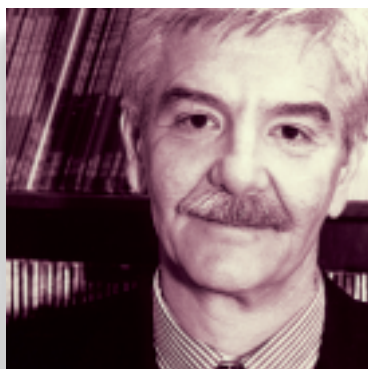


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Vascular depression: a new view of late-onset depression

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The National Institutes of Health (NIH) Consensus Development Conference noted that depression is one of the most frequent psychiatric disorders of old age, with a prevalence of 1% for major depression, 2% for dysthymia, and 8% to 15% for clinically significant depressive symptoms.¹ Over 50% of hospitalized depressed elderly patients are in their first episode.² Epidemiological studies have shown that the majority of individuals suffering from major depression or dysthymia have no history of previous psychiatric treatment.³

Earlier we suggested that late-onset depression is a heterogeneous syndrome, which, among others, encompasses patients with brain disorders that may or may not be clinically evident when the depression first appears.⁴

We have suggested that cerebrovascular disease may predispose, precipitate, or perpetuate some late-life depressive syndromes. The mechanisms of “vascular depression” include disruption of cortico-striato-pallido-thalamo-cortical (CSPTC) pathways or their modulating systems. This view is supported by the presentation of vascular depression, which consists of depressive symptoms, cognitive abnormalities, as well as neuroimaging findings that may result from CSPTC impairment. Moreover, clinical and electrophysiological evidence of CSPTC impairment, an abnormality frequently found in patients with vascular depression, appears to be associated with poor response to antidepressant treatment and early relapse and recurrence. The vascular depression hypothesis provides the conceptual background for studies that may have clinical and theoretical impact. Agents influencing dopamine, acetylcholine, and opioid neurotransmitters may be studied in vascular depression, since these are essential neurotransmitters of the frontostriatal circuitry. Drugs used for prevention and treatment of cerebrovascular disease may be shown to reduce the risk for vascular depression or improve its outcomes. The choice of antidepressants in vascular depression may depend on their effect on neurological recovery from ischemic lesions. Finally, identification of specific relationships between specific symptoms, cognitive deficits, and disability may lead to interventions that target the patients’ deficits as well as their interactions with psychosocial factors known to contribute to depression. Research can clarify the pathways to vascular depression by focusing on the site of lesion, the resultant brain dysfunction, the presentation of depression and time of onset, and the contribution of nonbiological factors.

Keywords: vascular depression; treatment resistance; recovery from ischemia; disability

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Late-onset depressives have more cognitive^{5,6} and neuroradiological abnormalities,^{7,9} greater disability,¹⁰ medical morbidity and mortality,^{11,12} and lower familial prevalence of mood disorders than elderly early-onset depressives,¹¹ although some disagreement exists.¹⁴⁻¹⁶ Studies of late-onset depression are confounded by: (i) difficulties in identification of age of onset¹⁷; and (ii) the assumption that depressive episodes have the same etiology over time, although some patients may experience episodes with different causes at different periods of their lives. Nevertheless, research on late-onset depression has provided a conceptual step for identifying more homogeneous groups of geriatric depression. Depression occurring in the context of vascular disease may account for many geriatric depression cases with rather homogeneous etiology.

Recently, we hypothesized that cerebrovascular disease can predispose, precipitate, or perpetuate a depressive syndrome in some elderly patients. We selected the term "vascular depression"¹⁸ because it is broad and encompasses depressive syndromes with diverse vascular pathogenesis. Direct testing of the vascular depression hypothesis is not possible since there is no biological test that can function as a validating criterion. However, the vascular depression hypothesis can generate studies of the outcomes, pathogenesis, and treatment of a large subgroup of geriatric depressives. We present below findings relevant to the vascular depression hypothesis and discuss their clinical and theoretical value.

Clinical studies

Depression and cerebrovascular disease often coexist. An early longitudinal study observed that cerebrovascular disease occurring 2 to 3 years prior to psychiatric admission may have contributed to the development of geriatric depression.¹⁹ Post and Schulman noted a high incidence of cerebrovascular disease in elderly depressed patients and suggested that the resultant brain damage predisposes to late-life depression.²⁰ Patients with vascular diseases often have depression. In a sample of 15 186 patients treated in a primary care setting, we observed that those with significant depressive symptomatology had a higher frequency of vascular disease than nondepressed patients. Approximately 8% of depressed patients had hypertension, 9% had ischemic heart disease, 13% had peripheral vascular disease, 7% had stroke, and 9% had heart failure.²¹ The

corresponding percentages for nondepressed patients were 4%, 4%, 4%, 5%, and 4%, respectively. In a prospectively followed population of 248 patients who underwent coronary artery bypass, 43% had significant depressive symptomatology prior to surgery.²² Similar findings have been reported by others who observed that patients with hypertension,²³ coronary artery disease,²⁴ and vascular dementia²⁵ often develop depression. Patients with vascular dementia have more retardation, depression, and anxiety than Alzheimer's patients with similar cognitive impairment.²² Unlike Alzheimer's disease, vascular dementia is a subcortical dementia. Therefore, these findings raise the question whether damage of subcortical structures by vascular lesions contributes to depression.

Ischemic brain lesions in geriatric depression

In a series of elegant studies, Robinson and Starkstein²⁶ and other investigators²⁷⁻²⁹ demonstrated that depression is a frequent complication of stroke. Stroke with neurological symptoms and signs occurs in a relatively small number of geriatric depressives. However, "silent stroke" without neurological signs is frequent in elderly depressed populations. In a Japanese sample, silent cerebral infarction was found in 83% of major depressives older than 65 years.³⁰ Silent cerebral infarction was observed in 94% of patients with onset of first depressive episode after 65 years of age. While this investigation did not include normal controls, other studies suggest that silent cerebral infarction occurs in 17% of healthy individuals in their fifties and 21% of individuals in their sixties.³¹ A study of Caucasian populations found that silent stroke occurs in 23% of individuals older than 65 years; in 72% of them the lesions exceeded 3 mm in diameter.³² These findings suggest that vascular brain lesions can be found in a significant number of elderly patients with late-onset depression.

Elderly depressives, and especially late-onset depressives, have white matter hyperintensities (WMHs) more frequently than nondepressed individuals.³³⁻³⁷ WMHs correspond to areas of arteriolar ectasia, enlargement of perivascular spaces, and myelin pallor associated with arteriosclerotic changes of perforating arteries.³⁸ In asymptomatic individuals, WMHs were found to be associated with extracranial carotid artery disease, reduced cerebral blood flow, and a history of hypertension, dia-

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betes, cardiac disease.³⁹ Not all WMHs are due to vascular disease. However, geriatric depressed patients without cerebrovascular risk factors were found to have similar degree of WMHs to nondepressed controls.⁴⁰ The temporal relationship between the formation of WMHs and development of depression has not been systematically investigated. However, in one case, depression developed following a large increase in WMHs.⁴¹

We used transcranial sonography to compare cerebral blood flow velocity between elderly patients with major depression and normal elderly controls.⁴² Depressed patients had reduced blood flow velocity in the middle, anterior, and posterior cerebral artery (*Figure 1*). Blood flow velocity was strongly correlated with overall cognitive dysfunction, but the strongest correlations were those with initiation/perseveration scores of the Mattis Dementia Rating Scale.⁴³

Lesions in the basal ganglia are associated with depression. Approximately 40% to 75% of depressed elderly patients have lesions of the thalamus and basal ganglia,³⁶ while only 5% of normal elderly controls have such lesions, and their lesions are smaller than the lesions of elderly depressives.

The clinical presentation of vascular depression

Vascular disease contributes to cognitive impairment. The incidence of dementia 1 year after the first cerebral infarct was found to be 9 times greater than expected.⁴⁴ Lacunar infarcts in the basal ganglia, thalamus, and deep white matter, but not cortical infarcts, appear to be associated with high prevalence of dementia in Alzheimer's patients.⁴⁵

Declining cognitive performance, perhaps due to unrecognized vascular disease, was found to be a stroke risk factor.⁴⁶ WMHs were correlated with impaired attention, mental speed, and executive functions⁴⁷⁻⁵⁰ in non-depressed subjects.

Late-onset depressives with vascular risk factors were reported to have greater cognitive impairment than elderly patients with early-onset depression without vascular risk factors.^{18,51} Executive functions were most affected. In vascular dementia, a subcortical syndrome frequently associated with depression, the extent of WMHs correlated with cognitive impairment.⁵² In cortical or basal ganglia stroke, cognitive impairment was associated with high incidence and increased severity

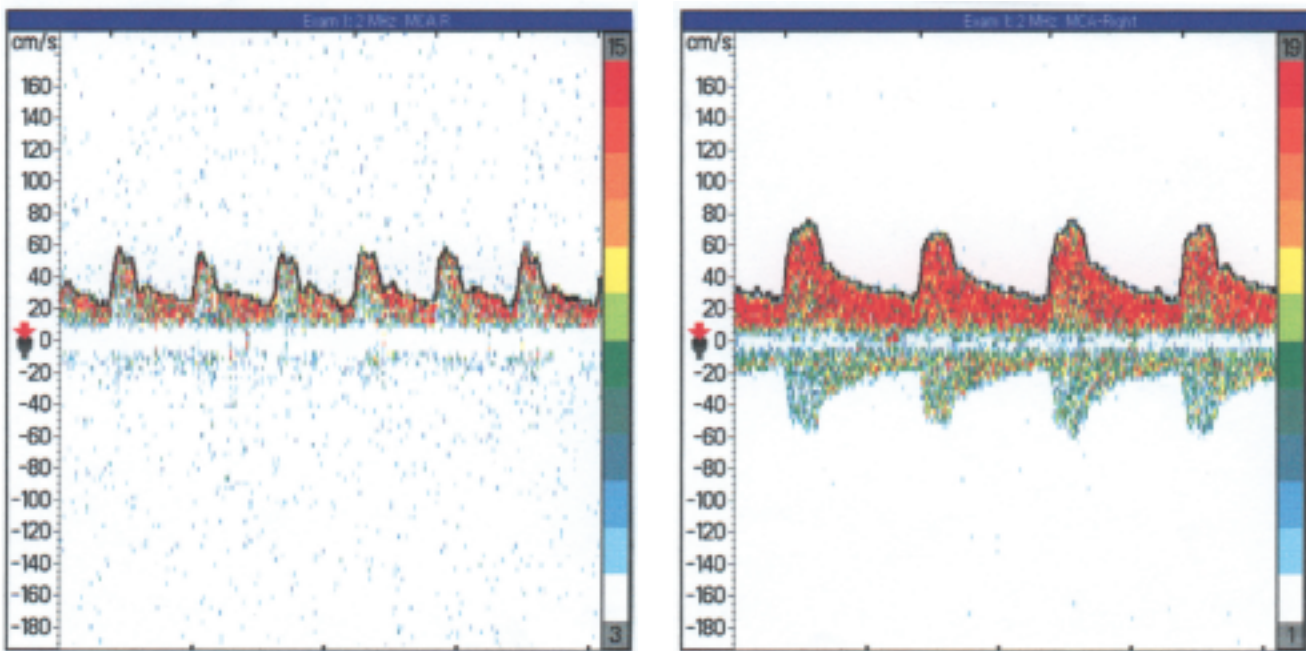


Figure 1. Blood flow velocity in the middle cerebral artery in an 82-year-old patient with major depression (left) and a 79-year-old psychiatrically normal subject (right). Blood flow velocity was measured with transcranial sonography.

of depression.²⁶ These findings suggest that cerebrovascular lesions lead to depression and cognitive impairment through related mechanisms.

Patients with late-onset major depression and vascular risk factors or ischemic brain lesions appear to have more psychomotor retardation, apathy, and lack of insight, and less agitation and guilt than geriatric patients with early-onset depression without vascular risk factors.^{42,53} Moreover, patients with vascular depression have greater impairment in frontal functions and more disability.¹⁸ Identification of relationships among specific symptoms, lesion location, and overall damaged tissue can provide information about the pathogenesis of vascular depression.

Localization of lesions

The clinical presentation of vascular depression suggests that damage of subcortical structures and their connections to some frontal lobe structures are the contributing pathophysiological abnormality. This view is further supported by the observation that subcortical dementing disorders, including vascular dementia, Parkinson's disease, and Huntington's disease, are more likely to result in depression than cortical dementias.⁵⁴ In contrast, patients with Alzheimer's disease develop depression less frequently and have less severe depressive syndromes than patients with subcortical dementias.⁵⁵ Moreover, development of depression is more likely to occur in Alzheimer's patients with subcortical atrophy.⁵⁶

The pathogenetic role of subcortical lesions in depression is supported by studies of stroke. Stroke of the caudate head is the most likely to result in depression, while thalamic stroke has a rather low incidence of depression.⁵⁷ Most depressed patients with silent cerebral infarction have lesions in the perforating arteries territory.³⁰ Similarly, WMHs of elderly depressives are most prominent in subcortical and frontal areas.³⁴⁻³⁶ Reduced size of the head of the caudate⁵⁸ and putamen⁵⁹ has been observed in neurologically unimpaired depressed patients.

Lesions of the left hemisphere often result in depression.²⁶ Depression may occur after right hemisphere stroke,^{60,61} despite difficulties in the recognition of depression due to anosognosia. Depressed mood is infrequent in right-sided stroke, but vegetative signs

and abnormal dexamethasone suppression test are equally frequent in left and right stroke.⁶⁰ In left hemisphere stroke, anterior lesions were associated with depression more often than posterior lesions.²⁶ A more complex lesion-location relationship was observed in right stroke. Immediately after right stroke, depression was more severe in patients with posterior lesions,⁶² while the severity of depression occurring within 3 to 6 months after right stroke was associated with anterior lesions.^{62,63} These observations suggest that poststroke depression is mediated by different mechanisms, especially in patients with right hemisphere lesions.

The pathogenetic contribution of the basal ganglia and their prefrontal connections is supported by functional neuroimaging studies. Most functional neuroimaging studies of major depression observed hypoactivity in frontal regions,⁶⁴⁻⁶⁶ including the dorsolateral, inferior and medial/anterior cingulate, and the caudate nucleus,^{67,68} but disagreement exists.⁶⁹

Prefrontal and limbic dysfunction in depression has been suggested by positron emission tomography (PET) activation studies of younger adults. Intravenous administration of procaine can induce emotional experiences associated with increased blood flow in the anterior temporal lobes, inferior frontal lobes, and anterior cingulate gyri in normal subjects.⁷⁰ However, minimal activation of these regions was noted in depressives who have the same experiences as the normal subjects.⁷⁰

Left prefrontal areas may participate in the development of sad mood. Transient sadness increases the activity of the left anterolateral prefrontal cortex,⁷¹ left anterior cingulate, left medial frontal cortex, and left anterior limbic system.⁷² The relationship of these findings to depression is unclear. However, they suggest that the left prefrontal system and its connections to limbic areas mediate some aspects of depressive symptomatology.

We used high-sensitivity H₂¹⁵O PET with an activation task to probe frontotemporal function in elderly patients with severe major depression (Hamilton Depression Rating Scale >30) and elderly controls.⁷³ Each session included 4 scans during a paced word generation condition with phonemic cues, and 4 scans in a paced letter repetition sensorimotor control state. Group differences in brain activity were identified with statistical parametric mapping according to the general linear model at each voxel. Brain activity during word

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generation (activation vs control states) was decreased bilaterally in the dorsal anterior cingulate ($P < 0.001$) and the hippocampal areas in depressed elderly patients compared to controls (*Figure 2*). These findings suggest that the striatofrontal circuitry and its connections to the hippocampus may be the neural substrates of some of the cognitive and psychomotor symptoms and signs of geriatric depression.

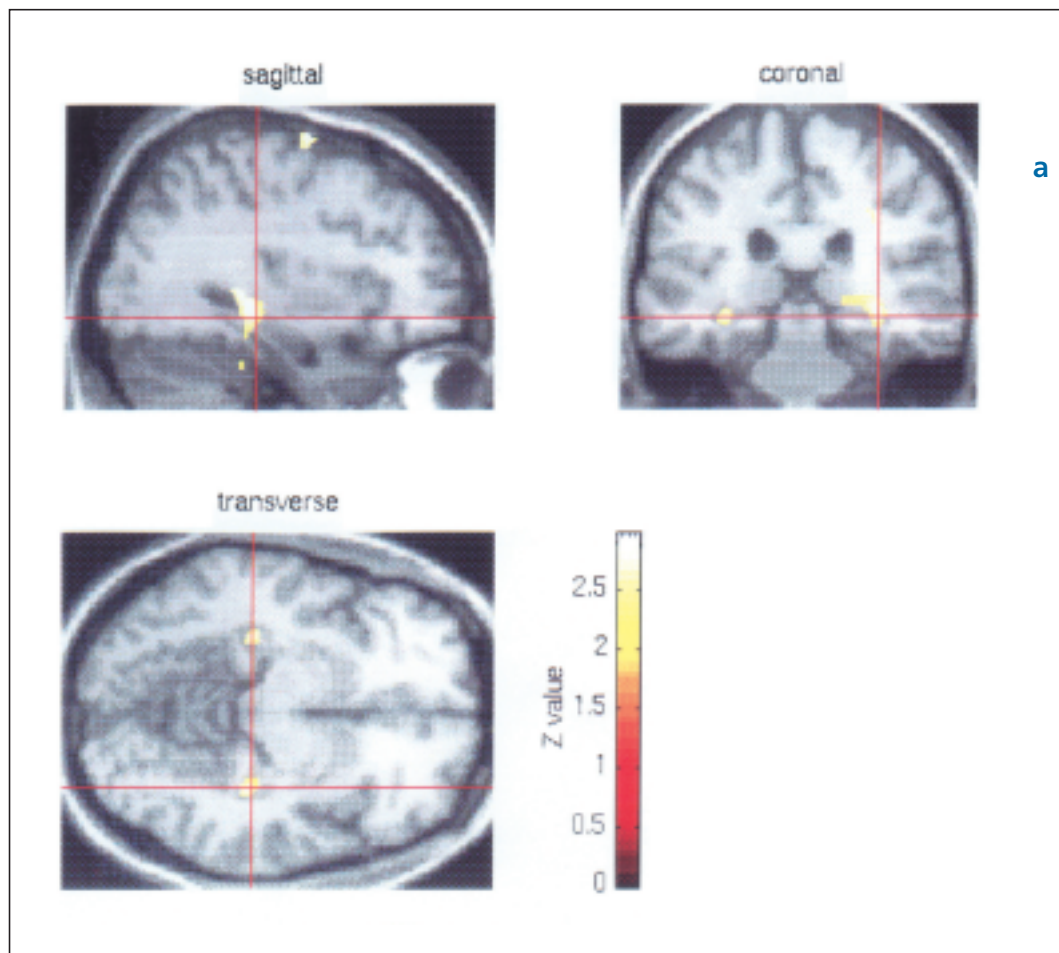
Some aspects of the depressive syndrome are associated with rather specific functional brain abnormalities in younger depressives. Psychomotor slowing was found to be correlated with decreased flow in the left anterolateral cortex, while cognitive impairment correlated with decreased activity in the left medial prefrontal area.⁷⁴ Anxiety occurring in the context of depression was associated with increased activity in the right posterior cingulate and bilateral inferior parietal areas.⁷⁵ These observations suggest that distinctive depressive syndromes may result from vascular lesions that disrupt specific prefrontal-subcortical circuits.

Three cortico-striato-pallido-thalamo-cortical (CSPTC) pathways may be relevant to depression.^{76,77} Damage of the orbitofrontal circuit may lead to disinhibition, irritability, and diminished sensitivity to social cues.⁷⁶ Damage of the anterior cingulate may result in apathy and reduced initiative.⁷⁶ Damage of the dorsolateral circuit may result in difficulties in set shifting, learning, and word list generation.⁷⁶ These behavioral abnormalities resemble in part the depressive syndrome.

Treatment response in vascular depression

Several studies suggest that vascular depression may have a poor outcome. Late-onset depression, an entity that often occurs in the context of vascular disease, is a rather chronic disorder.⁷⁸ In elderly depressives, leukoencephalopathy was found to be associated with low quantitative electroencephalogram (qEEG) coherence^{79,80}; low qEEG coherence predicted failure to recover, residual depressive symptomatology, increased mortality, and disability.^{79,80}

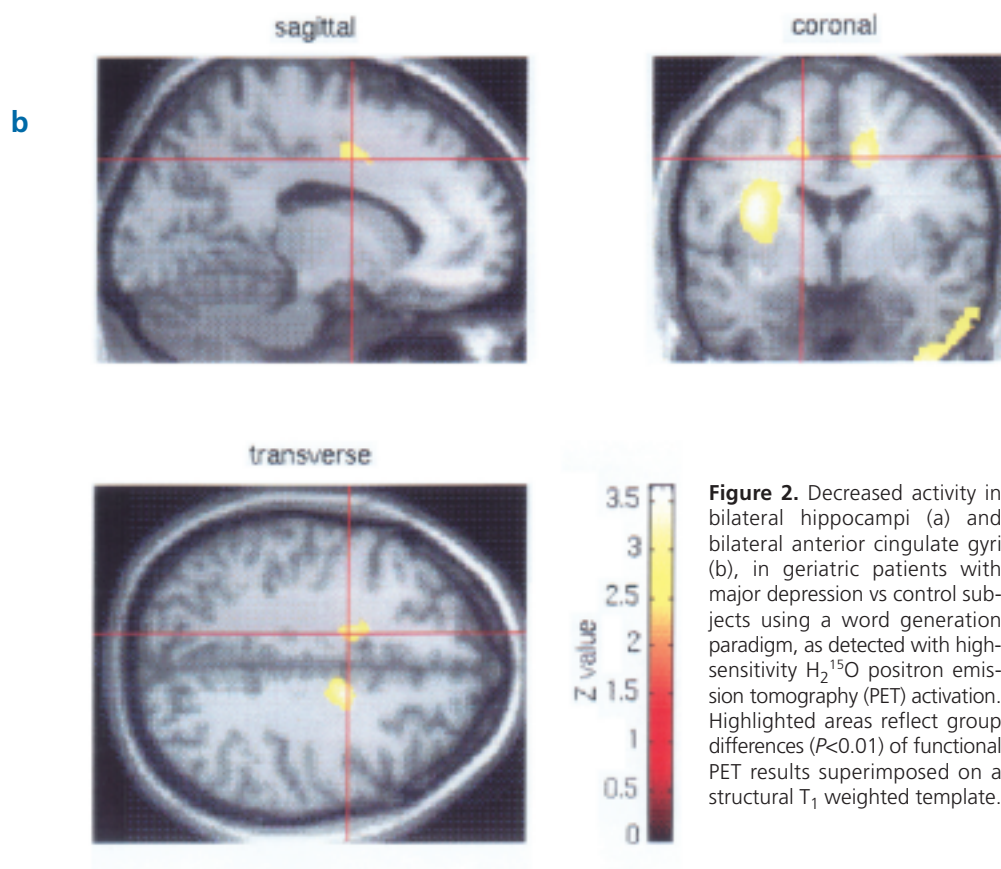
We studied the relationship of clinical, neuropsychological, and electrophysiological measures of prefrontal dysfunction with treatment response in elderly patients with major depression.⁸¹ Abnormal initiation/perseveration scores of the Dementia Rating Scale, psychomotor retardation, and long P300 latency



of the auditory evoked potential predicted 58% of the variance in change of depression scores from baseline to 6 weeks. Depressed patients who remained symptomatic had more abnormal initiation/perseveration scores and longer P300 latency compared with depressed patients who achieved remission and control subjects. There were no differences between the last two groups. These findings suggest that prefrontal dysfunction is associated with poor or delayed antidepressant response in depressed elderly patients. Although not very specific, abnormal initiation/perseveration scores, psychomotor retardation, and long P300 latency are thought to reflect striatofrontal impairment, an abnormality often caused by vascular disease.⁸² We are currently conducting a study of average evoked responses following the Stroop response inhibition test. The Stroop requires integrity of the anterior cingulate and thus is more specific to frontal

dysfunction than our earlier tests. Preliminary findings suggest that, compared with controls, depressed elderly patients overrecruit prefrontal neurons during the response inhibition task (Figure 3). Further research will examine whether this abnormality is associated with poor response to antidepressants.

In another study, we investigated the relationship of executive and memory impairment to relapse, recurrence, and the course of residual depressive symptoms and signs after remission of geriatric major depression.⁸³ The subjects of this study, after remission of depression, received continuation treatment with nortriptyline at plasma levels 60 to 150 ng/mL for 16 weeks and were then randomly assigned to either nortriptyline maintenance therapy or placebo for a period of up to 2 years. Abnormal initiation/perseveration scores, but not memory impairment, were associated with relapse (Figure 4) and recurrence (Figure 5) of geriatric depression and with fluctuations of depressive symptomatology in the whole group and in subjects who never met criteria for relapse or recurrence during the follow-up period. Memory impairment, disability, medical burden, social support, and history of previous episodes did not significantly influence the outcome of depression in this sample. These findings provide the rationale for studies of the role of specific prefrontal pathways in predisposing or perpetuating depressive syndromes or symptoms in the elderly. Abnormal initiation/perseveration scores reflect striatofrontal dysfunction, an abnormality associated with vascular depression. While direct studies are needed, these findings suggest that vascular depression has a chronic and relapsing course.



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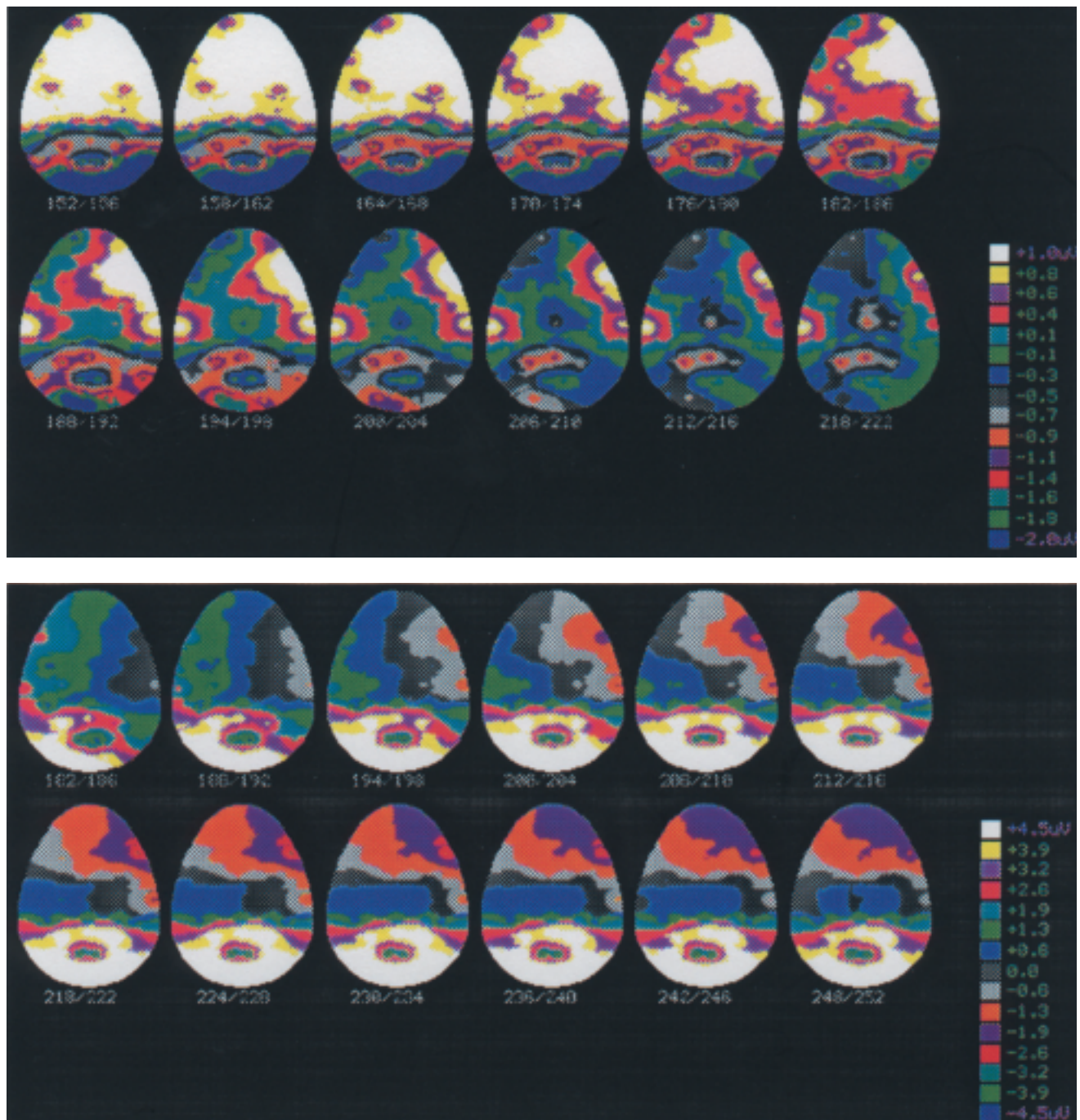


Figure 3. Increased frontal activation in a 73-year-old patient with major depression (top) compared with a 70-year-old psychiatrically normal subject (bottom). Evoked responses were recorded following the Stroop Color Interference task. A total of 162 color-congruent words and 162 color-incongruent words presented for 500 milliseconds every 2 seconds in random order. Topographical maps of evoked potential activity were constructed after sorting the correct responses to the incongruent task and estimating the voltage distributions across the scalp.

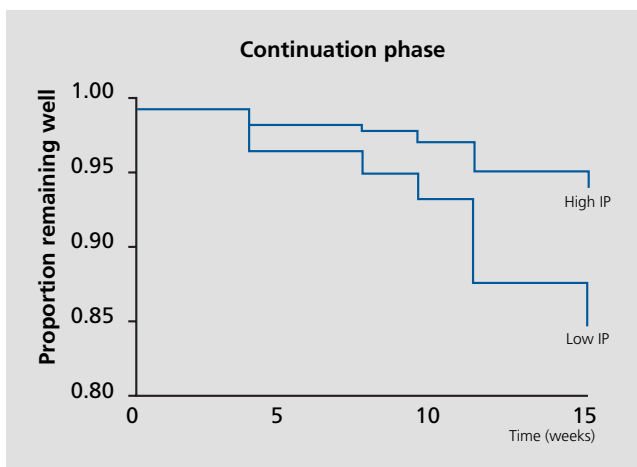


Figure 4. Cox proportional hazard analysis of 57 elderly patients who had recovered from major depression and received continuation treatment with nortriptyline at plasma levels of 60 to 150 ng/mL. Seven patients had a relapse during continuation phase. Fitted survival curves with low (first quartile) and high (3rd quartile) scores of the initiation/perseveration (IP) domain of the Mattis Dementia Rating Scale are shown.

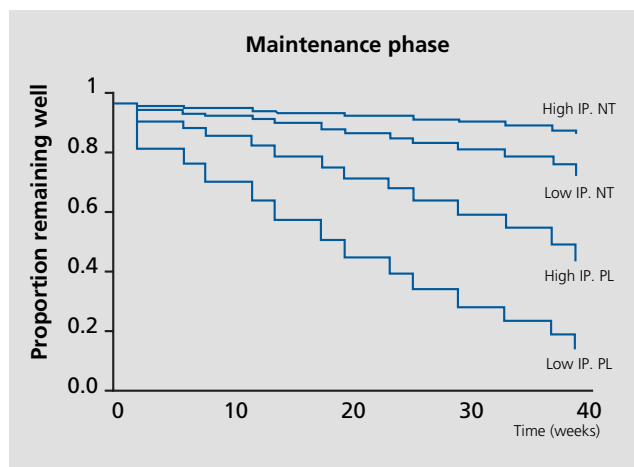


Figure 5. Cox proportional hazard analysis of 43 elderly patients who had recovered from major depression, completed a 16-week continuation treatment with nortriptyline at plasma levels of 60-150 ng/mL and were randomly assigned to nortriptyline (NT) or placebo (PL) maintenance treatment. Fifteen patients had a recurrence during maintenance treatment phase; 4 were on nortriptyline and 11 were on placebo. Fitted survival curves with low (first quartile) and high (3rd quartile) scores of the initiation/perseveration (IP) domain of the Mattis Dementia Rating Scale are shown.

Mechanisms of vascular depression

Two broad hypotheses can be tested regarding localization of lesions in vascular depression. The first hypothesis is that small lesions disrupting critical pathways may precipitate vascular depression. This hypothesis is supported by stroke studies showing that lacunar infarcts of the left caudate head or the left frontal pole often lead to depression.²⁶ The direct lesion-depression pathway may account for vascular depression cases that develop after stroke.

The second hypothesis is that accumulation of lesions exceeding a threshold predisposes to depression. This hypothesis is most applicable to patients with neurologically silent lesions or an old stroke. The threshold concept is supported by the observation that a total area of WMHs exceeding 10 cm² may result in impaired attention and executive skills.⁸² Similar impairments have been noted in late-onset depression with vascular risk factors.⁸⁴⁻⁸⁷ Vascular lesions may damage glutamergic fibers from cortical areas to the striatum, or the GABAergic neurons of the limbic-basal ganglia circuits and alter the input to cortex.⁸⁸ Since these systems are “redundant,” depressive symptoms may appear if the

overall damage exceeds a critical level and leads in increased inhibitory CSPTC input. Another mechanism may involve damage of catecholamine neurons by white matter lesions at the pons, resulting in reduction of stress responses.⁷⁴ A third mechanism postulates disruption of control exerted by the orbitofrontal cortex on the serotonergic raphe nuclei.⁸⁹ We have reported that depressives with vascular risk factors have greater dysfunction in auditory transmission at the pons than geriatric depressives without vascular risk factors or elderly normal controls.⁹⁰ These putative mechanisms suggest that lesions at various sites may result in depression through direct disruption of the CSPTC circuits or their modulating systems.

The “threshold hypothesis” postulates vulnerability that may be conferred by the lesions themselves or by a broader cerebrovascular disturbance that compromises pathways relevant to depression. Nonbiological factors may be required to trigger depression in predisposed patients. Depression developing 3 months after stroke was found to be predicted by impairment in activities of daily living, while depression occurring 12 months after stroke was predicted by social isolation.⁹¹ Other studies have shown that reverse occipital

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asymmetry (right larger than left), absence of ventriculomegaly, and absence of family history of mood disorders are associated with lower frequency of post-stroke depression.²⁶ Studies of outcomes of patients with vascular disease or risk factors can identify biological and nonbiological mechanisms that mediate or protect against depression.

Prevention of vascular depression

The vascular depression hypothesis provides the conceptual background for primary prevention of geriatric depression by modifying risk factors for cerebrovascular disease. Hypertension is a significant risk factor for stroke.⁹²⁻⁹⁴ Treatment of hypertension⁹⁵ and hypercholesterolemia⁹⁶ reduces cerebrovascular morbidity and mortality. Warfarin and aspirin reduce the risk of stroke in patients with atrial fibrillation.⁹⁷ Ticlopidine,⁹⁸ aspirin,^{98,99} and dipyridamole⁹⁹ may prevent future stroke in patients with transient ischemic attacks or ischemic stroke. Studies are needed to ascertain whether antihypertensive, anticholesterolemic, and antiplatelet agents alter the course of vascular depression. Antiplatelet agents may prove to be effective in preventing further vascular damage occurring during depressive episodes, when the serotonin-mediated thrombogenic platelet response is enhanced.^{100,101} In addition, longitudinal studies of patients with vascular depression can evaluate the efficacy of these agents in improving the course of illness. Drugs that reduce damage after stroke may be relevant to vascular depression. These include thrombolytic agents, calcium- and sodium-channel antagonists, *N*-methyl-*D*-aspartate (NMDA) receptor antagonists, glutamate synthesis inhibitors, glutamate-release inhibitors, γ -aminobutyric acid (GABA) antagonists, gangliocides, aminosteroids, antioxidants, growth factors, and antiapoptotic agents.¹⁰² The role of these drugs in the prevention and treatment of vascular depression can be examined in patients with ischemic events participating in acute intervention and secondary prevention trials.

Treatment of vascular depression

Psychotropic drugs used in depressed elderly patients may influence recovery from ischemic lesions. Animal studies suggest that the dopamine receptor blocker haloperidol, the α_1 -adrenergic receptor antagonists tra-

zodone and amitriptyline, the α_2 -adrenergic receptor clonidine, and GABA agonists such as diazepam and phenytoin interfere with motor recovery after ischemic lesions.¹⁰²⁻¹⁰⁴ In contrast, amphetamine, desipramine, the dopamine agonist bromocriptine, and the α_2 -adrenergic receptor antagonists yohimbine and idazoxan may be beneficial to recovery from ischemic injury.¹⁰²⁻¹⁰⁴ A clinical study has observed that fluoxetine may facilitate and maprotiline may hinder recovery in poststroke hemiplegic patients undergoing rehabilitation.¹⁰⁵ Studies may examine which psychotropic agents influence the incidence of poststroke depression or alter the course of vascular depression, and identify antidepressants suitable for prophylaxis of vascular depression.

The presence of subcortical abnormalities and their adverse impact on the treatment response and the long-term outcome of vascular depression provide the rationale for studies of agents that influence the neurotransmitter systems of frontostriatal circuitry. Further research may determine the efficacy of drugs acting on the dopamine, acetylcholine, and opiate systems of prefrontal pathways in patients with vascular depression. We have observed a relationship between disability and abnormal scores of initiation/perseveration and psychomotor retardation,¹⁰ abnormalities that frequently occur in vascular depression. Disability is also associated with anxiety and depressive ideation in depressed elderly patients.¹⁰ Cognitive behavioral therapy combined with rehabilitation approaches have been found to reduce depression and improve quality of life.¹⁰⁶ Such interventions may be useful in disabled patients with vascular depression provided that they are individualized and address the cognitive deficits of these patients.

Conclusion

Clinical and neuroimaging studies suggest that cerebrovascular disease may predispose, initiate, or perpetuate late-life depression, perhaps by compromising the integrity or regulation of CSPTC systems. The heuristic value of the vascular depression hypothesis is that it provides the background for studies of mechanisms of depression. Lesions at specific locations may promote, have no effect, or even protect patients from depression. The lesion burden concept may be relevant to some cases of vascular depression. Structural and functional imaging and electrophysiological techniques can quantify specific lesions and total lesion

burden and study the functional changes associated with lesions.

The clinical significance of the vascular depression concept is that it can lead to new pharmacological and psychosocial prevention and treatment models. Drugs used in the prevention and treatment of cerebrovascular disease may be studied for their ability to reduce the risk for depression in patients with vascular risk factors or reduce chronicity, recurrence, cognitive impairment, and disability in vascular depression. The long-term efficacy of specific antidepressants can be investigated in depressed patients at risk for new vascular lesions, since basic research suggests that some antidepressants, and not others, promote recovery after ischemic brain lesions. Finally, the efficacy of agents influencing dopamine, acetylcholine, and opioid neurotransmitters may be studied in vascular depression, since these neurotransmitters mediate the function of the CSPTC pathways, which are often compromised in vascular depression.

Studies of affective symptoms and cognitive deficits and their relationship to short-term and long-term outcomes of vascular depression can identify pathophysiological meaningful abnormalities. Linking a cognitive abnormality to a specific outcome of depression suggests that this abnormality is relevant to the mechanisms of the depressive disorder. Since some cognitive dysfunctions have known functional imaging correlates, it may prove feasible to use simple-to-administer neuropsychological tests and identify the role of specific functional abnormalities on the course of vascular depression. Finally, identification of specific relationships between symptoms, cognitive deficits, and disability may lead to sharply focused interventions that take into consideration the interaction of the patients' deficits with psychosocial factors that contribute to depression. □

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Depresión vascular : una nueva perspectiva de la depresión de comienzo tardío

Lemos sugerido que la enfermedad cerebrovascular puede predisponer, precipitar o perpetuar algunos síndromes depresivos que aparecen en la edad avanzada. Los mecanismos de la “depresión vascular” incluyen la interrupción de las vías córtico-estriato-pálido-tálamo-corticales (CEPTC) o de sus sistemas de modulación. Esta perspectiva se ve apoyada por el modo en que se manifiesta la depresión vascular, la cual consiste en síntomas depresivos, anomalías cognitivas, y constataciones específicas en neuroimágenes, que parecen resultar del deterioro de las vías CEPTC. Además, se asocia a las pruebas clínicas y electrofisiológicas del deterioro de estas vías, lo cual es una anomalía frecuentemente observada en pacientes con depresión vascular, una respuesta insuficiente al tratamiento antidepressivo y una pronta recaída y recidiva. La hipótesis de la depresión vascular aporta un sustrato conceptual para estudios que podrían tener un importante impacto clínico y teórico. Deberían estudiarse los fármacos que influyen en los neurotransmisores dopaminérgicos, acetilcolinérgicos y opiáceos en la depresión vascular, ya que se trata de neurotransmisores esenciales del circuito frontoestriatal. Los fármacos utilizados en la prevención y tratamiento de la enfermedad cerebrovascular parecen ser eficaces para reducir el riesgo de depresión vascular o para mejorar sus consecuencias. La elección de los antidepressivos para tratar la depresión vascular depende de sus efectos sobre la recuperación neurológica de las lesiones isquémicas. Finalmente, la identificación de las relaciones específicas entre los síntomas específicos, los déficits cognitivos y la consiguiente incapacidad puede conducir a intervenciones dirigidas a los déficits de los pacientes y sus interacciones con factores psicociales que, como es sabido, contribuyen a la depresión. La investigación puede esclarecer las causas de la depresión vascular, concentrándose en el sitio de la lesión, en la disfunción cerebral resultante, en la manifestación de la depresión en su momento de aparición y en la contribución de los factores no biológicos.

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La dépression vasculaire : une nouvelle approche de la dépression du sujet âgé

Nous avons suggéré que les maladies cérébrovasculaires favorisent, accélèrent ou perpétuent certains syndromes dépressifs du sujet âgé. Les mécanismes de la " dépression vasculaire " incluent une interruption des voies cortico-striato-pallido-thalamo-corticales (CSPTC) ou de leurs systèmes régulateurs. Ce point de vue est étayé par le tableau de cette forme de dépression qui combine des symptômes dépressifs, des troubles cognitifs et des données obtenues en imagerie cérébrale, lesquelles résulteraient des altérations des voies CSPTC. En outre, les altérations cliniques et électrophysiologiques reflétant un dysfonctionnement des voies CSPTC sont fréquemment retrouvées chez les patients souffrant de dépression vasculaire et sont associées à une réponse pauvre aux traitements antidépresseurs, à des rechutes précoces et à des récidives. L'hypothèse de la dépression vasculaire constitue une base conceptuelle pour des études qui peuvent avoir un impact clinique et théorique. Les agents qui influent sur certains neurotransmetteurs comme la dopamine, l'acétylcholine et les opioïdes peuvent être étudiés dans cette dépression, car ceux-ci jouent un rôle essentiel dans le circuit frontostriatal. Les médicaments utilisés dans la prévention et le traitement des maladies cérébrovasculaires pourraient avoir un effet démontré sur le risque de dépression vasculaire ou améliorer son pronostic. Le choix d'antidépresseurs adaptés à ce syndrome peut dépendre de leur effet sur la récupération neurologique qui succède aux lésions de nature ischémique. Au bout du compte, la mise en évidence de relations spécifiques entre les symptômes caractéristiques, les troubles cognitifs et le handicap pourrait déboucher sur des interventions visant à la fois les déficits et leurs interactions avec les facteurs psychosociaux qui contribuent à la dépression. La recherche peut clarifier les voies impliquées dans la dépression vasculaire en se focalisant sur le site des lésions, le dysfonctionnement cérébral qui en résulte et la présentation de la dépression au moment où elle s'installe, sans oublier la contribution des facteurs non biologiques.

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