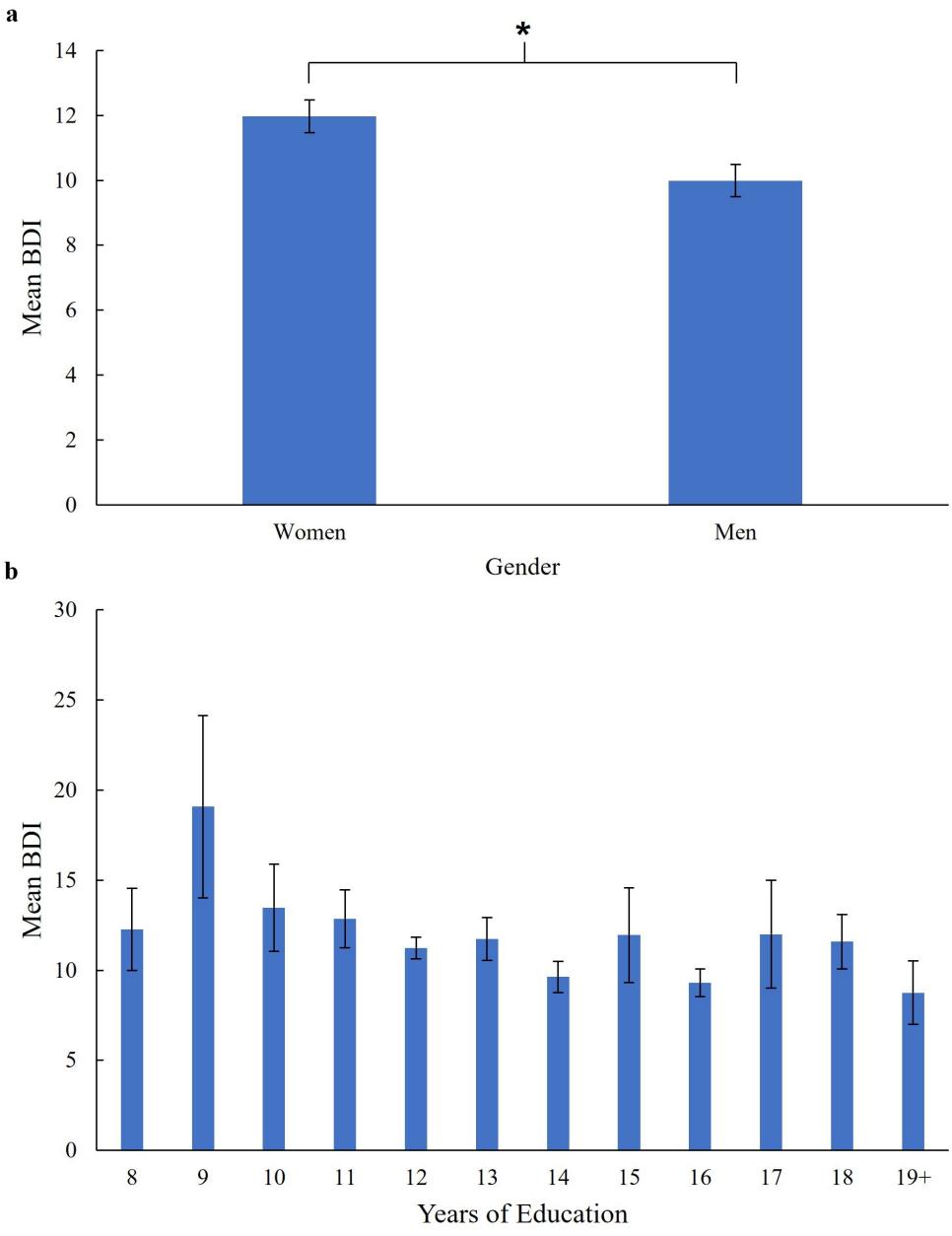

Figure 2. Mean BDI scores by demographic factors. Note. Bars reflect mean ± SEM. * indicates $p = .003$

multiple lesion etiologies had lower BDI scores than those with other lesion etiologies (Beta = −.10, $t = -2.00$, $p = .047$, $sr = -.09$). Lesion laterality and lesion volume were not significant predictors of BDI score ($ps > .100$). Adding all two-way interactions between lesion variables to the regression model was not significant ($R^2 = .05$, $F(23, 454) = 1.08$, $p = .368$). Figures 2–4 provide data regarding comparisons of mean BDI scores in the various subgroups.

Analyses were re-run after removing outliers for lesion volume. Using Tukey's method, 12 outliers were identified and removed. The results for the demographic and lesion predictors were unchanged. However, the results for the temporal factors went from being non-significant to being significant. Specifically, when controlling for demographic and lesion factors, the temporal variables were a significant predictor of BDI score ($R^2 = .05$, $F(2, 465) = 3.18$, $p = .043$). Age at lesion onset was a significant predictor of BDI score, whereby individuals with younger age at onset had higher BDI scores (Beta = −.13, $t = -2.27$, $p = .024$, $sr = -.10$). Time since lesion onset was also a significant predictor of BDI score, whereby individuals with a shorter time since onset had higher BDI scores (Beta = −.11, $t = -2.02$, $p = .044$, $sr = -.09$). Adding the two-way interaction between the temporal variables to the regression model

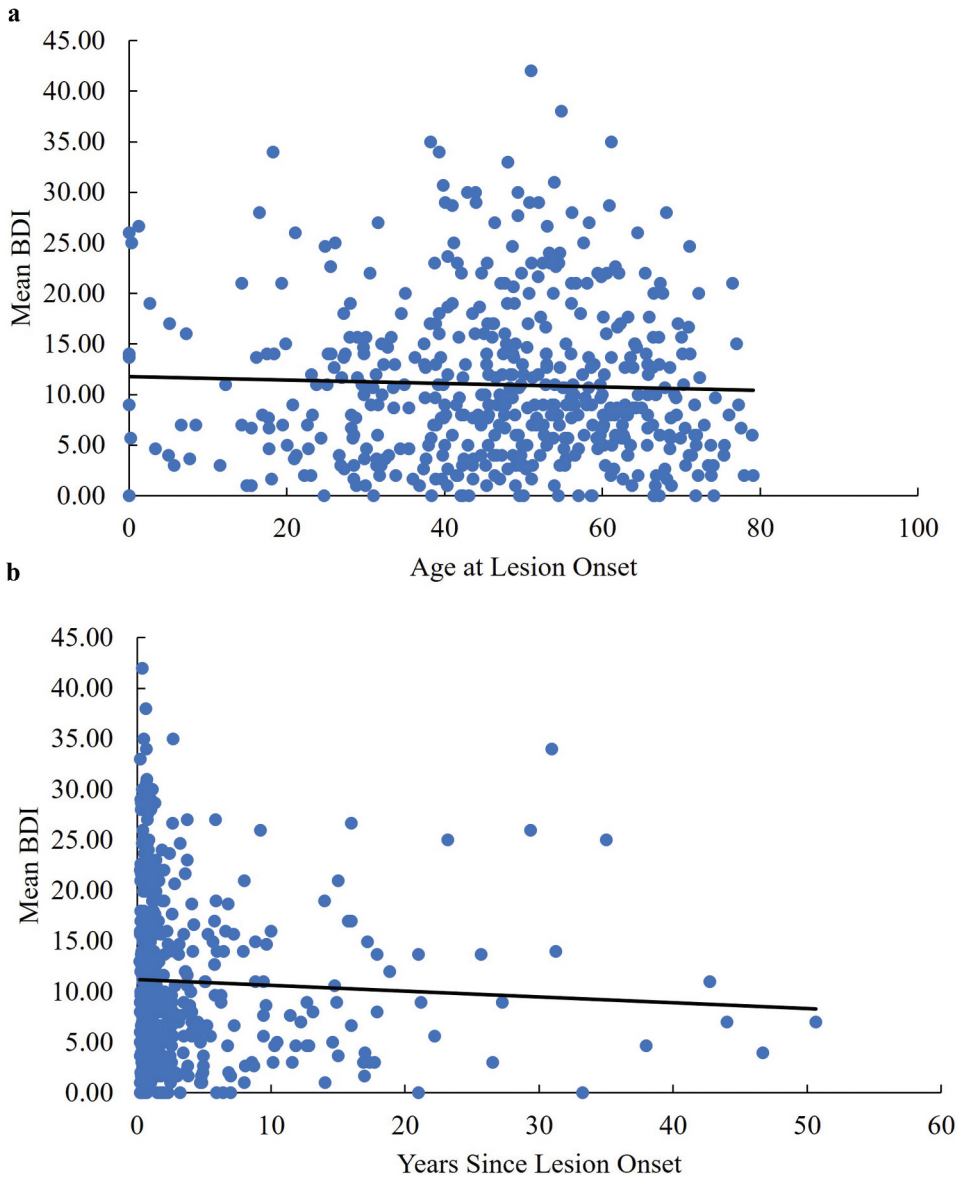

Figure 3. Mean BDI scores by temporal factors.

was significant (R^2 = .06, $F(1, 464) = 4.45$, p = .035). The interaction between age at lesion onset and time since lesion onset was significant, whereby those with younger age at onset and fewer years since onset had higher BDI scores (Beta = −.14, t = −2.11, p = .035, sr = −.09).

Analyses were re-run for the BDI-I and BDI-II separately. Analyses on patients who completed the BDI-I included only the ischemic and hemorrhagic stroke etiologies (sample sizes for the other etiologies were not large enough to support a meaningful statistical analysis). When looking at BDI-I scores alone, the final regression model was not significant ($F(17, 138) = 1.41$, p = .139), so we did not examine the individual effects of demographic, temporal, or lesion factors. Table 4 provides descriptive results for the BDI-I scores alone (156 patients).

When looking at BDI-II scores alone, the final regression model of all variables predicting level of depression was not significant ($F(35, 300) = 1.44$, p = .057), so we did not examine the individual effects of demographic, temporal, or lesion factors. Table 5 provides descriptive results for the BDI-II scores alone (336 patients).

As an exploratory analysis, we examined BDI scores over time in a subset of patients who had BDI scores at two different time points within the chronic epoch (n = 172). BDI scores at the first-time point were significantly correlated with BDI scores at the second time point (r = 0.485, p < .001). A repeated measures ANOVA showed no significant difference between

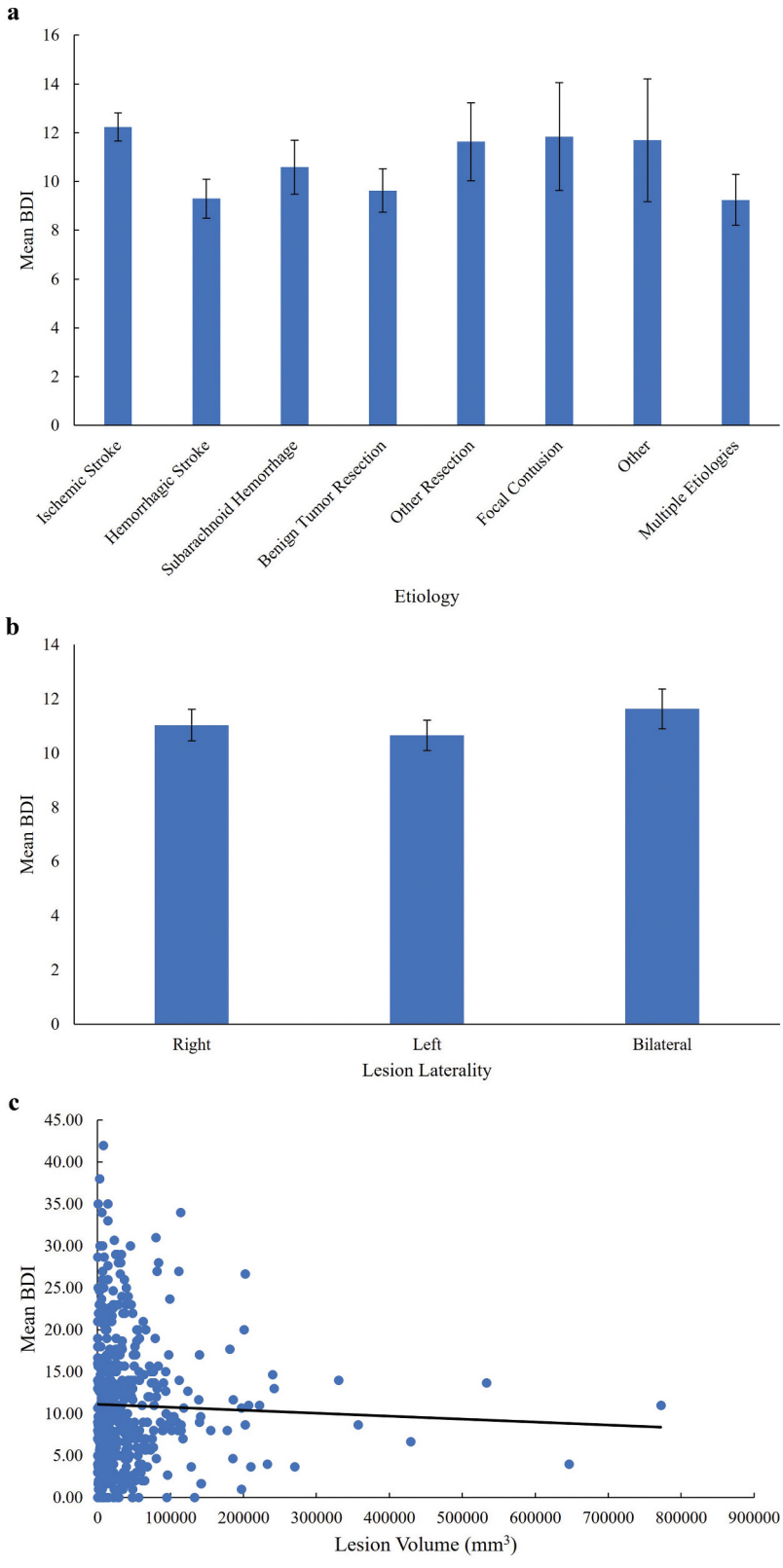

Figure 4. Mean BDI scores by lesion factors. Note. Bars reflect mean ± SEM.

Table 4. *BDI-I scores* (n = 156).

Severity					
Minimal (0–13)	107 (68.6%)				
Mild (14–19)	28 (17.9%)				
Moderate (20–28)	16 (10.3%)				
Severe (29–63)	5 (3.2%)				
	M	SD	MED	IQR	Range
Overall	10.59	7.79	9.00	4.00–15.00	0.00–35.00
Women	11.84	7.37	12.00	6.00–16.00	0.00–31.00
Men	9.57	8.01	8.00	4.00–14.00	0.00–35.00
Ischemic stroke	11.07	7.59	10.00	5.50–15.00	0.00–35.00
Hemorrhagic stroke	11.60	7.02	10.00	7.00–16.00	2.00–23.00
Subarachnoid hemorrhage	12.57	6.45	12.00	10.50–16.50	1.00–21.00
Benign tumor resection	5.63	4.75	5.50	1.50–8.50	0.00–14.00
Other resection	9.44	11.09	4.00	3.00–9.00	0.00–34.00
Focal contusion	11.88	10.30	5.50	4.50–22.00	3.00–28.00
Other etiology	9.67	9.59	6.00	3.00–12.00	3.00–28.00
Multiple etiologies	6.29	5.94	3.00	3.00–9.50	0.00–16.00
Right lateralized lesion	10.81	8.45	8.00	4.00–15.50	0.00–35.00
Left lateralized lesion	9.88	7.16	9.00	4.00–14.50	0.00–34.00
Bilateral lesion	11.47	7.66	11.00	5.50–15.50	0.00–29.00

Values are n (%) for severity. Means (M), standard deviations (SD), medians (MED), interquartile ranges (IQR), and ranges are provided for BDI-I scores overall and by gender, etiology, and laterality.

Table 5. *BDI-II scores* (n = 336).

Severity					
Minimal (0–13)	225 (67.0%)				
Mild (14–19)	51 (15.2%)				
Moderate (20–28)	45 (13.4%)				
Severe (29–63)	15 (4.5%)				
	M	SD	MED	IQR	Range
Overall	11.16	8.39	9.00	5.00–16.00	0.00–42.00
Women	12.08	8.40	10.00	6.00–18.00	0.00–38.00
Men	10.16	8.29	9.00	4.00–14.00	0.00–42.00
Ischemic stroke	13.26	9.48	10.00	6.00–21.00	0.00–42.00
Hemorrhagic stroke	8.81	7.17	7.00	3.00–13.00	0.00–31.00
Subarachnoid hemorrhage	9.94	5.74	8.50	6.00–14.00	0.00–23.00
Benign tumor resection	10.09	7.21	8.00	4.00–14.00	0.00–30.00
Other resection	12.50	7.85	11.00	7.00–17.00	0.00–27.00
Focal contusion	11.89	9.44	12.00	2.00–19.00	0.00–27.00
Other etiology	12.86	9.87	10.00	6.50–19.00	2.00–27.00
Multiple etiologies	9.65	7.90	8.00	3.00–14.00	0.00–30.00
Right lateralized lesion	11.27	8.64	9.00	5.00–16.50	0.00–38.00
Left lateralized lesion	10.89	8.68	9.00	4.00–15.00	0.00–42.00
Bilateral lesion	11.62	6.98	11.00	6.00–17.00	0.00–27.00

Values are n (%) for severity. Means (M), standard deviations (SD), medians (MED), interquartile ranges (IQR), and ranges are provided for BDI-II scores overall and by gender, etiology, and laterality.

BDI scores during the chronic epoch ($F(1, 169) < 0.01$, $p = .964$), even after controlling for time between assessments ($F(1, 169) = 0.57$, $p = .451$). Thus, BDI scores appear to be relatively stable during the chronic epoch.

Discussion

The aim of the present study was to characterize depression symptoms in individuals with stable focal brain lesions who are in the chronic epoch, as well as examine whether various demographic, temporal, and lesion factors predict severity of depression symptoms. Overall, the average BDI score in our sample was mildly elevated in reference to what was observed in a demographically comparable community sample (Segal et al., 2008) but still fell within the minimal range on average. Further, significantly more participants in our patient population reported depression symptoms at the mild- and moderate-range severity levels, compared to the Segal et al. community sample. However, we would note that the magnitudes of these differences tended to be small, and the overall mean depression score in our sample (10.97) was in the "minimal range" of severity per the BDI Manual, even if numerically somewhat higher than the mean value (8.59) from the Segal et al. sample. Additionally, our results showed that gender and lesion etiology may explain why some individuals report depression symptoms following focal brain lesions

while others do not. It appears that women (compared to men) and individuals with ischemic stroke (compared to various other lesion etiologies such as hemorrhage, benign tumor resection, and focal contusion) have higher levels of depression symptoms. This has important clinical implications for the identification of patients who are at higher risk of developing depression following a focal brain injury. Further, this could lead to earlier intervention for post-lesion depression in patients identified as higher risk, especially given that treatments such as psychotherapy and/or pharmacotherapy as well as transcranial magnetic stimulation have been shown to be effective for treating depression in neurological patients (Baker et al., 2018; Gu & Chang, 2017; Hordacre et al., 2021; Jorge et al., 2004; Robinson, 2003).

Our findings suggest that while on average the neurological patients reported sub-clinical depression symptoms, many individual patients reported elevated depression symptoms following their brain lesion. Across the "mild," "moderate," and "severe" ranges, a total of 150 patients reported symptoms in these severity ranges (see Table 3). It is still unclear as to why some individuals have elevated depression symptoms in the chronic epoch while others do not, but gender may be one explanation for why depression symptoms are higher following a brain lesion in some individuals. We found that on average, women reported higher levels of depression symptoms than men, which is in line with previous research on gender differences in depression symptoms in non-lesion populations (Roelofs et al., 2013; De Sá et al., 2019; Villarroel & Terlizzi, 2020). Previous work on gender differences in depression has suggested a diathesis-stress model whereby women are predisposed to depression (due to differences in gonadal hormones, personality, and/or socialization surrounding gender roles), which is then modulated by external factors, such as experiencing traumatic events or loss of employment (Parker & Brotchie, 2010). Under this framework, a neurological event leading to a focal brain lesion could be the stressor that, combined with women's predisposition for depression, could explain why women reported higher levels of depression symptoms in our sample. However, given that prevalence rates of depression in general tend to be higher in women than in men (Ferrari et al., 2013), it is also possible that women had higher levels of depression symptoms prior to lesion onset. Given that the mean BDI score in both men and women in our sample was higher than the mean BDI-II scores for men and women in a community sample (9.99 for men and 11.97 for women in our sample vs. 8.13 for men and 8.70 for women in the Segal et al. sample), experiencing a neurological event seems to confer greater risk for depression symptoms regardless of gender. Nevertheless, clinicians should be aware that women may be especially likely to report elevated levels of depression symptoms following a focal brain lesion. Knowing this could prompt clinicians to more thoroughly assess depression symptoms in these patients and potentially intervene earlier, which may lead to better patient outcomes.

In addition to gender, lesion etiology may also explain why some individuals report more severe depression symptoms following focal brain lesion than others. Specifically, in our sample, patients with ischemic stroke had elevated BDI scores compared to those with other lesion etiologies. This is in line with a large body of previous literature showing an association between stroke and elevated depression symptoms. Moreover, our results are in line with the vascular depression hypothesis, which posits that sustaining an ischemic stroke may put someone at greater risk of developing a depressive disorder due to vascular changes in the brain caused by the stroke (Taylor et al., 2013). Thus, in our sample, individuals with ischemic stroke may be at greater risk of elevated depression symptoms. However, this finding could also be driven by the fact that ischemic stroke was the predominant lesion etiology in our sample ($n = 217$ for ischemic stroke; n's < 80 for all other lesion etiologies). Thus, it is possible that lesion etiology plays a relatively small role in predicting depression symptom severity and ischemic stroke was the only etiology for which we were well-powered to detect a significant predictive effect. Regardless, it is important for clinicians monitoring patients following ischemic stroke to be aware that these individuals may be at risk for more severe depression symptoms in the chronic epoch. This could facilitate earlier detection and treatment of these symptoms.

Interestingly, neither of the temporal predictors (time since lesion onset and age at lesion onset) were associated with depression symptom severity. This could indicate that these factors are not as predictive of depression symptom severity as other factors included in our analyses, or it could be the result of our sample characteristics. Although we included some individuals with childhood onset lesions (lesions sustained prior to age 18; $n = 27$), most of our patients had their lesion onset in adulthood. This limits our ability to examine the effects of lesion onset during brain development compared to the effects of lesion onset when the brain is generally less plastic. Further, we examined whether there was a linear relationship between age at lesion onset and depression symptom severity, but some

work in stroke patients has posited a nonlinear relationship between age and depression symptom severity whereby symptoms peak in middle adulthood (McCarthy et al., 2016). Thus, we would be cautious about interpreting our findings and would acknowledge that age at lesion onset may be an important factor in depression symptom severity in neurological populations with attributes different from ours. Future work could examine whether there is a nonlinear relationship between age at lesion onset and depression symptom severity.

Time since lesion onset was also not a significant predictor of depression symptom severity. Given our finding that BDI scores are relatively stable during the chronic epoch, this may well be a true null finding. However, again, we would urge caution in interpreting these findings. Although our sample had a wide range of times since lesion onset (0.25–50.63 years), the distribution was highly right-skewed with around half of patients having had lesion onset between 3 and 12 months prior to our assessment. Future work could examine depression symptom severity in a patient sample with a wider range of long-term measurements post-lesion onset. Finally, when we removed outliers for lesion volume, the temporal set became a significant predictor of BDI score, whereby patients with younger age at lesion onset and a longer time since lesion onset had higher BDI scores. This suggests that there may be a small effect of temporal predictors on BDI score that was diminished when patients with particularly large lesion volumes were included. Future work could replicate the findings here in a larger sample with more homogenous lesion volumes to see if there is an effect of age at lesion onset and time since lesion onset on depression symptoms.

Lesion volume and lesion laterality were also not significant predictors of depression symptom severity in our sample. These findings may seem somewhat surprising. For example, it could be expected that larger lesions might be associated with worse outcomes generally, and with more severe depression symptoms specifically. Similarly, previous work on poststroke depression has found that left-lateralized lesions are associated with more severe depression symptoms (e.g., Robinson & Jorge, 2016). It is possible that other variables, such as gender and lesion etiology, are stronger predictors of depression symptom severity than lesion volume and laterality, which could explain why we failed to find a significant association between lesion volume and laterality, and BDI scores. We would also note that the evidence for an association between left-sided lesions and poststroke depression is actually quite mixed (Nickel & Thomalla, 2017). There is also substantial heterogeneity in patient outcomes following a brain lesion, and it is possible that our sample is different compared to patient samples in previous studies; again, this could explain why we failed to find lesion volume and laterality to be significant predictors of depression symptom severity. These are open questions that could be pursued further in additional research.

Strengths, limitations, and future directions

A strength of our study is the size and heterogeneity in lesion etiology of our sample. No previous work has examined depression symptoms in a sample of this size with several different lesion etiologies. Much of the previous literature has examined depression symptoms in individuals with ischemic stroke (Robinson & Spalletta, 2010), while few studies have looked at other lesion etiologies included in our study. For example, previous studies of brain tumor resection and depression had small sample sizes and few examined depression symptoms more than one-year post-lesion onset (Keng et al., 2020). Thus, we were able to examine whether particular lesion etiologies are associated with depression symptoms. Another strength of our study is that it focused exclusively on the chronic phase of recovery. Many previous studies included patients in both the acute and chronic phases of recovery, which may have an effect on the findings (Espárrago Llorca et al., 2015). By focusing solely on patients in the chronic epoch, we were able to limit variability caused by phase of recovery. Specifically, individuals in the acute epoch may be more likely to report more severe depression symptoms, possibly due to the acute adjustment demands of coping with a newly acquired neurological deficit (e.g., a motor or sensory impairment, speech impairment, or cognitive impairment). On the other hand, individuals in the chronic epoch may have adjusted to and recovered from the acute effects of their lesion and hence report fewer depression symptoms. This is another area that would benefit from further research.

One limitation is the fact that our sample was overwhelmingly non-Hispanic white (98.2%), so we were not able to evaluate the effect of race or ethnicity on depression symptoms post-lesion. Future work could consider these and other factors, such as nationality and socioeconomic status, when evaluating potential predictors of depression following brain lesion. Similarly, we only collected data on patients' self-reported gender and did not collect direct information on their sex, so we cannot draw any conclusions about the role of biological sex in the development of post-lesion depression symptoms or compare that to the

role of gender. Future work could compare and contrast the roles of sex and gender as well as replicate this work in a more diverse sample that includes people of other gender identities, such as non-binary and transgender.

We also did not have access to an aggregate measure of post-lesion impairment (e.g., an NIH Stroke Scale) in our analyses, so we cannot draw conclusions about the effect of general impairment or disability on depression symptoms. We included lesion volume, which may serve as a good proxy for impairment, but future work could include measures of impairment or disability (e.g., Barthel Index) to assess the extent to which post-lesion depression may be influenced by ability to perform activities of daily living and other day-to-day functions.

Another limitation is that we used a self-report measure of depression symptoms. Although the BDI is a commonly used and psychometrically sound measure of depression symptoms, previous literature has shown that rates of depression can vary depending on the type of measure used (Robinson & Spalletta, 2010). Furthermore, we used two versions of the BDI and did not identify any significant predictors of depression symptoms when using the BDI-I or BDI-II alone, although this was likely due to insufficient power. Future studies could employ other methods of evaluating depression in neurological patients, such as a structured diagnostic interview. Similarly, the aim of this study was to examine overall depression symptom severity, but previous literature suggests that some symptoms, such as vegetative symptoms, may be more common in patients with brain lesions (Paradiso et al., 1997). Future work could examine symptom severity for specific types of depression symptoms following a brain lesion. A final limitation of this study is the fact that it is cross-sectional and correlational, so we cannot establish a causal relationship between depression symptoms and a brain lesion. Although challenging, some patient samples, such as those undergoing brain resection surgery, do lend themselves to examining depression symptoms pre- and post-lesion onset, so future studies of such samples could compare depression symptom severity using a longitudinal design that might allow cause-and-effect conclusions.

Conclusions

Depression following focal brain lesion is a complex condition, affected by many factors. The present study provides severity rates for depression symptoms in patients with stable, focal brain lesions in the chronic phase of recovery. We found that gender and lesion etiology were predictors of post-lesion depression symptoms, such that women and those with ischemic stroke had more severe depression symptoms. These findings provide a fuller understanding of post-lesion depression symptoms and could aid in the diagnosis, prognosis, and treatment of depression in neurological patients.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

This research was partially supported by grants from the National Institute of General Medical Sciences (T32GM108540), the National Institutes of Mental Health (P50 MH094258 to DT; R01NS114405 to ADB; and R21MH120441 to ADB), and the Kiwanis Neuroscience Research Foundation (to DT).

References

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). American Psychiatric Association.

Angeleri, F., Angeleri, V. A., Foschi, N., Giaquinto, S., Nolfe, G., Saginario, A., & Signorino, M. (1997). Depression after stroke: An investigation through catamnesis. *Journal of Clinical Psychiatry*, *58*(6), 261–265. https://doi.org/10.4088/JCP.v58n0605

Ayerbe, L., Ayis, S., Wolfe, C. D. A., & Rudd, A. G. (2013). Natural history, predictors and outcomes of depression after stroke: Systematic review and meta-analysis. *British Journal of Psychiatry*, *202*(1), 14–21. https://doi.org/10.1192/bjp.bp.111.107664

Baker, C., Worrall, L., Rose, M., Hudson, K., Ryan, B., & O'Byrne, L. (2018). A systematic review of rehabilitation interventions to prevent and treat depression in post-stroke aphasia. *Disability and Rehabilitation*, *40*(16), 1870–1892. https://doi.org/10.1080/09638288.2017.1315181

Bar, M., Skoloudik, D., & Roubec, M. (2009). Post-stroke depression: A one year prospective follow-up study. *Journal of the Neurological Sciences*, *285*(S1), S172. https://doi.org/10.1016/s0022-510x(09)70658-6

Beck, A. T., Steer, R. A., Ball, R., & Ranieri, W. F. (1996b). Comparison of beck depression inventories -IA and -II in psychiatric outpatients. *Journal of Personality Assessment*, *67*(3), 588–597. https://doi.org/10.1207/s15327752jpa6703_13

Beck, A. T., Steer, R. A., & Brown, G. (1996a). *Beck Depression Inventory-II (BDI-II): Manual and questionnaire*. The Psychological Corporation.

Bowren, M., Adolphs, R., Bruss, J., Manzel, K., Corbetta, M., Tranel, D., & Boes, A. (2020). Multivariate lesion-behavior mapping of general cognitive ability and its psychometric constituents. *Journal of Neuroscience*, *40*(46), 8924–8937. https://doi.org/10.1523/JNEUROSCI.1415-20.2020

De Sá, A. R., Liebel, G., De Andrade, A. G., Andrade, L. H., Gorenstein, C., & Wang, Y. P. (2019). Can gender and age impact on response pattern of depressive symptoms among college students? A differential item functioning analysis. *Frontiers in Psychiatry*, *10*(50), 10. https://doi.org/10.3389/fpsyt.2019.00050

Eastwood, M. R., Rifat, S. L., Nobbs, H., & Ruderman, J. (1989). Mood disorder following cerebrovascular accident. *British Journal of Psychiatry*, *154*(2), 195–200. https://doi.org/10.1192/bjp.154.2.195

Espárrago Llorca, G., Castilla-Guerra, L., Fernández Moreno, M. C., Ruiz Doblado, S., & Jiménez Hernández, M. D. (2015). Post-stroke depression: An update. *Neurología (English Edition)*, *30*(1), 23–31. https://doi.org/10.1016/j.nrleng.2012.06.006

Ferrari, A. J., Somerville, A. J., Baxter, A. J., Norman, R., Patten, S. B., Vos, T., & Whiteford, H. A. (2013). Global variation in the prevalence and incidence of major depressive disorder: A systematic review of the epidemiological literature. *Psychological Medicine*, *43*(3), 471–481. https://doi.org/10.1017/S0033291712001511

Fiez, J. A., Damasio, H., & Grabowski, T. J. (2000). Lesion segmentation and manual warping to a reference brain: Intra- and interobserver reliability. *Human Brain Mapping*, *9*(4), 192–211. https://doi.org/10.1002/(SICI)1097-0193(200004)9:4<192::AID-HBM2>3.0.CO;2-Y

Gu, S. Y., & Chang, M. C. (2017). The effects of 10-Hz repetitive transcranial magnetic stimulation on depression in chronic stroke patients. *Brain Stimulation*, *10*(2), 270–274. https://doi.org/10.1016/j.brs.2016.10.010

Hackett, M. L., & Pickles, K. (2014). Part I: Frequency of depression after stroke: An updated systematic review and meta-analysis of observational studies. *World Stroke Organization*, *9*(December 2014), 1017–1025. https://doi.org/10.1111/ijs.12357

Haghgoo, H. A., Pazuki, E. S., Hosseini, A. S., & Rassafiani, M. (2013). Depression, activities of daily living and quality of life in patients with stroke. *Journal of the Neurological Sciences*, *328*(1–2), 87–91. https://doi.org/10.1016/j.jns.2013.02.027

Hordacre, B., Comacchio, K., Williams, L., & Hillier, S. (2021). Repetitive transcranial magnetic stimulation for post-stroke depression: A randomised trial with neurophysiological insight. *Journal of Neurology*, *268*(4), 1474–1484. https://doi.org/10.1007/s00415-020-10315-6

Irle, E., Peper, M., Wowra, B., & Kunze, S. (1994). Mood changes after surgery for tumors of the cerebral cortex. *Archives of Neurology*, *51*(2), 164–174. https://doi.org/10.1001/archneur.1994.00540140070017

Jorge, R. E., Robinson, R. G., Tateno, A., Narushima, K., Acion, L., Moser, D., Arndt, S., & Chemerinski, E. (2004). Repetitive transcranial magnetic stimulation as treatment of poststroke depression: A preliminary study. *Biological Psychiatry*, *55*(4), 398–405. https://doi.org/10.1016/j.biopsych.2003.08.017

Kanner, A. M. (2003). Depression in epilepsy: Prevalence, clinical semiology, pathogenic mechanisms, and treatment. *Biological Psychiatry*, *54*(3), 388–398. https://doi.org/10.1016/S0006-3223(03)00469-4

Keng, A., Stewart, D. E., & Sheehan, K. A. (2020). Examining the neuropsychiatric sequelae postsurgical resection of adult brain tumors through a scoping review. *Psychosomatics*, *61*(3), 209–219. https://doi.org/10.1016/j.psym.2019.12.008

McCarthy, M. J., Sucharew, H. J., Alwell, K., Moomaw, C. J., Woo, D., Flaherty, M. L., Khatri, P., Ferioli, S., Adeoye, O., Kleindorfer, D. O., & Kissela, B. M. (2016). Age, subjective stress, and depression after ischemic stroke. *Journal of Behavioral Medicine*, *39*(1), 55–64. https://doi.org/10.1007/s10865-015-9663-0

Nazarinasab, M., Motamedfar, A., Neamatpour, S., & Javadi, S. (2018). Assessment of depression after stroke and its relation to brain lesion. *Minerva Psichiatrica*, *59*(1), 39–44. https://doi.org/10.23736/S0391-1772.17.01956-2

Nickel, A., & Thomalla, G. (2017). Post-stroke depression: Impact of lesion location and methodological limitations-a topical review. *Frontiers in Neurology*, *8*(498), 1–8. https://doi.org/10.3389/fneur.2017.00498

Norrving, B. (2003). Long-term prognosis after lacunar infarction. *Lancet Neurology*, *2*(4), 238–245. https://doi.org/10.1016/S1474-4422(03)00352-1

Paradiso, S., Ohkubo, T., & Robinson, R. G. (1997). Vegetative and psychological symptoms associated with depressed mood over the first two years after stroke. *International Journal of Psychiatry in Medicine*, *27*(2), 137–157. https://doi.org/10.2190/BWJA-KQP3-7VUY-D06T

Parker, G., & Brotchie, H. (2010). Gender differences in depression. *International Review of Psychiatry*, *22*(5), 429–436. https://doi.org/10.3109/09540261.2010.492391

Przewoźnik, D. A., Rajtar-Zembaty, A. M., Bober-Płonka, B., Starowicz-Filip, A., Nowak, R., & Przewłocki, R. (2015). PSDRS, BDI, MoCA and MMSE as screening tools for the evaluation of mood and cognitive functions in patients at the early stage of cerebral stroke. *Archives of Psychiatry and Psychotherapy*, *3*(3), 32–39. https://doi.org/10.12740/APP/59066

Robinson, R. G. (2003). Poststroke depression: Prevalence, diagnosis, treatment, and disease progression. *Biological Psychiatry*, *54*(3), 376–387. https://doi.org/10.1016/S0006-3223(03)00423-2

Robinson, R. G., & Jorge, R. E. (2016). Post-stroke depression: A review. *American Journal of Psychiatry*, *173*(3), 221–231. https://doi.org/10.1176/appi.ajp.2015.15030363

Robinson, R. G., & Spalletta, G. (2010). Poststroke depression: A review. *Canadain Journal of Psychiatriy*, *55*(6), 341–349. https://doi.org/10.1177/070674371005500602

Roelofs, J., van Breukelen, G., de Graaf, L. E., Beck, A. T., Arntz, A., & Huibers, M. J. H. (2013). Norms for the Beck Depression Inventory (BDI-II) in a large dutch community sample. *Journal of Psychopathology and Behavioral Assessment*, *35*(1), 93–98. https://doi.org/10.1007/s10862-012-9309-2

Segal, D., Coolidge, F., Cahill, B., & O'Riley, A. (2008). Psychometric properties of the Beck Depression Inventory-II (BDI-II) among community-dwelling older adults. *Behavior Modification*, *32*(1), 3–20. https://doi.org/10.1177/0145445507303833

Sharpe, M., Hawton, K., House, A., Molyneux, A., Sandercock, P., Bamford, J., & Warlow, C. (1990). Mood disorders in long-term survivors of stroke: Associations with brain lesion location and volume. *Psychological Medicine*, *20*(4), 815–828. https://doi.org/10.1017/S0033291700036503

Sharpe, M., Hawton, K., Seagroatt, V., Bamford, J., House, A., Molyneux, A., Sandercock, P., & Warlow, C. (1994).

Depressive disorders in long-term survivors of stroke. Associations with demographic and social factors, functional status, and brain lesion volume. *British Journal of Psychiatry*, *164*(3), 380–386. https://doi.org/10.1192/bjp.164.3.380

Taylor, W. D., Aizenstein, H. J., & Alexopoulos, G. S. (2013). The vascular depression hypothesis: Mechanisms linking vascular disease with depression. *Molecular Psychiatry*, *18*(9), 963–974. https://doi.org/10.1038/mp.2013.20

Townend, B. S., Whyte, S., Desborough, T., Crimmins, D., Markus, R., Levi, C., & Sturm, J. W. (2007). Longitudinal prevalence and determinants of early mood disorder post-stroke. *Journal of Clinical Neuroscience*, *14*(5), 429–434. https://doi.org/10.1016/j.jocn.2006.01.025

Tranel, D. (2019). Cognitive neuroscience and neuropsychology. In R. Lim, F. Fecto, & G. Richerson (Eds.), *100 years of neurology at the university of Iowa* (pp. 62–68). University of Iowa Carver College of Medicine.

Tranel, D., Bechara, A., & Denburg, N. L. (2002). Asymmetric functional roles of right and left ventromedial prefrontal cortices in social conduct, decision-making, and emotional processing. *Cortex*, *38*(4), 589–612. https://doi.org/10.1016/S0010-9452(08)70024-8

Tranel, D., Damasio, A. R., & Damasio, H. (1988). Intact recognition of facial expression, gender, and age in patients with impaired recognition of face identity. *Neurology*, *38*(5), 690–696. https://doi.org/10.1212/wnl.38.5.690

Villarroel, M. A., & Terlizzi, E. P. (2020). Symptoms of depression among adults: United States, 2019. *NCHS Data Brief*, *379*(September 2020), 1–8.

Wade, D. T., Wood, V. A., & Hewer, R. L. (1985). Recovery after stroke - The first 3 months. *Journal of Neurology, Neurosurgery, and Psychiatry*, *48*(1), 7–13. https://doi.org/10.1136/jnnp.48.1.7

Wang, Y. P., & Gorenstein, C. (2013). Psychometric properties of the beck depression inventory-II: A comprehensive review. *Revista Brasileira de Psiquiatria*, *35*(4), 416–431. https://doi.org/10.1590/1516-4446-2012-1048

White, C. L., McClure, L. A., Wallace, P. M., Braimah, J., Liskay, A., Roldan, A., & Benavente, O. R. (2011). The correlates and course of depression in patients with lacunar stroke: Results from the secondary prevention of small subcortical strokes (SPS3) study. *Cerebrovascular Diseases*, *32*(4), 354–360. https://doi.org/10.1159/000330350