

Cerebral Blood Flow

Jennifer Horner and Rebecca Chacko
Duke University Medical Center, Durham, North Carolina

Panel: Application of Special Neurodiagnostic
Techniques to Aphasiology

INTRODUCTION

The purpose of this paper is to provide the reader a general understanding of the technology, advantages, and limitations of the cerebral blood flow (CBF) technique as it applies to clinical aphasiology. From our review of over 100 studies in neurology, neurosurgery, neuropsychology, and neuro-linguistic journals, abstracts of the International Neuropsychological Society and various symposia proceedings and texts, we have abstracted those we consider to be both representative and important (see Appendix).

Hundreds of studies have been published since the first CBF research by Kety and Schmidt (1945). The work of Meyer and his colleagues (Meyer, Shinohara, Kanda, et al., 1970; Meyer, Kanda, Fukuuchi, et al., 1971) was a milestone for CBF research as it pertains to our special interest, stroke and aphasia. The following discussion provides an overview of CBF literature regarding 1) methodological considerations, 2) normal brain-behavior relationships, 3) diagnosis and management of neurogenic disorders, 4) recovery from stroke, and 5) recovery from aphasia per se.

METHODOLOGICAL CONSIDERATIONS

Four major methodological considerations for CBF research are described by Stump and Williams (1980). The first is choice of radioisotope. While different radioisotopes can be used in CBF studies, Xenon 133 is popular in current CBF methodology because it is inert (i.e., chemically stable), odorless, and readily diffusible.

The second methodological consideration is the mode of infusion of the radioisotope into the brain; either injection or inhalation. The injection technique has several disadvantages. Intracarotid injection is invasive. Injection study of CBF is limited to 1 hemisphere at a time. Injection studies usually are limited to patients requiring diagnostic angiography. In contrast, the inhalation approach is noninvasive. Equally important to neuro-behavioral studies is the fact that both hemispheres can be studied at the same time. The inhalation technique places no restriction on patient type. Finally, because of rapid clearance, exposure to radiation is minimal. For these reasons, the inhalation technique is widely used in current research. It is beyond the scope of this paper to discuss all the pros and cons of each approach. A study by Reivich and colleagues (Reivich, Obrist, Slater, et al., 1975) describes a strong correlation between the 2 approaches, but others have challenged this finding, with arguments on both sides.

The third methodological consideration is the method of monitoring radiation uptake into, and clearance from, the brain. Such monitoring is vital to the validity and reliability of CBF studies (Deshmukh and Meyer, 1978). One type of apparatus for setting up radiation detector probes is the so-called "block," shown in Figure 1. The other type is the "helmet," also shown in Figure 1. The placement and angle of the probes is important to

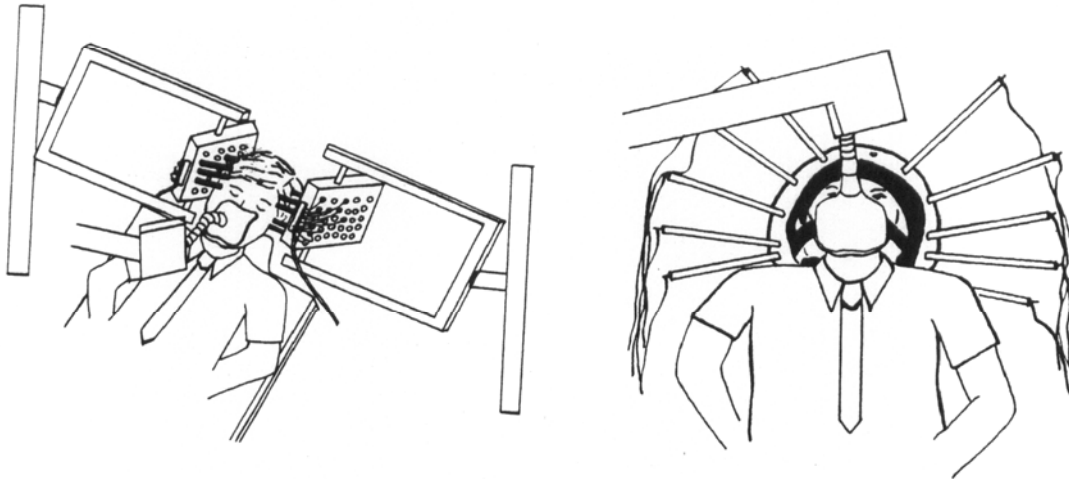


Figure 1. Apparatus used in CBF studies showing the placement of radioisotope detector probes on the skull. Left=block. Right=helmet. (Artist's reproduction based on illustration in Desmukh and Meyer, 1978.)

obtaining accurate measurements. Similarly, the number of probes is important. The literature describes the use of as few as 8 probes per hemisphere and as many as 254. A popular number is 16, or 32 for the whole brain.

The fourth methodological consideration is the approach to data analysis and graphic display of CBF values. Blood flow is measured in milliliter/gram/minute (ml/gram/min.). Typically, a computerized visual display is provided, with different colors representing different blood flow rates, ranging from 20 to 80 ml/gram/min. (e.g., Hougaard, Oikawa, Sveinsdottir, et al., 1976).

NORMAL BRAIN-BEHAVIOR RELATIONSHIPS

Brain-behavior relationships have been studied widely using the CBF technique with neurologically normal individuals. For example, Lassen and Roland (1983) studied regional CBF (rCBF) in normal adults under 3 modalities of stimulation. They found distinct regional differences in blood flow across stimulus conditions. As expected, auditory stimulation resulted in increased temporal lobe blood flow; tactile stimulation resulted in increased parietal flow; and, visual stimulation resulted in increased occipital flow. Moderate flow increases occurred in the frontal lobe also in all conditions. In this study, multimodality stimulation did not result in increased blood flow in the temporal-parietal-occipital junction, disputing the concept of a multimodality or "supramodal" association area in the posterior hemisphere.

As stated earlier, the use of the inhalation approach allows the simultaneous measurement of both hemispheres either at rest or during stimulation. First, a mean hemisphere blood flow value for each hemisphere is obtained. Then, a percentage of deviation in blood flow from the hemispheric mean is determined for each region. Maximilian's (1982) study of neurologically normal individuals showed two things: 1) in normal individuals,

rCBF at rest is remarkably similar in the left and right hemispheres, and 2) again, at rest, homologous areas in the frontal lobes show relatively greater flow than posterior cortical areas.

This pattern of relatively high rates of blood flow frontally at rest changes when the brain is aroused or activated, or must accomplish a mental task that requires effort. For example, Ingvar (1975) studied normal rCBF responses under various stimulus conditions. The pattern of rCBF at rest (that is, in the pre-stimulation baseline) was distinctly frontal. Of special interest were his findings regarding rCBF during talking and reading. During talking (automatic speech), an upward shift in blood flow occurred in premotor, Rolandic, and Sylvian regions. This pattern has been referred to as the "z pattern." Oral reading of a simple text showed a similar "z pattern" but with more pronounced rCBF in the occipital cortex. In this and other studies of rCBF during speech, the participation of Broca's area (paradoxically) is not consistently seen (e.g., Larsen, Skinhoj and Lassen, 1978; Soh, Larsen, Skinhoj and Lassen, 1978).

CLINICAL APPLICATIONS

The clinical applications of CBF studies to medical management of neurologic disorders have been broad and varied. Deshmukh and Meyer's (1978) text describes the Baylor University CBF Laboratory and provides an excellent overview of these clinical applications. They report that CBF has been used to study the physiology of cerebrovascular disorders, including ischemia, embolism, subarachnoid and intracerebral hemorrhage, hypertensive encephalopathy, and so on. In these conditions, medical treatment can be monitored using repeated blood flow measurements. Blood flow has been used in the diagnosis and management of headache and migraine, seizure disorders, demyelinating diseases, psychiatric disorders, and toxic and metabolic disorders. CBF has been useful in surgical cases such as arteriovenous malformation, brain tumors, endarterectomy, and extracerebral to intracerebral artery bypass. Head trauma and comatose patients have been studied using the CBF technique, and features of brain death have been identified. Finally, the technique has been used to study degenerative diseases such as Alzheimer's dementia versus multi-infarct dementia versus pseudodementia.

STROKE

The understanding of recovery from stroke has been advanced through the application of CBF technology. In 1914, Von Monakow described the phenomenon of diaschisis. Diaschisis refers to temporary depression (or suppression) of function in remote areas of the brain following localized injury to the brain (Von Monakow, 1914, in Meyer et al., 1970). Hoedt-Rasmussen and Skinhoj (1964) were the first to report bilateral reduction of CBF after unilateral stroke. Meyer and colleagues in the early 1970's (Meyer et al., 1970, 1971) extended this research. They reported that bilateral depression of CBF lasts two to three weeks, and that diaschisis is more severe and lasts longer in older patients with acute stroke. Fujishima, Tanaka, Takeya and Omae (1974) found that loss of consciousness at stroke onset, associated with decreased blood flow, was a poor prognostic indicator. Heiss, Zeiler, Havelec et al. (1977) reported that blood flow rates were different across patients presenting as neurologically severely impaired at stroke onset. These patients could be separated into two groups. Severe patients with high perfusion showed better recovery than severe patients with low perfusion. Finally, a

2-compartmental analysis proposed by Wilkinson, Bull, DuBoulay et al. (1971) has not yet been fully explored. Basically, this approach analyzes early, rapid clearance and late, slow clearance of the radioisotope. The early component is thought to represent subcortical blood flow, and the late component, cortical blood flow.

APHASIA

Our final interest is the use of the CBF technique to study aphasia. Researchers in this area have looked at correlations between rCBF and specific aphasia types and the possible role of the right hemisphere in aphasia recovery. For example, Soh and colleagues (Soh et al., 1978) reported consistently different rCBF patterns for motor, sensory, and global aphasia types. However, neither this study nor that of Maly and associates (Maly, Turnheim, Heiss and Gloning, 1977) found a close correspondence between rCBF patterns and classical localization models. Maly et al. (1977) studied rCBF and aphasia type and found that, in most cases, rCBF disturbances did not correspond to anterior - posterior expectations for Broca's and Wernicke's aphasia, respectively. Of the verbal tests given to their patients, the strongest correlations between language performance and the severity of blood flow disturbance were obtained for word fluency tasks (such as rapid animal naming) and the Token Test. A key point was that rCBF disturbances were positively correlated not to aphasia type but to aphasia severity. Maly et al. (1977) concluded: "...test results were influenced primarily by the severity of perfusion disturbances within the foci. The size of foci themselves and the perfusion of the total hemisphere had less effect upon test results" (p. 90).

Regarding right hemisphere activation or participation in the speech and language of aphasic patients, Halsey, Blauenstein, Wilson and Wills (1980) reported bilateral increases in rCBF in frontal regions in left hemisphere stroke patients. Meyer, Sakai, Yamaguchi et al. (1980) and Yamaguchi, Meyer, Sakai and Yamamoto (1980) found right hemisphere frontal-temporal increases in lieu of increases in the damaged left hemisphere. These studies support the idea that positive prognosis for recovery from aphasia may be related to right hemisphere participation and/or takeover of language functions. However, the influence on rCBF of task type, modality condition, type of instructions, effect of incentives, effect of practice, and so on are not known for the normal brain.

ADVANTAGES AND LIMITATIONS

Cerebral blood flow research is one approach to the study of brain-behavior relationships in both neurologically normal and brain-damaged individuals. An advantage of this approach is that CBF is closely related to tissue function. The use of CBF with the neurologically impaired individual allows a study of dysfunction separate from tissue destruction (Soh et al., 1978). CBF reflects neuronal activity as a function of oxygen utilization. Raichle, Grubb, Gado et al. (1976) reported that oxygen consumption and blood flow in normally functioning brains and chronic stable diseases are positively correlated (cf. luxury perfusion [Deshmukh and Meyer, 1978], and acute stroke [Raichle et al., 1976]). Limitations of the CBF technique are summarized by Stump and Williams (1980). They include (1) amount of Xenon 133 inhaled, (2) recirculation artifact, (3) extracerebral contamination, (4) number of probes, (5) placement of probes, (6) adequacy of resting baseline, (7) habituation to stimuli, (8) individual differences, (9) type and amount of "brain work," in the stimulation phase.

SUMMARY

We have briefly described CBF methodological considerations, normative studies, the use of CBF in medical diagnosis and management, the study of stroke, and the study of aphasia following stroke. Despite a number of possible limitations, the study of brain-behavior relationships in normal and brain-damaged individuals has been advanced using the CBF approach. In the area of aphasia following stroke, we have a better understanding of prognosis for recovery, and of right hemisphere participation in recovery. Finally, we recognize the potential application of the CBF technique to the study of treatment approaches.

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APPENDIX

Select Abstracts

1. rCBF Studies: Normal

- Carmon et al., 1975 Compared auditory-verbal (digits) and auditory-nonverbal (music) stimulation. The rCBF for verbal stimuli showed increases in the left hemisphere [LH], decreases in the right hemisphere [RH]; for nonverbal, increases occurred in both LH and RH, but much more so in RH.
- Falgout et al., 1983 Tested run-to-run variability of rCBF. Authors question an underlying premise of the rCBF model which assumes a "steady state" of the "resting" brain.
- Gelmers, 1981 Studied voluntary hand movements and rCBF. In general, rCBF increased in the contralateral hemisphere. Repetitive hand contractions showed increased rCBF in the supplementary motor area [SMA]; sequential movements, in parietal lobe; and "motor ideation," SMA, parietal lobe, and entire frontal lobe.
- Gur et al., 1981 Found rCBF to increase in LH relative to RH on a verbal task, and RH relative to LH on a nonverbal spatial task.
- Ingvar, 1975 Studied a variety of stimulus conditions. For automatic speech and reading, found a "z-pattern" of rCBF in LH. Resting rCBF was distinctly frontal.
- Johansen et al., 1981 In patient with symptoms of anxiety, resting mean flow values were normal. During states of anxiety, rCBF increased in frontotemporal areas of both hemispheres.
- Knopman et al., 1982 Compared rCBF bilaterally during rhyme detection and meaning detection (single words). The rhyme task was associated with greater LH rCBF increases than the meaning task; the latter showed bilateral increases.
- Larsen et al., 1978 During automatic speech, found premotor increases bilaterally. A "z-pattern" of activation, not including Broca's area, was seen in the LH.
- Leli et al., 1984 Compared identical cognitive tasks with different response modalities: oral vs manual. The response modalities resulted in highly divergent rCBF landscapes.
- McLain et al., 1984 Describe test-retest reliability of rCBF, baseline vs activation, over a one-week interval on a verbal task.
- Maximilian et al., 1980 Found significant bihemispheric postcentral rCBF increases during Raven's Matrices activation.
- Maximilian, 1982 Found significant rCBF asymmetry in temporoparietal cortices: rCBF in LH was greater than RH regardless of ear of presentation of auditory word lists.
- Raichle et al., 1976 Compared rCBF and regional metabolic activity for oxygen (rCMRO₂). In normal subjects and patient with chronic stable diseases of the brain, correlations were positive, but in acute disease, the correlations were unpredictable.
- Wallesch et al., 1984 rCBF was studied by single photon emission computerized tomography (SPECT). Increased rCBF in LH was seen in cortical and subcortical areas during language production.
- Warren et al., 1984 Though depressed subjects had a lower resting flow than normal subjects, the pattern of rCBF was nearly identical. Both groups showed the same pattern of rCBF increases when offered monetary incentives, but only on the first run. The effects of incentives, practice effects, and task complexity are discussed.

2. rCBF Studies: Abnormal

- Butler et al., 1982 Studied young and aged normals and various types of dementia. Found a significant correlation between CBF and measured intelligence. Suggest that reduced CBF is a function of the severity rather than the cause of the abnormality.

- Deutsch, 1982 In arteriovenous malformation [AVM] patients, resting rCBF measured showed higher flow in the AVM region. During activation, flow approached (i.e., decreased to) normal flow levels.
- Deutsch & Tweedy, 1983 In closed head injury [CHI] patients, improvement in neuropsychological status correlated better with normalization of rCBF pattern than with changes in overall cerebral blood flow.
- Francis et al., 1981 Schizophrenic patients showed reduced mean hemispheric flow in both hemispheres, but was significantly below normal in the RH.
- Gustafson et al., 1978 Presenile dementia patients showed a marked reduction in mean hemispheric blood flow. rCBF patterns corresponded to receptive and/or expressive language deficits
- Hougaard et al., 1976 Studied patients with focal cortical epilepsy and found marked flow increases in areas presumed to participate in the seizure activity, even though EEG's often showed no epileptic foci.
- Hoyer, 1982 Describes deviations from normal of CBF and metabolism in Alzheimer's dementia [AD] and dementia of vascular origin. Findings dispute the idea that dementia represents accelerated aging.
- Johansen, 1981 Compared strategies of solving Koh's Block designs in patients with dementia. Patients with frontal rCBF decreases lack systematic solutions, error awareness, and anxiety. Patients with postcentral rCBF decreases showed these behaviors.
- Largen et al., 1981 Found mean resting levels of hemispheric blood flow to be significantly below normal but near normal during activation (Raven's Matrices) in early AD as compared to age-matched normals.
- Okabe et al., 1983 CBF was measured before and after surgery for AVM. Before surgery, rCBF was reduced in areas adjacent to the AVM; after excision, rCBF in gray and white matter increased significantly to normal.
- Overgaard & Tweed, 1983 Studied CHI patients' rCBF values in the acute phase relative to outcome. CHI patients with lower mean flow rates had a poorer prognosis. The rCBF pattern of borderzone flow deprivation was also related to poor neurological outcome.
- Risberg et al., 1983 Found significant rCBF differences in different types of dementia. In AD, flow decreases were in temporal-parietal and temporal-occipital regions; in Pick's, in frontal-temporal; in multi-infarct dementia [MID], asymmetries and irregular flow patterns were seen.
- Shakhnovich et al., 1980 In patients with surgical lesions, rCBF pattern was related to task difficulty and emotional state.
- Silfverskiold et al., 1979 Found rCBF to be normal in pseudodementia but reduced in AD.
- Thomas et al., 1984 In patients with unilateral carotid stenosis, rCBF was decreased on the affected side. Patients undergoing extracranial to intracranial [EC-IC] artery bypass showed improved rCBF on the operated side.
- Wood et al., 1980 (a) Studied rCBF in a patient with acute onset retrograde amnesia. Found suppression of blood flow in the occipital region in RH but not LH. Assuming that an "up-stream" flow from the occipital to the medial temporal lobe(s) occurs during memory activation in normals, it was concluded that memory was supported by RH not LH in this patient.
- Wood et al., 1980 (b) Compared to normals who show decreased rCBF in frontal lobes during mental activation, the amnesic patient studied showed: 1) low blood flow throughout the cortex, and 2) generalized increased flow especially in frontal areas. Results were consistent with the idea that the amnesic syndrome reflects inadequate focusing of attention with resulting pathologically diffuse flow.

3. rCBF Studies: Stroke

- Fujishima et al., 1974 Studied stroke patients and found that many had abnormal CBF on both the lesion side and the contralateral side. In patients who had loss of consciousness [LOC] at onset, CBF remained depressed bilaterally for over 2 months. Those without LOC showed better neurologic recovery.
- Grubb et al., 1975 Studied rCBF and cerebral blood volume [CBV] and other parameters in subarachnoid hemorrhage [SAH] due to aneurysm and other causes. Found the most striking changes in patients who had cerebral vasospasm: namely, CBF decreased as CBV increased. Suggest that extraparenchymal vessels and small intraparenchymal vessels are differently affected by vasospasm in SAH, the latter opposing or compensating for the former.
- Gur et al., 1982 Comparisons of resting CBF data did not differentiate stroke or TIA patients from controls. During cognitive stimulation, in contrast, CBF abnormalities were found in 96% of stroke and 38% of TIA patients studied.
- Heiss et al., 1977 Studied clinical neurologic deficits in stroke patients with rCBF and final outcome. Neurologic deficits and rCBF were positively correlated. Initial rCBF correlated positively with final outcome. Severe patients with high perfusion showed better recovery than severe patients with low perfusion.
- Hoedt-Rasmussen & Skidnhoj, 1964 First report of bilateral reduction of CBF after unilateral stroke.
- Keating et al., 1975 Studied stroke patients longitudinally. Found that unilateral stroke often causes bilateral CBF reduction. Abnormal blood flow shows most improvement within the first 2 weeks post onset. CBF values correlated significantly with neurologic status.
- Meyer et al., 1970 Found a bilateral depression of CBF for 2-3 weeks post stroke with a subsequent increase on the healthy side. CBF abnormalities were not related to increased intracranial pressure, generalized cerebral arteriosclerosis, or severe hyper- or hypotension. Findings provided quantitative proof for Von Monakow's concept of diaschisis.
- Meyer et al., 1971 Found that diaschisis, related to abnormal CBF, was more severe and lasts longer in older patients with acute stroke. Stated that collateral circulation is the most important single factor influencing recovery.
- Von Monakow (1914) Diaschisis refers to the idea that "following localized injury to the brain, temporary depression of function may occur in remote areas of the nervous system" (in Smith, 1972, p. 241), either intra- or interhemispherically.
- Wilkinson et al., 1971 Used a 2-compartmental rCBF analysis: early rapid clearance as an index of gray matter perfusion; late slow clearance as an index of white matter perfusion. This approach allows for a refined appreciation for cortical vs sub-cortical deficits relative to neurobehavioral profiles in stroke patients.

4. rCBF Studies: Aphasia

- Halsey et al., 1980 Found that in normal adults, LH aphasic, and RH nonaphasic patients discussing banal topics or answering questions, showed fairly symmetric bilateral increases of rCBF in the inferior frontal regions. Conclude, "the effort to speak. . . engages both sides of the brain mainly in the effort to activate the muscles of articulation" (p. 59).
- Maly et al., 1977 Studied rCBF and aphasia type and found, in most cases, CBF disturbances did not correlate with anterior - posterior expectations for Broca's and Wernicke's aphasia, respectively. Used a battery of neuropsychological tests. Concluded that performance was influenced primarily by the perfusion disturbance within the foci, while size of the foci and the perfusion of the total hemisphere had less effect on test results (p. 90).

Meyer et al., 1980

Studied LH aphasic patients over time using rCBF at rest and during behavioral activation. State, ". . . one of the few areas failing to show an [rCBF] increase was in Broca's area in the left hemisphere, but there were sizeable increases in the corresponding posterior frontal and sylvian areas of the right hemisphere, suggesting the possibility of transfer of motor speech function from the left to the right hemisphere which was only seen in [those] patients who showed good recovery of motor speech" (p. 69).

Soh et al., 1978

Studied CBF in motor, sensory and global aphasias. Found consistently abnormal rCBF patterns corresponding to aphasia types. Broca's area was not consistently involved in either motor or global aphasia. Inter-subject variability was significant. Stress the potential usefulness of rCBF measures for developing classification and prognostic criteria because ". . . the rCBF technique allows the study of dysfunction as separate from actual tissue destruction" (p. 632).

Yamaguchi et al., 1980

Report 3 aphasic patients' rCBF response during behavioral activation. Found poor prognosis associated with failure to increase rCBF in fronto-temporal regions bilaterally, and good prognosis associated with increased rCBF in the RH homologous to Broca's area.
