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Effects of Post-Stroke Depression on Cognitive and Linguistic Recovery

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Effects of Post-Stroke Depression on Cognitive and Linguistic Recovery

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Dedication

This report is dedicated to my parents and Jon, for their unconditional love and support.

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Abstract

Effects of Post-Stroke Depression on Cognitive and Linguistic Recovery

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Abstract: The aim of this paper is to explore the relationship between functional recovery from stroke and depression. Stroke leads to depression both directly (through the location of the lesion) and indirectly (through decreased functional status and aphasia secondary to stroke). Consequently, depression may limit functional recovery and recovery from aphasia. The relationship between decreased functional status post-stroke and depression appears to be bidirectional and mutually-reinforcing (decreased functional status leads to depression and depression limits functional recovery). Similarly, the relationship between aphasia recovery and depression is likely bidirectional and mutually reinforcing. Antidepressants may be useful in disrupting these relationships and thereby improving functional recovery from stroke.

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Introduction

Stroke, the second leading cause of long-term disability in older Americans (Ramasubbu, Robinson, Flint, Kosier, & Price, 1996), is associated with declines in independent functioning. Post-stroke patients may have difficulty performing daily tasks and activities, including self care and ambulation, in addition to cognitive and communication deficits that affect daily functioning. Two common effects of stroke, aphasia and depression, may impact a person's functional independence in the immediate and chronic post-stroke periods. Post-stroke aphasia has an incidence of more than 80,000 new cases each year in the United States. At least 20–30% of stroke survivors experience chronic aphasia ("Aphasia," 2000). The incidence of post-stroke depression may be as high as 50-60% (Starkstein & Robinson, 1988, as cited in Code & Herrmann, 2003). In the acute post-stroke stage, depression may stem from the site of neurological damage, as evidenced in research that has found a common site of subcortical lesion in these patients, involving the putamen and external globus pallidus (Herrmann, Bartels, & Wallesch, 1993). In the chronic stages of recovery from stroke, depression may be considered a reaction to the impairment and loss of functioning that the patient experiences (e.g., Code & Herrmann, 2003). The aim of this paper is to explore the relationship between recovery from stroke and depression. More specifically, what impact does depression have on recovery from stroke with respect to functional status and aphasia?

The accumulated evidence (e.g., Sinyor, Amato, Kaloupek, Becker, Goldenberg, and Coopersmith, 1986; Parikh, Robinson, Lipsey, Starkstein, Fedoroff, and Price, 1990) shows that the presence of depression in post-stroke patients leads to decreased functional recovery from stroke. Additionally, depressive symptoms, especially in patients beyond the acute stage of recovery, often result from this decreased functional status. That is, the relationship between depression and decreased functional status is bidirectional and perhaps mutually-reinforcing; depression hinders functional recovery while decreased functional status contributes to depression.

There are several reasons to think that a bidirectional relationship might exist between aphasia and depression as well. Aphasia causes decreased functional status in that it limits a person's ability to communicate. Insofar as depression limits functional recovery, it may also limit recovery from aphasia. Further, there is evidence that the communicative deficits experienced in chronic aphasia often lead to depression in post-stroke patients (e.g., Kauhanen, et al., 1999; Herrmann, et al., 1993**)**. Thus, the bidirectional relationship between functional recovery and depression is likely to be operating between aphasia recovery and depression as well. The lack of studies directly supporting the claim that depression limits recovery from aphasia, and the resulting conclusion that the relationship between aphasia and depression is bidirectional, suggests that this would be a fruitful area for future research.

If clinicians working with post-stroke patients were more informed about the detrimental effects of depression on recovery from aphasia and general functional recovery, they might be more likely to refer patients for appropriate mental health services. Treatment for depression would then decrease the effect of depressive symptoms on cognitive, linguistic, and functional recovery from stroke, and ultimately save healthcare resources by shortening the duration of institutionalized care (Kotila, Numminen, Waltimo, & Kaste, 1999).

Effects of Depression on Functional Status and Recovery

Depression after a stroke may be categorized as a major or minor depressive episode. Major post-stroke depression is characterized by a dysphoric mood or loss of interest or pleasure in many or all of a person's usual activities and pastimes, accompanied by at least four of the following symptoms: loss of energy, poor appetite or significant weight loss, psychomotor retardation, insomnia, decreased concentration, feelings of worthlessness, and suicidal ideation. Symptoms must persist for two years to support a diagnosis of major post-stroke depression. Minor post-stroke depression has many of the same signs and symptoms as major depression, but does not require a two-year duration of symptoms for diagnosis (Starkstein & Robinson, 1988).

Depression has been found to be a significant predictor of functional impairment in several large-scale stroke studies. Sinyor, et al. (1986) found that patients who were depressed presented with decreased functional status at the outset of the rehabilitation program under their investigation. A more recent study (Ramasubbu, et al., 1998) evaluated 626 patients who were between seven and ten days post-stroke, using the *Center for Epidemiological Studies Depression Scale* (CES-D; Radloff, 1977) and the *Barthel Index* (BI; Mahoney & Barthel, 1965), which measures independence in activities of daily living (ADLs). Results indicated that the presence of depression was significantly associated with decreased functional performance in the acute post-stroke period.

Depression affects functional recovery. Several prospective, longitudinal studies have found that depression negatively affects recovery in functional status after a stroke. Among a group of 63 stroke patients followed by Parikh, Robinson, Lipsey, Starkstein, Fedoroff, and Price (1990), 25 were diagnosed with depression in the acute stage (less than two weeks post-stroke). This diagnosis was based on symptoms of depression or anxiety elicited during a structured psychiatric interview (The *Present State Examination*; PSE; Wing, Cooper, & Sartorius, 1974). Because of the use of this verbal interview, patients with significant comprehension deficits were excluded, but patients with other types of aphasia (N=15) were included if they could participate reliably in the PSE. During the initial examination patients also completed the *Mini-Mental*

State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) to gauge their cognitive performance and a 10-item questionnaire evaluating their participation in ADLs, including: walking, eating, dressing, comprehension of spoken and written language, performance of routine tasks, expressing their needs, and finding their way around.

Parikh, et al. (1990) found that at the two-year follow-up evaluation, patients who were depressed during the acute stage showed significantly less recovery in ADLs than patients who were not depressed, despite initial scores in daily functioning that were similar between the two groups. Participation in rehabilitation programs lasting 30 days or more was approximately equal between the depressed and non-depressed groups (about half of the participants in each group), suggesting that participation in rehabilitation was not a factor in the varied recovery rates between the two groups. Additionally, the presence of aphasia or other cognitive deficits (as assessed by the MMSE) did not explain the slower rate of recovery among the depressed patients. ADLs were further grouped into three categories of functioning: those related to self-care (walking, dressing, eating, etc), those related to comprehension and production of language, and one related to sphincter control. The rate of recovery in self-care and language comprehension/production was significantly reduced in patients with depression, suggesting that depression may act as a significant hindrance in recovery from aphasia or other cognitive/communicative deficits resulting from stroke. The effects of depression on recovery from stroke appeared to be long lasting as well; depressive symptoms had subsided in most patients well before the two-year follow up, while rates of recovery continued to be slower among those patients who had previously been depressed.

Morris, Raphael, and Robinson (1992) examined recovery in functional status among stroke patients with and without depression using the *Karnofsky Performance Status Scale* (KPSS; Karnofsky, Abelmann, & Kraver, 1948), ADLs using the *Barthel Index*, and cognitive performance using the *Mental Status Questionnaire*. Diagnosis of clinical depression was based on a semi-structured psychiatric interview (the *Composite International Diagnostic Interview*; CIDI; World Health Organization, 1987). Patients with severe aphasia or comprehension deficits

were excluded from the study. Among the remaining patients, 20 were diagnosed with depression and 29 were not. Depressive episodes began soon after the onset of stroke (mean=2.7 weeks) and lasted, on average, about five months. Based on assessments completed at two months and 16 months post-onset, patients who were depressed at two months showed significantly less improvement in functional status and showed a slight decline in cognitive performance. Patients in the non-depressed group made modest gains in cognitive performance in the 14 months after the initial evaluation. Depressed and non-depressed patients did not show significant differences in recovery of ADLs, as measured by the BI. However, scores on the BI only took into account physical independence and may not have reflected patients' ability to understand written and verbal language or express their needs. Functional status, in this study, was based on the KPSS, a scale that rated overall function from "moribund, near death" to "normal, no complaints, no evidence of disease" (Morris, Raphael, & Robinson, 1992, p. 240), which may have captured areas of functional independence that the Barthel Index did not assess. If so, results of this study would be in concordance with those found in Parikh, et al. (1990), in that post-stroke depression seemed to negatively affect recovery in independent functioning, even after clinical symptoms of depression had subsided.

Another prospective, longitudinal study investigating the effects of post-stroke depression on functional outcomes (Hermann, Black, Lawrence, Szekely & Szalai, 1998) followed consecutive entries (N=136 at conclusion of study) to a stroke center for one year. Factors investigated included neurological status, functional outcome (measured with the *Functional Independence Measure*; FIM; Keith, Granger, Hamilton, & Sherwin, 1987), social handicap (measured with the *Oxford Handicap Scale*; OHS; Bamford, Sandercock, Warlow, & Slattery, 1989), lesion location, and volume. The FIM scale assessed function in mobility, locomotion, sphincter control, self-care, communication and social cognition, while the OHS assessed limitation in the patient's social roles. Patients in this study were not excluded based on the presence of aphasia and assessments were attempted unless the patient had global aphasia or severe comprehension deficits.

Because the FIM measured levels of independence in communication and social cognition, it could act as a measure of recovery in language and cognition among stroke patients. Hermann, et al. (1998) attempted to determine whether depressive symptoms at three months predicted functional outcome at one year by calculating correlations between scores on depression rating scales at three months with scores on the FIM and OHS at one year. The resulting correlations were significant ($p<.003$) in most cases, suggesting that early depression was related to significantly decreased recovery in FIM scores and in the patients' social roles, as measured by the OHS. Because patients in this study often had relatively mild depression, the effects of even mild depressive symptoms on functional outcomes after stroke were highlighted.

Another study that followed patients for one year, with assessments at admission and at three-, six-, and twelve-month follow ups, from a population-based stroke register, was completed by Kotila, et al. (1999). The specific research questions posed were whether depressed patients required greater assistance in activities of daily living and whether they were more often in institutionalized care than post-stroke patients who were not depressed. Unlike some of the studies reviewed, the researchers in this study specifically reported on the bidirectional relationship between depression and recovery in functional outcomes. Patients who were depressed at three months were more dependent in ADLs at twelve months than non-depressed patients. Additionally, patients who were more dependent in ADLs at three months were more likely to be depressed at twelve months. Moreover, patients who were depressed at three months were more likely to be in institutionalized care during the study period than those patients who had not been depressed at three months. This suggests that in addition to its detrimental effects on functional outcome, depression may raise the costs of healthcare associated with recovery from stroke, as institutionalized care is likely to cost more than outpatient rehabilitation or in-home care.

Although patients with severe aphasia were excluded in the study by Kotila, et al. (1999), patients with aphasia who were able to complete the assessments were included in the results; thus, results found in this study may be generalized from this group of post-stroke patients to a

group of patients with post-stroke aphasia, insofar as these patients are representative of the group. Two outcome measures that were included in some follow-up assessments but not reported were a "Speech Scale," administered at admission, three, and 12 months post-onset, and the MMSE. Since these measure linguistic and cognitive performance, respectively, analysis of changes in patients' scores on these two assessments could have made this study more relevant to the question of whether post-stroke depression limits cognitive and linguistic recovery.

Conflicting results were found in one study investigating the relationship between post-stroke depression and functional recovery. Sinyor, et al. (1986) followed a group of 64 patients who presented to a rehabilitation program within weeks after stroke onset to determine the impact of post-stroke depression on rehabilitation outcomes. The presence of depression was assessed using a combination of self-rating scales to determine a *Composite Depression Index* (CDI) as well as through a *Nurses' Rating Scale* (NRS), completed by the patients' primary nurses. Patients with receptive aphasia or comprehension problems were excluded; however, patients with expressive aphasia (but adequate auditory/written comprehension) could provide responses to interview questions by pointing to responses on cards. Dependent variables in this study included ratings from physical therapy and occupational therapy staff at admission and discharge from the rehabilitation program. Physical therapists rated the overall motor functioning of patients, and occupational therapists rated their capacity for independent living, which may have included measures of how well patients could communicate, although the parameters upon which they were assessed was not stated explicitly. Results of the study indicated that depressed patients had lower scores on functional status than non-depressed patients at both time points (admission and discharge). However, patients in both groups made similar gains in functional status during the time spent in the rehabilitation program.

Depressed and non-depressed patients also differed with respect to their coping strategies, with depressed patients less likely to report "behavioral action" (e.g. "I take some positive action to regain strength") or "rational cognition" (e.g. "I take things one step at a time") as coping strategies. The other coping mechanisms listed in the *Coping Scale* (COPE; Billings & Moos,

1981), included worry, suppression, and denial; each were more commonly reported by depressed than non-depressed patients. In conjunction with findings that depressed and non-depressed patients made similar gains in functional status, this suggests that depressive symptoms and a lack of positive coping strategies were not necessarily predictive of decreased recovery in functional outcome. However, unlike many of the studies cited thus far, in which patients were drawn from consecutive hospital admissions or from population-based stroke registers (e.g., Herrmann, et al., 1998), patients in Sinyor, et al. (1986) each voluntarily participated in physical and occupational therapy after their stroke. Hermann, et al. (1998) noted that rehabilitation-center-based groups of post-stroke patients may be self-selected for positive rehabilitation potential, in that these patients may be more motivated to improve their functional status, and are less likely to be in institutionalized care (e.g. a long-term care facility or skilled nursing facility). Self-selection could account for why the results of Sinyor, et al. (1986) are at odds with the results of virtually every other study investigating the relationship between functional recovery and depression. Sinyor, et al. (1986) should have also noted whether the rehabilitation center at which the study was conducted served inpatients, outpatients, or both, as these populations of patients may have had very different prognoses for recovery.

Taken together, these studies strongly support the proposition that depression limits functional recovery after stroke. The results of Sinyor, et al. (1986), the one study which found that depression did not significantly hinder functional recovery, can be accounted for by the fact that it only used patients from a rehabilitation center, who are more likely to have positive functional outcomes. Every other study either found that depression limits functional recovery or is at least associated with decreased initial functional status. Thus, depression does indeed hinder functional recovery.

Effects of Functional Status on Depression

Decreased functional status can cause depression. Sinyor, et al. (1986) found that depressed patients had lower scores on measures of functional status than non-depressed patients both initially and at discharge. Ramasubbu, et al. (1998) noted that patients with decreased functional status were more depressed in the acute post-stroke stage. Kotila, et al. (1999) found that patients with poor functional outcome at three months were more often depressed at twelve months. There is not only a correlation between functional status and depression, but a causal relationship: decreased functional status leads to depression. However, the Kotila study also notes that depression at three months was associated with poor functional performance at 12 months. This suggests a bidirectional relationship between functional status and depression: depression limits functional recovery, and decreased functional status in turn leads to depression.

While many post-stroke patients receive therapy for their decreased functional status, Kotila et al., found that relatively few received treatment for depression. If the relationship between decreased functional status and depression is in fact bidirectional and mutually-reinforcing, then patients should be treated for both problems. Treatment for depression is less likely to be effective without dealing with the underlying cause, which is often decreased functional status. Similarly, if depression limits functional recovery, treatment for the depression should come at the same time that the patient receives therapy to improve functional status. Kotila, et al. concluded as much, noting that "[i]f depression were diagnosed and treated early, it might help patients recover more completely and/or faster, which could save community health care resources by avoiding or shortening the time of institutional care or by reducing the need for home care" (Kotila, et al., 1999, p. 311). In short, the relationship between depression and decreased functional status is bidirectional and mutually reinforcing, and post-stroke patients with low functional status would benefit from treatment for their depression in addition to physical, occupational, and speech therapy aimed at functional recovery.

Pharmacological Treatments for Post-Stroke Depression

Hackett, Anderson, and House (2005) reviewed anti-depressant medications for the treatment and prevention of post-stroke depression. Pharmacological agents used in these randomized, placebo-controlled studies included tricyclic antidepressants (TCAs), tetracyclic antidepressants (TeCAs), selective serotonin reuptake inhibitors (SSRIs), and monoamine oxidase inhibitors (MAOIs). Seven treatment trials (with 615 patients at entry) and nine prevention trials (with 479 patients at entry) were identified for inclusion in the review. Treatment duration ranged from several weeks to 12 weeks for the treatment trials and from two weeks to 12 months for the prevention trials. The most commonly used depression assessment was the *Hamilton Depression Rating Scale* (HDRS; Hamilton, 1960). Characteristics and results of the included trials are summarized in Table 1 (Treatment trials) and Table 2 (Prevention Trials). Results indicated a skewed distribution of reduced (improved) scores on mood rating scales across studies, for those patients who received antidepressant medications. However, no clear benefit of antidepressants for the treatment or prevention of depression was found.

A combination of antidepressant medication and a brief psychosocial-behavioral intervention was found to be highly effective in reducing depression in the short- and long-term (one and two years post-entry) among 101 clinically depressed patients within four months post-stroke (Mitchell, et al, 2009). Patients were randomized into a psychosocial-behavioral group that met nine times over eight weeks, or to their usual care, which included antidepressant medication. Patients in the psychosocial-behavioral intervention were taught to view depressive symptoms as "observable and modifiable behaviors that are initiated and maintained by person-environment interactions" (Mitchell, et al., 2009, p. 3072). Patients in each group were evaluated with the *Hamilton Rating Scale for Depression* (HRSD). Patients in the intervention group demonstrated significantly greater decreases in HRSD scores at one year when compared with the control group. Additionally, significantly more of the intervention group was in remission immediately post-treatment and at a one-year follow up.

Aphasia as a Cause of Depression

Aphasia affects a person's language processing. The effects of aphasia on a person's ability to communicate can range from relatively mild word-finding difficulties that occasionally lead to breakdowns in communication, to an inability to answer yes/no questions in order to have basic needs met by medical staff and other caregivers. A person with expressive aphasia can have relatively intact language comprehension, which may be especially frustrating. The person can understand language and have an idea of what he would like to contribute in a conversation, and yet be unable to access the words and grammatical constructions to do so in a coherent, intelligible manner.

Communication is the foundation of our social relationships; therefore, a person with aphasia may find his social roles severely restricted after a stroke. Hemsley and Code (1996), following a small group of individuals with aphasia, found that aphasia severity and severe depression decreased over time, while social dysfunction remained. All participants who began the study with global or expressive aphasia had improved to expressive or anomic aphasia, respectively, meaning that some had improved to a point where word-finding difficulties represented their most severe deficits, which is considered a relatively mild form of aphasia. Participants were asked to self-rate their participation in social activities at three months and nine months post-onset. Decreased participation in social activities was found at nine months, suggesting that the subjective experience of social impairment lingered even after communicative deficits had improved.

Herrmann, Bartels and Wallesch (1993) investigated depressive changes in two groups of patients with aphasia: those in the acute stage (less than three months post-onset) and those in the chronic stage (more than six months post-onset). Patients' depressive symptoms were measured using the Cornell Depression Scale (CDS; Alexopoulos, Abrams, Young, & Shamoian, 1988), which primarily involved observer ratings of the patient's symptoms, but also included a patient interview and a review of the patient's case history. Patients were rated on mood-related signs of depression, behavioral disturbances, physical signs, disturbance of cyclic functions, and

ideational disturbances. Major depression was only found in aphasic patients who were in the acute stage of recovery from stroke. However, there were no significant differences between the groups (i.e., chronic vs. acute patients with aphasia) in terms of mood-related signs, and patients with chronic aphasia were more likely to exhibit ideational disturbances, such as thoughts of suicide. Patients with chronic aphasia, while not suffering from major depression, may present with signs and symptoms of depression. In terms of the association between aphasia type and severity of depression, in the acute stage patients with non-fluent aphasia (i.e., patients with prominent expressive language deficits) had significantly higher depression scores than patients with fluent aphasia (i.e., those with impaired language comprehension); this association between aphasia type and presence of depression was not found in the group of patients with chronic aphasia. The authors concluded that the presence of depressive symptoms in acute patients with aphasia was more than a reactive depression as a result of acute illness/impairment. Rather, the profile of symptoms in these patients reflected a major depressive episode, as defined by the *Research Diagnostic Criteria* (RDC; Spitzer, Endicott, & Robins, 1978).

Hemsley and Code (1996) stated that depression in the acute post-stroke stage results from the brain damage itself, and is not an emotional reaction to the loss of functioning associated with stroke and aphasia. This was found to be the case in Herrmann, et al. (1993), in that a common site of subcortical lesion, involving the putamen and external globus pallidus, was found in all acute post-stroke patients with major depression. This association with site of lesion was not found in the chronic stages of recovery from aphasia, suggesting that depressive symptoms in these cases may be reactions to the neuropsychological, psychosocial, and functional impairments caused by the stroke (Hemsley & Code, 1996, p.568). This finding, however, would not preclude depression from also being a limiting factor in recovery from aphasia.

While depression in the acute post-stroke stage is likely due to the site of lesion, depression in the chronic post-stroke stage is more readily explained as resulting from aphasia and other neuropsychological, psychological, and functional impairments caused by the stroke.

Aphasia hinders a person's ability to interact socially and function independently, which would negatively impact emotional and psychosocial adjustment. Further, this is consistent with the earlier conclusion that decreased functional status leads to depression, as aphasia is closely analogous to decreased functional status.

Effects of Depression on Aphasia Recovery

Impairments in communication and psychosocial functioning can lead to depressive symptoms. These deficits in functional communication can be viewed much like the functional deficits observed in several large-scale stroke studies (e.g., Ramasubbu, et al., 1998) that were associated with an increased presence of depression. Given the bidirectional relationship between functional recovery and depression, the relationship between cognitive and linguistic recovery and depression is also likely to be bidirectional; cognitive and linguistic deficits may often lead to depression, and the presence of depression may limit cognitive and linguistic recovery.

Only a few studies have investigated the implications of depression for patients recovering from aphasia secondary to stroke. Astrom, Adolfsson and Asplund (1993) followed a consecutive series of stroke admissions for three years. The study set out to determine the relative contributions of cognitive impairment, lesion location and volume, cerebral atrophy, functional impairment, and social contact to post-stroke depression. However, based on assessments performed during the acute stage, three months-, twelve months, one year and two years post-onset, results of the study could also be used as evidence that post-stroke depression may limit recovery in activities of daily living. Patients who were depressed in the acute stage, based on a psychiatric interview, did not make gains in functional ability, whereas patients who were not depressed during the acute stage made significant recovery in the first twelve months after stroke. Patients in this study did not seem to recover from depression as quickly as in other studies, with only 57% recovering in the first year, and only one additional patient recovering by the three-year follow-up. However, studies used various criteria for recovery or remission of depression, which may explain the lower recovery rates found in Astrom, Adolfsson, and Asplund (1993).

Patients with aphasia in this study were significantly more likely to be depressed during the acute stage and at three months post-stroke than patients who did not have aphasia. Because patients with aphasia have been excluded from other studies investigating post-stroke depression, this association has not been widely reported (Astrom, Adolfsson & Asplund, 1993, p. 981).

Because language measures were not assessed in this study, patients with aphasia who did or did not have depression may have demonstrated different rates of recovery in cognitive and linguistic variables. However, the finding that aphasia was an independent predictor of depression has clinical significance to clinicians working with aphasic individuals, in that the presence of depression is common in this patient population and may impact recovery.

Another prospective study designed to evaluate the associations between cognitive deficits (as measured by the MMSE) and depression in a series of consecutive admissions to a university hospital was completed by Kauhanen, et al. (1999). Patients in this study were evaluated one to seven days after admission and at three and 12 months post-onset. As in other studies, functional dependence was measured with the *Barthel Index* and degree of handicap was scored with the *Rankin Scale*. Several interesting findings came from this study. First, the presence of aphasia was associated with more severe depression; 47% of patients with major depression at the 12-month follow-up had aphasia, which further supports the conclusion reached by Astrom, Adolfsson and Asplund (1993), that depression and aphasia frequently co-occur during the recovery period after a stroke. Second, at both three and 12 months post-stroke, patients with minor or major depression were more dependent in ADLs and had a greater degree of handicap, as measured by the *Barthel Index* and *Rankin Scale*. Kauhanen, et al. (1999) did not discuss the rates of recovery in ADLs or degree of handicap between the two groups, however. Nonetheless, the results suggest that depressed post-stroke patients, who often have aphasia, may present with greater deficits in cognition and independence in activities of daily living.

Fucetola, Connor, Perry, Leo, Tucker, and Corbetta (2006) conducted a cross-sectional examination of 57 patients at varying times post-onset of aphasia. The investigation primarily aimed to determine which factors most influenced functional communication in this population. Functional communication was measured with the *Communication Activities of Daily Living-2nd Edition* (CADL-2; Holland, et al., 1998), which is a structured set of tasks designed to assess a range of skills, including nonverbal communication, reading, writing, appreciation of humor, and the use of numbers. Responses are scored on the basis of how effectively the patient

communicated in a variety of contexts, with verbal and nonverbal responses accepted in most cases. Depression in this study was assessed using two of the *Visual Analog Mood Scales* (VAMS; Stern, 1997), "sad" and "angry," in which patients indicated the degree to which they experienced either of these mood states, by placing a mark on a vertical line that had a neutral face on the top and either a sad face or an angry face on the bottom.

Results of the study indicated that the combined depression measure (i.e. the combined VAMS sad and angry scales) accounted for a small, but significant proportion of the variance in CADL-2 scores. In conjunction with several measures of aphasia severity, reading comprehension at the sentence and paragraph level, presence of depression became a more significant predictor of functional communication ability. For patients with specific language deficits (in this case, deficits in reading comprehension), depression may act as a significant hindrance on functional communication, and perhaps recovery from language-based deficits as well.

Depression appears to limit recovery from aphasia, just as it limits functional improvement more generally. While the clinical evidence for this conclusion may not be as definitive as it is for some of the other conclusions of this report, the above studies are at least suggestive that depression has an independent, negative impact on recovery from aphasia. More importantly, a finding that depression limits recovery from aphasia would not be at all surprising in light of how closely analogous aphasia is to other forms of functional impairment. Insofar as depression limits functional recovery generally, it would be surprising if it did not also limit recovery from aphasia. Clearly, additional research is needed on the effects of depression on recovery from aphasia. However, the relationship between aphasia and depression, like the relationship between decreased functional status and depression, is likely to be bidirectional and mutually reinforcing.

Conclusion

Depression appears to limit functional recovery from stroke. The evidence for decreased functional recovery among depressed patients after a stroke is well-established in the literature (e.g., Morris, et al., 1992; Herrmann, et al., 1998), with consistent findings that these patients make fewer gains in functional status and cognitive performance. The evidence that depression also limits recovery from aphasia secondary to stroke is not quite as robust. However, the few studies investigating this relationship (e.g., Fucetola, et al., 1996) indicate that depression may also limit aphasia recovery. Further, both aphasia and decreased functional status are associated with an increased incidence of depression among stroke patients; patients who have difficulty communicating or performing basic ADLs are more likely to suffer from depression. One may conclude from the available literature that the relationship between low functional status and depression is bidirectional and mutually reinforcing; while decreased functional status leads to depression, depression also limits functional recovery. In light of how closely analogous aphasia is to low functional status more generally, the relationship between aphasia and depression is likely to be bidirectional and mutually reinforcing as well, although more research is needed to address this specific question.

If these relationships are bidirectional, patients should be treated for both depression and decreased functional status. While the efficacy of antidepressant medications for post-stroke patients has not been well-established, there is at least some evidence that these medications led to improved mood among patients. Clinicians working with post-stroke patients should be informed about the detrimental effects of depression on recovery from aphasia and general functional recovery, and these patients should be assessed for depression and treated if necessary. Early and effective treatment for depression would lead to better functional outcomes and help to conserve healthcare resources.

Table 1. Antidepressant Treatment Trials

Primary Author (date)	Randomization sample (active/placebo)	Assessment and Outcome Measures	Medications used	Duration	Outcome (95% CI)*
Anderson (1994)	33/33	HDRS	Citalopram (SSRI)	6 weeks	-3.2 (-5.2 to 1.3
Fruehwald (2003)	28/26	HDRS	Fluoxetine (SSRI)	12 weeks	-4.2 (-11.8 to 3.4)
Lipsey (1984)	17/22	HDRS	Nortriptyline (TCA)	4-6 weeks	-4.6 (-9.5 to 0.3)
Murray (2002)	62/61	MADRS	Sertraline (SSRI)	26 weeks	-0.9 (-4.1 to 2.3)
Ohtomo (1991)	150/135	Physician assessment	Aniracetam	12 weeks	N/A
Reding (1986)	11/6	Clinical diagnosis	Trazodone-HCl	4 weeks	N/A
Wiart (2000)	16/15	MADRS	Fluoxetine (SSRI)	45 days	-8.2 (-13.7 to -2.7)

*Outcomes reflect the differences in average change in mood scores between baseline and end of treatment, with more negative differences favoring treatment groups and more positive differences favoring control groups.

Key: DSM: *Diagnostic and Statistical Manual of Mental Disorders,* HDRS: *Hamilton Depression Rating Scale,* MADRS: *Montgomery-Asberg Depression Rating Scale,* N/A: Not available, SSRI: Selective serotonin reuptake inhibitor, TCA: Tricyclic antidepressant, TeCA: tetracyclic antidepressant.

Table 2. Prevention Trials

Primary Author (date)	Randomization sample (active/placebo)	Assessment and Outcome Measures	Medications used	Duration	Outcome (95% CI)*
Creytens (1980)	25/25	Modified SGRS	Piracetam	30 days	N/A
Dam (1996a)	18/8	HDRS	Fluoxetine (SSRI)	10 weeks	-2.4 (-7.4 to 2.6)
Dam (1996b)	17/9	HDRS	Maprotiline (TeCA)	10 weeks	-1.5 (-6.5 to 3.5)
Grade (1998)	10/11	HDRS	Methylphenidate	3-4 weeks	N/A
Palomaki (1999)	51/49	DSM-III-R	Mianserin (TeCA)	52 weeks	N/A
Rafaele (1996)	11/11	ZDS	Trazodone-HCl	45 days	-15.9 (-24.7 to -7.1)
Rasmussen (2003)	70/67	HDRS	Sertraline (SSRI)	52 weeks	N/A
Reading (1986)	3/2	Clinical diagnosis	Trazodone-HCl	4 weeks	N/A
Robinson (2000a)	17/8	HDRS	Fluoxetine (SSRI)	12 weeks	1 (-2.4 to 4.4)
Robinson (2000b)	15/8	HDRS	Nortriptyline (TCA)	12 weeks	-1 (-4.5 to 2.5)
Roh (1996)	32/33	Physician assessment	Indeloxazine	12 weeks	N/A

*Outcomes reflect the differences in average change in mood scores between baseline and end of treatment, with more negative differences favoring treatment groups and more positive differences favoring control groups.

Key: DSM: *Diagnostic and Statistical Manual of Mental Disorders,* HDRS: *Hamilton Depression Rating Scale,* N/A: Not available, SGRS: *Stockton Geriatric Rating Scale,* SSRI: Selective serotonin reuptake inhibitor, TCA: Tricyclic antidepressant, TeCA: tetracyclic antidepressant, ZDS: *Zung Depression Scale*.

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