

CROFT GUIDELINES –

Classifications & Treatment Protocols of Cervical Acceleration/Deceleration (CAD) Trauma

Types of Collisions: (Occupant maybe driver or passenger. Criteria does not consider loss of consciousness, the use of seat belts, shoulder harnesses or other factors).

Type I** Primary rear impact (struck car moving or stationary)

Type II** Primary side impact

Type III** Primary frontal impact

Other: Multiple Impacts, Rollover, Spinout etc.

CAD Grades of Severity of Injury:**

Grade I: Minimal; No limitations of motion or ligamentous injury, No neurological findings

Grade II: Slight; Limitations of motion no ligamentous injury, no neurological findings

Grade III: Moderate; Limitations of motion; some ligamentous injury, neurological findings may be present.

Grade IV: Mod/severe; Limitations of motion; ligamentous instability; neurological findings present.

Fracture or disc derangement

Grade V: Severe; requires surgical management/stabilization post-surgical chiropractic follow-up may be appropriate.

Stages of Injury:**

Stage I: acute; inflammatory phase; 0 - 72 hours

Stage II: sub-acute; repair phase; 72 hours - 14 weeks post MVC/OI

Stage III: remodeling phase; 14 weeks - 12 months or more post MVC/OI

Stage IV: chronic; permanent injury

Protocol Frequency and Duration of Care in CAD Traumatology**

	5x/w	3x/w	2x/w	1x/w	1x/mos.	T _D	T _N
Grade I	1w	1-2w	2-3w	<4w	*	<11w	<21
Grade II	1w	<4w	<4w	<4w	<4mo.	<29w	<33
Grade III	1-2w	<10w	<10w	<10w	<6mos.	<56w	<76
Grade IV	2-3w	<16w	<12w	<20w	prn	prn	prn
Grade V	Surgical stabilization necessary--chiropractic care is post-surgical, prn.						



TD = treatment duration

* Possible follow-up at one month

TN = treatment total number

prn May require permanent monthly or prn (as needed) treatment

There are factors that potentially complicating CAD trauma management & medical treatment duration. Please see PI ONLINE Trainings for details. See web site for courses on these guidelines.

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Vertebral Artery Injury

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Continuing Education Activity

Injuries to the vertebral artery may either be traumatic or spontaneous. Traumatic injuries are most frequently due to blunt injury to the head and neck but may be due to penetrating trauma. Spontaneous injuries are caused by intrinsic weakness of the vessel wall, often due to underlying vascular or connective tissue disorder, leading to a dissection of the vessel. This activity describes the causes, pathophysiology, and diagnosis of vertebral artery injury and highlights the role of the interprofessional team in the management of these patients.

Objectives:

- Identify the etiology of vertebral artery injury.
- Review the presentation of a patient with vertebral artery injury.
- Outline the treatment and management options available for vertebral artery injury.
- Summarize interprofessional team strategies for improving care and outcomes in patients with vertebral artery injury.

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Introduction

Injuries to the vertebral artery may either be traumatic or spontaneous. Traumatic injuries are most frequently due to blunt injury to the head and neck but may be due to penetrating trauma. Spontaneous injuries are caused by intrinsic weakness of the vessel wall, often due to underlying vascular or connective tissue disorder, leading to dissection of the vessel. Spontaneous dissections are frequently associated with minor precipitating events. A grade of injury can range from an irregularity of the vessel wall to complete transection with intracranial or extracranial hemorrhage. Patients commonly initially present with a headache and neck pain but may be asymptomatic. Vertebral artery injury is an important cause of stroke and transient ischemic attack, particularly in younger patients. The vertebral arteries perfuse the posterior fossa so the patient will present with stroke symptoms consistent with posterior circulation deficits. Symptoms may include difficulty speaking, swallowing, or maintaining their balance. Loss of coordination or vision changes may also be present. The modified Denver screening criteria are used to identify patients at high risk for cerebrovascular injury. The initial diagnostic imaging study of choice is a CT angiogram. Treatment depends on

location, symptoms, and degree of injury and may involve fibrinolysis, anticoagulation, antiplatelet therapy, endovascular therapy, or open surgical repair.[1][2][3][4]

Etiology

Vertebral artery injuries can be due to blunt trauma, penetrating trauma, or can occur spontaneously. The majority of vertebral artery injuries are due to blunt trauma from motor vehicle crashes. Falls, strangulation, and pedestrian accidents are less common causes. Closed injuries to the vertebral arteries are usually due to hyperextension coupled with lateral flexion or rotation of the head.

Penetrating trauma to the neck, such as from a gunshot wound, is a rare but devastating cause of vertebral artery injury with high mortality. Injury to the vertebral artery may result from minimal trauma. Multiple case reports describe various sports, trampoline use, amusement park rides, coughing, sneezing, vomiting, childbirth, sexual intercourse, yoga, scuba diving, and chiropractic neck manipulation among several other potential triggers.

Spontaneous vertebral artery injuries occur when the structural integrity of the arterial wall is compromised. While this condition may be associated with vascular or connective tissue disorders such as fibromuscular dysplasia, Ehlers-Danlos syndrome and Marfan syndrome, the majority of patients diagnosed with a spontaneous cerebral artery dissection have no known history of the underlying predisposing disease. Most “spontaneous” cases correlate with a mildly traumatic event.[5][6][7]

Epidemiology

Spontaneous: Spontaneous cerebral artery dissections, both carotid and vertebral, account for about 20% of strokes in young adults. Vertebral artery dissections are less common than carotid dissections, occurring in about 1 in 100000 individuals in population studies. The actual incidence may be higher since many may be asymptomatic. The mean age ranges from 44 to 46 years, and there is no evident racial or gender prevalence. Dissection may be more common in the winter but the reason for season variation is unclear.

Traumatic: Traumatic vertebral artery injury is a relatively rare condition, reported in less than 1% of trauma admissions. However, the incidence is increasing, most likely due to increased awareness and screening for this finding in high-risk patients. Vertebral artery injury may be as high as 11% in patients with blunt traumas that meet specific clinical and physical examination criteria. The modified Denver screening criteria are used to identify patients at high risk for cerebral artery injuries. Patients with cervical transverse foramen fractures or facet dislocations have an associated vertebral artery injury in 27.5% of cases.

Pathophysiology

The neurologic consequences of injury to the vertebral artery are due to cerebral ischemia from thromboembolism, hypoperfusion, hemorrhage, or a combination of the three. In most cases, vertebral artery injury is due to an intimal tear. The torn, exposed endothelium promotes platelet aggregation and thrombus formation. This thrombus may cause local occlusion of the vessel, but more commonly, the clot will embolize to the cerebral circulation resulting in a stroke. Intimal tears may also dissect and create a false lumen that may lead to arterial occlusion. Partial transection of the artery may result in pseudoaneurysm. A pseudoaneurysm can be a source of emboli or hemorrhage if it ruptures. Complete vertebral artery transections may result in hemorrhage, which may be intracranial or extracranial depending on the location.

Histopathology

Patients with spontaneous vertebral artery dissection have histopathologic findings of intramural hemorrhage with disruption of the intimal planes. Pathologic changes primarily involve the adventitial and medial layers of the vessel. This finding is not as common in patients with a cerebrovascular injury resulting from acute trauma.

History and Physical

The history can be quite variable depending on whether the vertebral artery injury is spontaneous or due to acute trauma. Many cases thought to be spontaneous have antecedent minor trauma as an associated factor. Spontaneous dissections are more common in patients with connective tissue disorders, but most patients will not present with any known history of connective tissue disease.[8][9]

The most commonly reported symptoms are the head, and neck pain, vertigo, and dizziness but many patients with small dissections may be asymptomatic. In diagnosed cases, the presenting finding is often a transient ischemic attack or acute stroke. The risk of stroke is greatest in the first two weeks after the dissection occurs. Young patients presenting with acute stroke should have cerebrovascular dissection considered, especially if their symptoms are associated with a headache or neck pain. It is important to note that while neck pain is a common complaint, only 46% will initially report it. Additional clinical manifestations include scalp tenderness, tinnitus, bruits, or even cervical nerve root involvement. Vertebral artery dissection may also lead to lateral medullary infarction, posterior cervical vestibular symptoms, vision loss, or spinal cord ischemia.

Patients presenting with acute trauma should first have a primary and secondary survey and should undergo stabilization following Advanced Trauma Life Support guidelines. Like with spontaneous dissections, some patients may initially have no neurologic findings. In one study by Biffi et al., a time-lapse of 18 hours existed between the time of injury and onset of neurologic symptoms in 44% of cases. Patients with blunt cervical trauma who meet the modified Denver Screening criteria should undergo evaluation for cerebrovascular injury.

Denver Screening Criteria:

- Lateralizing neurologic deficit (not explained by head CT)
- Infarct on head CT
- Nonexpanding cervical hematoma
- Massive epistaxis
- Anisocoria /Horner syndrome
- Glasgow coma score (GCS) less than 8 without significant CT finding
- Cervical spine fracture
- Basilar skull fracture
- Le Forte II or III facial fractures
- Seatbelt sign above the clavicle
- Cervical bruit/thrill

Evaluation

CTA is the most reliable non-invasive neurovascular imaging modality and is the initial test of choice for patients with suspected cerebral artery injury. CTA should be performed in patients meeting the modified Denver Screening Criteria and in this population has a sensitivity of nearly 100%. Digital subtraction arteriography (DSA) has long been described as the gold standard but is more invasive, less readily available, and requires more contrast than CTA. DSA itself also carries an increased risk of stroke (0.5%). DSA is still a choice when concurrent endovascular therapy is under consideration or when other imaging modalities are inconclusive or unavailable. CTA has largely replaced DSA.

MRI is recommended to screen for vertebral artery injury in patients with blunt spinal cord or vertebral subluxation injuries. Magnetic resonance angiography (MRA) has shown inferior or equivalent specificity for detecting vertebral artery injury as compared to CTA and MR and is often unavailable or impractical in the emergency setting. MR angiography is not used independently to screen for blunt cerebrovascular injury. While duplex ultrasonography is the least invasive and perhaps the most widely available imaging modality, there is no data to support its use in assessing for vertebral artery injury. Ultrasound's poor sensitivity for detecting vertebral artery injury is due to anatomic constraints that limit visibility in areas obscured by bone.

Young patients presenting with acute ischemic stroke should have spontaneous cerebral artery dissection considered as an inciting cause. CTA is commonly performed after non-contrast head CT to evaluate for this diagnosis.

Treatment / Management

Symptomatic patients who present with acute ischemic stroke due to spontaneous vertebral artery dissection without associated injuries or contraindications should be considered for systemic thrombolytic therapy (recombinant tissue plasminogen activator) if they present within 3 hours of the onset of symptoms. Patients who present up to 4.5 hours from symptom onset and those who are otherwise not candidates for systemic thrombolytic therapy should merit consideration for catheter-directed thrombolysis. Patients who are not appropriate for thrombolytic therapy can receive anticoagulation, antiplatelet therapy, endovascular or open operative repair depending on the grade of injury. [3][10][11]

Clinicians can manage symptomatic patients with anticoagulation versus antiplatelet therapy based on bleeding risk, the location of the lesion, and the grade of injury. Endovascular therapy and operative repair are reserved for patients with higher-grade lesions and those with contraindications to anticoagulation or antiplatelet therapy that are at high risk for progression.

There are no proven methods to reduce the risk of a neurologic event or recurrent dissection in patients with known dissections, but patients are advised to limit contact sports, neck manipulation or any other activity that involves the abrupt movement of the neck. Hypertension should be well-controlled and estrogen-containing medications avoided.

Differential Diagnosis

- Cervical spine fracture evaluation
- Cervical strain
- Emergent management of subarachnoid haemorrhage
- Migraine headache

- Haemorrhage stroke
- Tension headache
- Vasculitis affecting the vertebrobasilar circulation
- Vertebrobasilar atherothrombotic disease

Staging

Denver Radiologic Grading Scale for Blunt Cerebrovascular Injury:

Grade I: Irregularity of the vessel wall or dissection/intramural hematoma with less than 25% stenosis

- Management: Anticoagulation or antiplatelet therapy, endovascular repair for symptomatic patients who are not candidates for anticoagulation or antiplatelet therapy

Grade II: Intramural thrombus or raised intimal flap or dissection/intramural hematoma with greater than 25% stenosis

- Management: endovascular therapy if symptomatic, anticoagulation, antiplatelet therapy, deferred endovascular repair in high-risk asymptomatic patients

Grade III: Pseudoaneurysm

- Management: endovascular therapy if symptomatic, anticoagulation, antiplatelet therapy, deferred endovascular repair in high-risk asymptomatic patients

Grade IV: Vessel Occlusion

- Management: endovascular therapy if symptomatic, anticoagulation, antiplatelet therapy, deferred endovascular repair in high-risk asymptomatic patients

Grade V: Vessel transection

- Management: Vascular sacrifice, either open or endovascular if symptomatic followed by anticoagulation or antiplatelet therapy. Asymptomatic patients have their condition managed with observational, operative, or endovascular treatment for ongoing hemorrhage.

Prognosis

Traumatic vertebral artery injuries can have devastating complications. Sanelli et al. reported a stroke rate of 24% and a death rate of 8% in patients with traumatic vertebral artery injury. Mortality in patients with associated cervical spine injury is even higher and approaches 40%. Highest mortality occurs in those with bilateral injury or injury due to penetrating, high-velocity trauma such as blast injury or gunshot wound.

The prognosis in patients with spontaneous vertebral artery dissections depends on location as well as the degree of associated ischemic stroke or subarachnoid hemorrhage. In patients with extracranial dissections, an excellent outcome is reported in up to 85% with 5% to 25% have poor neurologic outcome or death. Poor outcome is associated

with older age, arterial occlusion, and higher stroke scores at diagnosis.

Enhancing Healthcare Team Outcomes

Injury to the vertebral artery is managed by an interprofessional team that consists of a vascular surgeon, radiologist, neurologist, and an internist. Once the clinician makes the diagnosis, the treatment depends on whether the patient is symptomatic or asymptomatic

Symptomatic patients who present with acute ischemic stroke due to spontaneous vertebral artery dissection without associated injuries or contraindications should be considered for systemic thrombolytic therapy if they present within 3 hours of the onset of symptoms. Patients who present up to 4.5 hours from symptom onset and those who are otherwise not candidates for systemic thrombolytic therapy should be a consideration for catheter-directed thrombolysis. Clinicians can manage patients who are not appropriate for thrombolytic therapy with anticoagulation, antiplatelet therapy, endovascular, or open operative repair depending on the grade of injury.

Asymptomatic patient management is with anticoagulation versus antiplatelet therapy based on bleeding risk, the location of the lesion, and the grade of injury. Endovascular therapy and operative repair are reserved for patients with higher-grade lesions and those with contraindications to anticoagulation or antiplatelet therapy that are at high risk for progression.

The prognosis for patients with vertebral injury varies from a stroke rate of 24% to a death rate of 8%. Mortality rates are even higher in the presence of another brain injury. Poor outcome is associated with older age, arterial occlusion, and higher stroke scores at diagnosis.[12][13]

Vertebral artery injuries require the efforts of a coordinated interprofessional healthcare team. The physician (MD, DO, NP, PA) should assess the case and determine the course of treatment. If thrombolytic medication is the chosen route, coordination with a pharmacist is advisable; the pharmacist can verify dosing, perform medication reconciliation, and discuss drug agent options. If a catheter-based solution is necessary, then an interventional radiologist or a vascular surgeon should perform the procedure. Nursing will play a crucial role in quickly preparing the patient, as well as administering care and medication post-procedure. If the physician elects to use anticoagulation or antiplatelet therapy, the pharmacist will again assist in agent selection and dose verification, and nursing will administer the drugs in the inpatient setting. The pharmacist and nursing staff should all be empowered to communicate any concerns they have to the physicians and the rest of the healthcare team. This type of collaborative interprofessional team approach can lead to better patient outcomes through coordinated care. [Level V]

Review Questions

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Neuroanatomy, Brain Arteries

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Introduction

The brain receives vascular supply from a network of arteries that anastomose to form the circle of Willis. Because the brain has a constant high metabolic demand and no energy supply of its own, it requires a significant blood supply, consuming 15% of total cardiac output; any blockage of blood flow leads to severe damage and a host of neurological pathologies (see **Figure**. Diagram of the Brain Blood Circulation).[1]

The brain is supplied by the internal carotid arteries (ICAs), which branch from the common carotid arteries, and the vertebral arteries, which branch from the subclavian. The ICA gives rise to the anterior cerebral artery (ACA) and the middle cerebral artery (MCA). The 2 vertebral arteries unite to form the basilar artery, terminating in the 2 posterior cerebral arteries (PCA). The circle of Willis is the combination of these anterior and posterior divisions (see **Image**. Outer Surface of the Cerebral Hemisphere).[2]

Structure and Function

The internal carotid arteries penetrate the temporal bone through the carotid canal before giving off branches supplying the eyes via the ophthalmic artery and its daughter, the central retinal artery.[3] It then gives off branches supplying the hypothalamus regions via the posterior communicating arteries, the areas surrounding the globus pallidus, and the amygdala via the anterior choroidal arteries, and the medial surfaces of the anterior segment of the brain via the anterior cerebral artery.[4][5] The 2 anterior cerebral arteries then connect by the anterior communicating artery (ACoA), the junction with which is a frequent location of berry aneurysms.[6] Finally, the internal carotid arteries end in the middle cerebral arteries, which, together with the anterior cerebral arteries, represent its terminal branches and supply a wide territory of the lateral aspects of the cerebral hemispheres (see **Image**. Arterial Circulation of the Brain). These broad territories include the centers controlling speech production: Broca and Wernicke areas.[7] The lenticulostriate arteries, which branch from the proximal part of the middle cerebral arteries, further serve the deeper structures of this region.

Several small branches of the ACA branch at or near its junction with the ACoA. These include the recurrent artery of Heubner (RAH), the orbitofrontal artery, and the frontopolar artery. Identification of these arteries is essential, particularly the RAH, as their location places them at risk of injury in surgery for aneurysms and tumors.[8] The RAH is the largest medial lenticulostriate arteries, which also branch from the ACA and serve the basal ganglia with lateral branches from the MCA. In addition to those lenticulostriate arteries, the MCA also gives off the polar and anterior temporal arteries and the uncus artery, followed by numerous cortical branches that come off the distal part of the MCA.[9]

The vertebral arteries arise from the corresponding subclavian arteries and course via the transverse foramina of the cervical spine into the foramen magnum.[10] Before joining to form the basilar artery, they give off the posterior inferior cerebellar arteries and the anterior spinal arteries. Following the joining, the basilar artery gives off the paramedian pontine arteries, labyrinthine arteries, the long circumferential anterior inferior cerebellar arteries, and superior cerebellar arteries. Cranial nerve III passes between the superior cerebellar and posterior cerebral arteries as it exits the midbrain.[11] The anterior inferior cerebellar arteries supply various brainstem territories and pontine cranial nerve nuclei. Finally, the basilar artery bifurcates into its 2 terminal branches, the posterior cerebral arteries, which supply the midbrain and much of the posterior brain, including the visual cortex and related centers in the occipital and temporal lobes (see **Figure**. Diagram of the Posterior Cerebral Artery and its Branches). They also give off the medial and lateral posterior choroidal arteries supplying deeper structures and cortical branches, including the splenial artery.[12]

Occlusion of each arterial territory causes damage to different functional areas of the brain. As a result, each branch has a unique constellation of symptoms that may present when affected.

Embryology

The proximal ICA originates from the third aortic arch, and the distal portions come from the dorsal aorta. At roughly 28 to 30 days, the ICA has fully divided into cranial and caudal segments. The cranial segment includes the primitive olfactory artery (POA) that eventually forms the anterior choroidal and MCA. Together with the median artery of the corpus callosum (MACC), the POA is involved as part of the normal development of the ACA. Failure of the MACC to regress can lead to a variant called azygos ACA, described below. The MCA develops later, beginning around 32 to 40 days, and develops together with the cerebral hemispheres. Initially, numerous anastomoses exist between the carotid and vertebrobasilar systems, most of which regress. Occasionally, the hypoglossal artery or the trigeminal artery may persist into adulthood. The PCA develops from the caudal segments of the ICA; it is initially a continuation of the posterior communicating artery, which regresses in most individuals.[13]

Blood Supply and Lymphatics

Vasa vasorum, the microscopic vessel networks supplying large blood vessels, are rarely found in the brain and, when present, are usually related to intracranial cardiovascular pathologies such as atherosclerosis. Rather than through vasa vasorum, intracranial vessels likely get their blood supplied by simple diffusion with the cerebrospinal fluid (CSF). [14]

The brain does not have a lymphatic system as peripheral tissues do; instead, it has a similar system by which CSF enters the brain parenchyma, known as the glymphatic system. CSF initially travels through the pial arteries into the perivascular Virchow-Robin space, entering brain cells via aquaporin channels found on astrocytes. Eventually, it exits into lymphatics running along the spinal and cranial nerves and through the arachnoid granulations.[15]

Physiologic Variants

The ACA is divided into 5 segments, denoted A1 through A5. Its distal part runs along the corpus callosum, sometimes called the pericallosal artery. The largest branch of this pericallosal segment is the callosomarginal artery, which can be present in more than half of individuals. Most branches of the ACA serve the cortex branch either from the callosomarginal artery or, if it is not present, directly from the pericallosal artery. There are numerous additional variants, of which significant examples are the azygos ACA, in which the A2 segments of the 2 ACAs fuse before dividing again; bihemispheric, in which the A2 segment of 1 ACA diminishes and the other divides to feed both hemispheres; and medial ACA, in which a third ACA appears and feeds the distal territories.[16] Also, many

individuals have fenestration of the anterior communicating artery, which can mimic an aneurysm.[13]

The MCA is divided into 4 parts: M1, from the ICA bifurcation through M4 to the lateral cerebral cortex. Corresponding with their relative locations, they are alternatively called the sphenoidal, insular, opercular, and cortical segments, respectively.[9] There may be a duplicate or accessory MCA in rare cases.[13]

The PCA is divided into 4 sections: P1, P2A (anterior), P (posterior), P3, and P4. The anastomosis with the posterior communicating artery separates P1 and P2.[17] As mentioned above, the PCA derives from the caudal segments of the ICA that form the posterior communicating artery. In many patients, the posterior communicating artery does not regress to a normal degree and remains a significant contributor to the PCA; the term for this is a "fetal" PCA.[13]

Surgical Considerations

As mentioned above, knowing cerebral branches and variants during surgery for intracranial aneurysms and neoplasms is vital. For example, avoiding occlusion of the fetal PCA is important, as it provides much of the posterior circulation during treating aneurysms of the posterior communicating artery.[13]

Clinical Significance

Occlusion of the cerebral arteries can lead to stroke, leading to significant morbidity and mortality (see **Image. Anterior Cerebral Artery Stroke**). Understanding cerebral arterial anatomy is also significant in diagnosing and managing intracranial aneurysms and tumors.

Ischemic occlusion of branches of the ICA results in anterior circulation strokes. Occlusion of cortical (pial) branches of the anterior circulation results in cortical stroke syndromes with clinical findings of aphasia, apraxia, cortical sensory impairment such as neglect or agrophesthesia, and contralateral hemiparesis. Occlusion of deep perforating branches, most commonly the lenticulostriate arteries, results in lacunar infarcts with the most common type of pure motor hemiparesis. Cortical infarction of the posterior cerebral artery results in homonymous hemianopia. Occlusion of the perforators from the PCA (thalamic perforators) may result in the lacunar syndrome of pure sensory hemianesthesia.

The ophthalmic artery arises from the ICA. A transient ischemic attack presenting with transient monocular blindness indicates a transient ischemic attack (TIA) in the ipsilateral ICA territory. The imaging modality of choice is a carotid duplex ultrasound or computed tomogram (CT) angiogram.

The anterior circulation supplies 80% of the brain, and the posterior circulation 20% of the brain. Logically, 80% of strokes occur in the anterior and 20% in the posterior circulation.

Moyamoya disease is an occlusive condition resulting from bilateral blockage of the terminal ICA and the development of abnormal collateral vessels in the basal ganglia and internal capsule region. These tiny collaterals give rise to the radiological appearance of a "puff of smoke," which is the literal meaning of Moyamoya in Japanese. It is a major cause of both ischemic and hemorrhagic strokes in childhood and early adulthood and is often treated with surgical bypass to revascularize the MCA distribution.[18]

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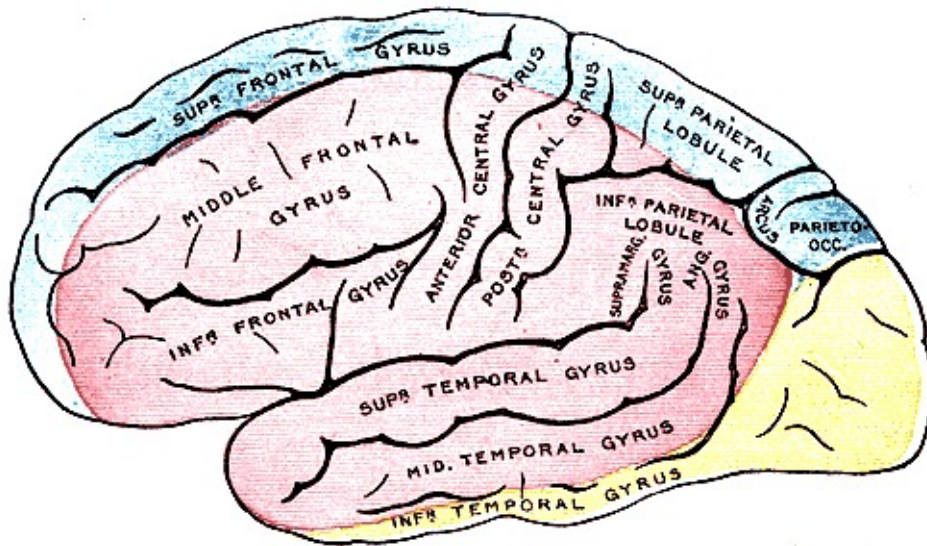
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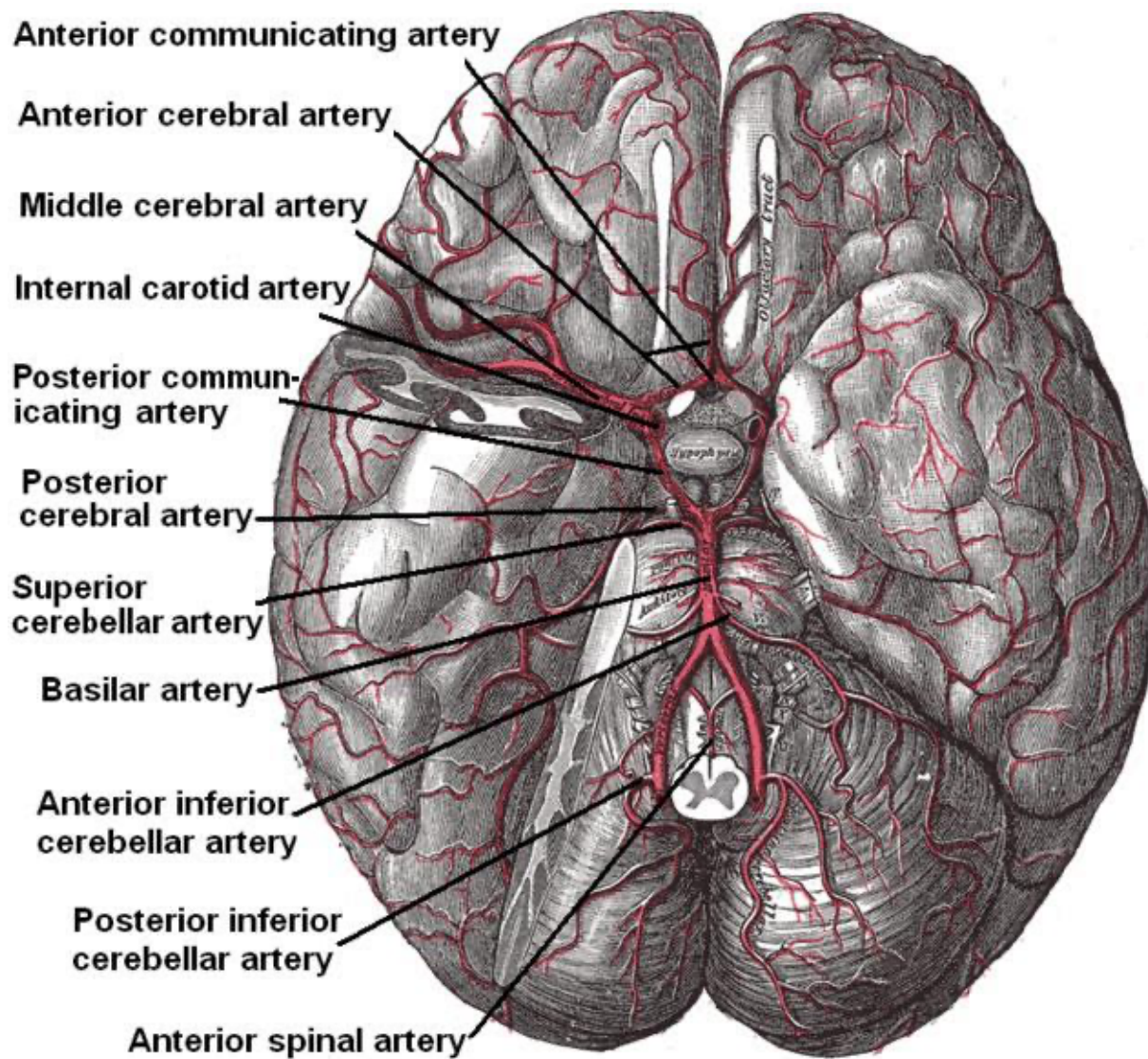
Disclosure: Richard Yu declares no relevant financial relationships with ineligible companies.

Disclosure: Forshing Lui declares no relevant financial relationships with ineligible companies.

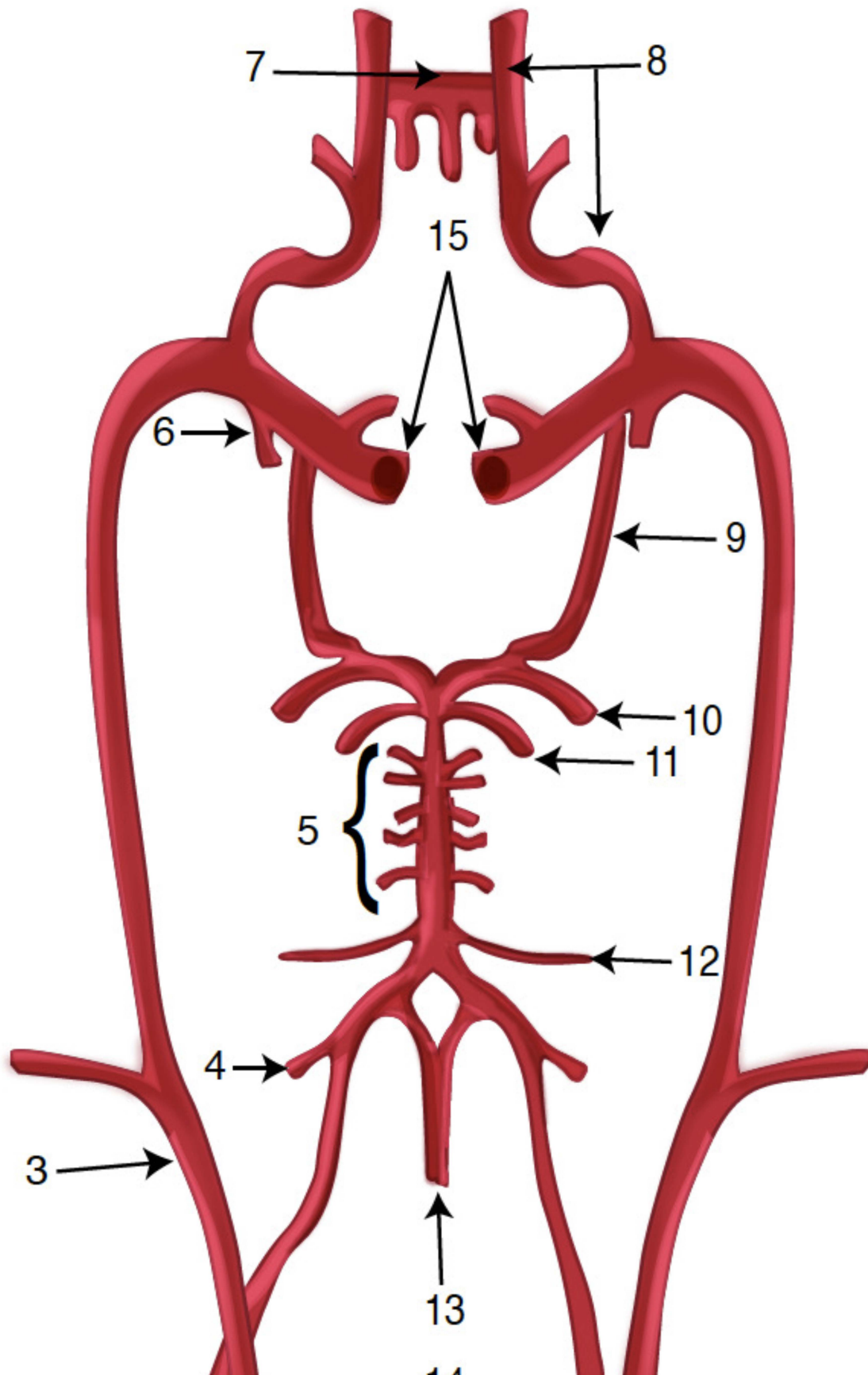
Figures



Outer Surface of the Cerebral Hemisphere. The outer surface of the cerebral hemisphere shows areas supplied by cerebral arteries. The blue areas are supplied by the anterior cerebral artery, the pink areas by the middle cerebral artery, and the yellow areas by the posterior cerebral artery. Henry Vandyke Carter, [Public Domain](#), via Wikimedia Commons



Arterial Circulation of the Brain. This inferior view shows the circle of Willis at the base of the brain formed by the anterior communicating, anterior cerebral, middle cerebral, internal carotid, posterior communicating, posterior cerebral, and basilar arteries. The temporal pole of the cerebrum and a portion of the cerebellar hemisphere have been removed on the right side. Other arteries in this illustration include the superior cerebellar, anterior inferior cerebellar, posterior inferior cerebellar, and anterior spinal arteries. Henry Vandyke Carter, [Public Domain](#), via Wikimedia Commons



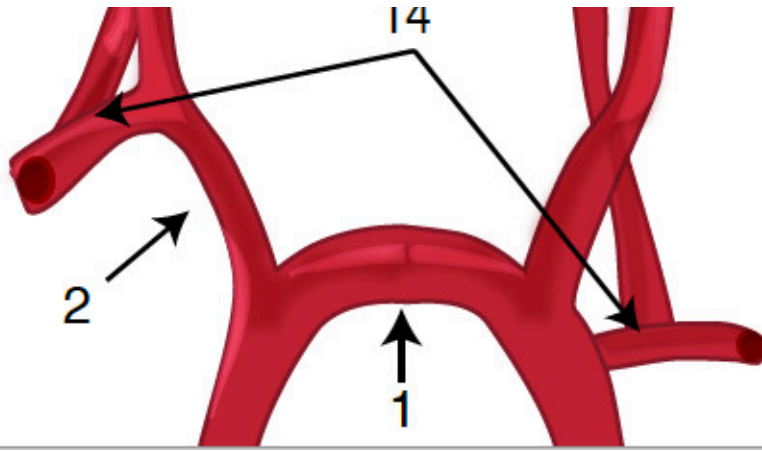
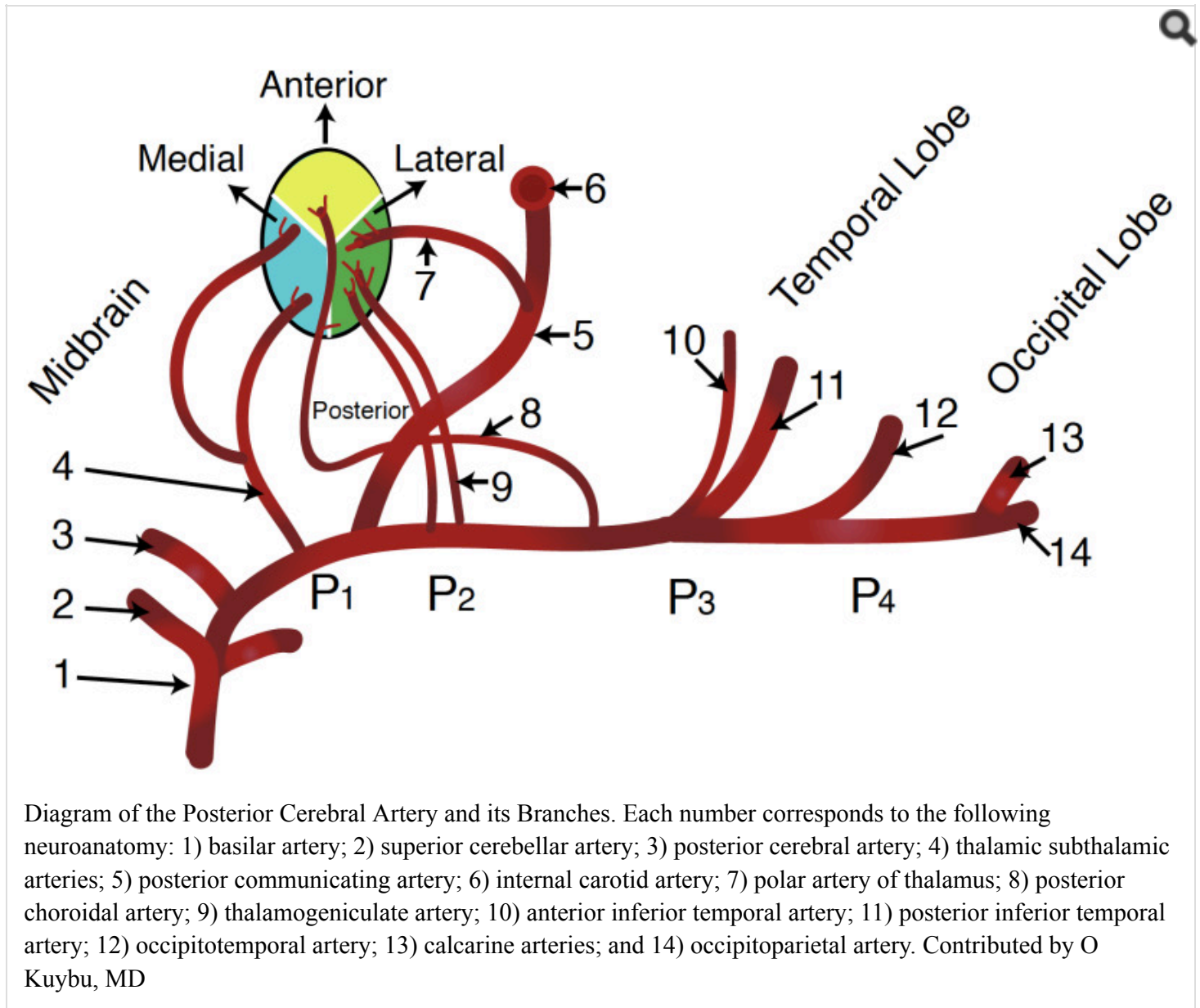
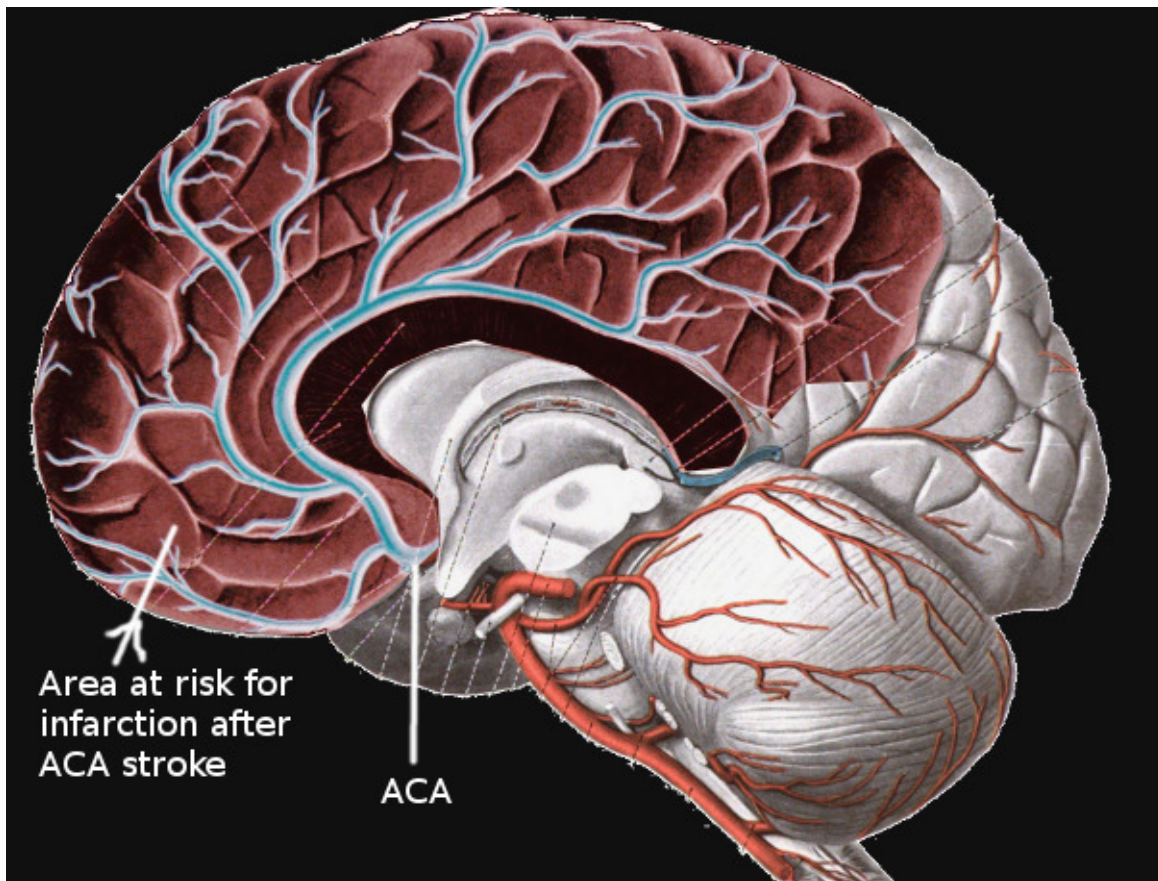


Diagram of the Brain Blood Circulation. Each number corresponds to the following neuroanatomy: 1) aortic arch; 2) brachiocephalic artery; 3) common carotid artery; 4) posterior inferior cerebellar artery; 5) pontine arteries; 6) anterior choroidal artery; 7) anterior communicating artery; 8) anterior cerebral artery; 9) posterior communicating artery; 10) posterior cerebral artery; 11) superior cerebellar artery; 12) anterior inferior cerebellar artery; 13) anterior spinal artery; 14) arches of vertebral arteries; and 15) internal carotid arteries. Contributed by O Kuybu, MD





Anterior Cerebral Artery Stroke Contributed by S Bhimji, MD

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ON THE FUNCTION OF THE CIRCLE OF WILLIS.*

By S. P. KRAMER, M.D.

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PLATES 52-56.

In 1664, Dr. Thomas Willis, of Oxford, published his "Cerebri Anatome," in which he described, at the base of the brain, the arterial anastomosis which since then has borne his name. In this book, there is a very interesting description of an experiment.¹

* Read before the Physiological Society at Oxford, England, July 1, 1911. Received for publication, November 24, 1911.

¹ The following account of this experiment is taken from Dr. Willis's Practice of Physick (English translation by S. Pordage, London, 1684, pt. vi, p. 59). "Let the Carotidick Arteries be laid bare on either side of the *Cervix* or the hinder part of the Head, so that their little Tubes or Pipes, about half an inch long, may be exhibited together to the sight; then let a dyed liquor, and contained in a large Squirt or Pipe, be injected upwards in the trunk of one side, after once or twice injecting, you shall see the tincture or dyed liquor to descend from the other side by the trunk of the opposite Artery: yea, if the same be more copiously injected towards the Head, from thence returning through the Artery of the opposite side, it will go thorow below the *Praecordia*, even to the lower Region of the Body; when in the meantime, little or nothing of the same tincture is carried thorow the outward and greater Jugular Veins. Then the Head being opened, all the Arteries, before the entrance of the Head, and the Veins of the same band with them, will be imbued with the color of the same injected liquor. Further, in the Vessels which constitute the wonderful Net, and which cover the Basis of the Brain, some footsteps of the same tincture will appear. But that this liquor doth descend so plentifully by the opposite Artery, and not by the Jugular Vein, either associate or opposite, the reason is, because it cannot enter those Veins, unless the region of the whole Brain, being first passed thorow, it had entered the bosom; but the liquor being plentifully injected, could not so suddenly pass thorow the very small Vessels covering the Brain: wherefore rather than the force should be carried to the Brain by the violent impulse of the liquor, it returning from the injection, and otherwise threatening a flood to the Brain, finds the way of receding also by the opposite Arteries, for that end, both before they enter the Brain, and after they have entered it, communicating among themselves.

"And here we cannot sufficiently admire so provident (and to be equalled by no mechanical Art) a dispensation of the blood within the confines of the Brain.

As the result of this experiment and of the conclusions drawn therefrom by Willis, for two hundred and fifty years we have believed that it was the function of the circle of Willis to equalize the blood supply to all parts of the brain. We had come to regard this anastomosis as a kind of reservoir from which the different parts of the brain drew their blood supply through the various arteries leading from the circle.

The conditions in the living animal under physiological conditions seemed, however, worthy of investigation. In the experiments now to be described, fifty dogs and three monkeys were used.

The animals were anesthetized with ether, and two cubic centimeters of a 3 per cent. solution of methylene blue were injected into a carotid or vertebral artery by means of a fine hypodermic needle. The circulation of the blood in the artery that was being injected was not interfered with except by the insertion of the needle. Just enough pressure was used in the syringe to overcome the arterial blood pressure. The animals were killed by opening the heart two minutes after the injection of the methylene blue. The brain and spinal cord were then removed and the distribution of the methylene blue was noted. The results obtained were surprisingly constant.

Area of the Carotid Artery.—On injection into one carotid artery, the other carotid and both vertebrales being unobstructed, the methylene blue was distributed to all that part of the cerebral hemisphere which is supplied by the anterior and middle cerebral arteries, by the anterior choroid, and by the posterior

For in as much as the Carotidick Arteries do communicate between themselves in various places, and are mutually ingrafted; from thence a double benefit results, though of a contrary effect: because by this one and the same means care is taken, both lest the brain should be defrauded of its due watering of the blood, and also lest it should be overwhelmed by the too impetuous flowing of the swelling stream or torrent. As to the first, lest that should happen, one of the *Carotids* perhaps being obstructed, the other might supply the provision of both; then, lest the blood rushing with too full a torrent, should drown the channels and little Ponds of the brain, the flood is chastised or hindered by an opposite emissary, as it were a Flood-gate, and so is commanded to return its flood, and haste backward by the same ways, and to run back with an ebbing Tide."

communicating arteries on the same side as that on which the injection was made. As a rule, the anterior portion of the frontal lobe on the opposite side was also stained; that is, there was some crossing over of the stain in the region of the anterior cerebral artery, but not into the other vessels.

The following parts of the cerebrum were stained after carotid injection in the living dog: The entire surface of the cortex of the cerebrum on the side of the injection, except the posterior aspect of the occipital lobe which rests on the tentorium. On the median and basal surfaces of the homolateral cerebral hemisphere, all that area which is in front of and above the section of the corpus callosum. The part that is below and behind was unstained. On the side opposite the injection, the olfactory lobe and the anterior central gyrus were stained. The centrum ovale was stained in the areas corresponding to the stained cortex outside of it. The following structures were also stained: the corpus callosum, both caudate nuclei, the anterior commissure, the anterior pillars of the fornix, the tela and choroid plexuses of the third and lateral ventricles, the septum lucidum, the optic chiasm, the infundibulum, and pituitary gland; and on the homolateral side, the anterior third of the crista of the peduncle, the lenticular nucleus, the internal capsule, and the regio subthalamica and the claustrum.

In *Macacus sinicus*, the posterior two thirds of the occipital lobe was unstained after carotid injection. Otherwise the staining corresponded to that described in the dog (figures 1, 2, and 3).

Area of the Vertebral Artery.—If methylene blue is injected into one of the vertebral arteries in the living dog, the other vertebral artery and both carotids being unobstructed, the stain is distributed to those parts of the brain and spinal cord supplied by both vertebral arteries, the basilar artery and both posterior cerebral arteries and their branches.

The following structures were stained on both sides: the upper dorsal and the entire cervical part of the spinal cord, the medulla oblongata, the tela and choroid plexus of the fourth ventricle, the pons, the cerebellum, the corpora quadrigemina, the nucleus ruber, the posterior two thirds of the crura of the peduncles, the pulvi-

nar, the optic thalamus, the corpora mammillaria, and the body and posterior pillars of the fornix.

In addition, the following structures were stained: all that portion below and behind the corpus callosum on the median and basal surfaces of both hemispheres; the posterior or tentorial surface of both occipital lobes, and both the first external (medial) gyri on the upper surface. In the dog, the distribution of the carotid and vertebral cortical areas overlap in both external or medial gyri (figure 4). In *Macacus sinicus*, the posterior two thirds of both occipital lobes was stained after vertebral injection.

If one vertebral artery is tied and the other injected, then the distribution of the stain is incompletely bilateral in the parts supplied by the vertebrales; that is, the staining is incomplete on the side on which the vertebral was tied. If one carotid was tied and the other injected, no appreciable or constant difference in distribution could be noted; that is, the parts were stained as in the experiments in which one carotid was injected, the other carotid being unobstructed. If both carotids or both vertebrales are tied and one of the other arteries is injected, then the separation of the areas disappears and the stain is carried forward or backward as the case may be. In other words, the circle of Willis is an antero-posterior anastomosis between the carotids and the vertebrales, which under physiological conditions does not permit the mingling of the blood streams. When, however, either the anterior or posterior arteries are completely blocked, then the anastomosis will supply blood to the areas of the central nervous system supplied by the blocked vessels.

It may be said, in passing, that this separation of the areas of supply is true of all arterial anastomoses under physiological conditions. Thus, if one injects the carotid artery of one side in the living dog with methylene blue, the other carotid being unobstructed, one lobe and the homolateral half of the isthmus of the thyroid gland, and the homolateral half of the tongue are stained blue, although both of these organs have a very rich anastomosis crossing the middle line. If, however, the injection is made into one carotid after the other is tied, then the stain crosses the middle line in both the tongue and the thyroid gland.

If the above experiments have been correctly interpreted, we ought to have a pharmacological method of verifying our results. If, namely, only the blood of the vertebral artery goes to the medulla oblongata, and not that of the carotid or a mixture of both, then the injection into the vertebral artery of a very minute quantity of certain "bulbar" poisons ought to produce on the centers in the medulla results which they would not cause when injected into the carotid. Such experiments were accordingly made, and these have given results that are entirely confirmatory.

The method was as follows: Dogs were narcotized with ether, the blood pressure in the femoral artery was recorded with a mercury manometer, and the respirations by means of the Gad aeroplethysmograph, which gives a quantitative record of both inspiration and expiration. In all the tracings, the upstroke represents expiration, and the downstroke inspiration. The moment of injection was recorded by means of an electric signal. The experiments here described were made with alcohol, ether, and chloroform.

If two cubic centimeters of a 25 per cent. solution of ethyl alcohol are injected into a carotid artery (figure 5), no effect on the circulation or respiration is regularly produced. At times the injection may be followed by a slight fall in blood pressure, but oftener there is no change in the circulation. If the same or even a smaller amount of the same solution is injected into one of the vertebral arteries, it is immediately followed by lessened respiration, then a stoppage of breathing in inspiration lasting for a few seconds, with a gradual recovery of respiration. The blood pressure curve is very characteristic: immediately following the injection there are a few "vagal" beats, that is, a slowing of the heart with wide excursions, due to irritation of the vagus centre, followed by a prolonged fall in pressure to be succeeded by a gradual recovery to the pressure which obtained before the injection (figure 6).

With stronger alcohol, such as a 50 per cent. solution, similar effects though of greater intensity are produced. That is, the stoppage of respiration is more prolonged and may return only after artificial respiration, and the fall in blood pressure is more pronounced (figure 7).

Exactly the same results follow the injection of ether in minute doses. Figures 8 and 9 are tracings obtained from a dog following the carotid and vertebral injection of two cubic centimeters each, of a solution of ether in water at 24° C.

If pure ether in amounts as low as 0.2 of a cubic centimeter is injected into the vertebral artery, the respiratory center may be completely and permanently narcotized and cannot be restored by artificial respiration (figure 10). The injection of the same amount into the carotid artery produces little or no effect.

Chloroform is soluble in water in amounts that are less than 1 per cent., but the difference in effect between carotid and vertebral injection may be plainly demonstrated with chloroform water.

Figure 11 is a tracing obtained while injecting two cubic centimeters of chloroform water into the right carotid artery of a dog. No effect upon either respiration or circulation was produced.

Figure 12 is a tracing from the same dog while injecting the same amount of chloroform water into the vertebral artery. We see the slow "vagal" heart beats and the drop in blood pressure. Expirations are markedly diminished in amplitude, though there is no complete stoppage of respiration.

If we inject into the vertebral artery of a dog 0.13 of a cubic centimeter of pure chloroform, it is followed by complete stoppage of respiration in inspiration. No recovery takes place after artificial respiration for fifteen minutes; the heart beats are markedly slowed, and the blood pressure falls (figure 13).

The injection of twice the amount into the carotid artery produces no effect on the respiration. There is a fall in blood pressure from which the recovery is prompt, but there is no slowing of the heart such as follows irritation of the vagus center (figure 14).

If, in all these experiments, the drug is dissolved in defibrinated blood obtained from the same animal, exactly the same results are obtained. This was done to rule out the possible production of embolism in the vessels of the brain.

It is also to be noted that if these injections be made with both vagus nerves divided, then the vagal slowing of the heart and the drop in blood pressure does not occur. Instead, there is a marked

rise in blood pressure due to stimulation of the vasomotor center in the medulla oblongata.

The fact that the circle of Willis is an antero-posterior anastomosis that operates only when either the carotid or vertebral arteries are tied, may also be demonstrated pharmacologically.

The injection of 0.33 of a cubic centimeter of chloroform into the right carotid produced a fall in blood pressure from which there was a quick recovery (figure 15). The respiratory and vagus centers were unaffected. Both vertebral arteries were then tied, and the same amount of chloroform injected into the right carotid produced complete and permanent stoppage of respiration with vagal slowing of the heart and fall in pressure, the usual effect after vertebral injection.

One may also demonstrate by a glass model of the circle of Willis the separation of the areas supplied by the carotid and the vertebral arteries.

I have constructed such a model (figure 16). It has four rubber tubes representing the two carotid and the two vertebral arteries. These are connected with a large tube, which represents the aorta, and the aorta is connected with a pressure bottle filled with water. Water under a pressure of 150 millimeters of mercury was then circulated through the entire system. While the water was running through and out of the six capillary tubes that represent the anterior, middle, and posterior cerebral areas, a few drops of a methylene blue solution were injected into one of the rubber carotid tubes. The blue colored water was distributed to the two anterior branches, to the homolateral middle branch, to the homolateral posterior communicating branch up to the posterior cerebral branch. Here, however, it stopped and none of the blue fluid was carried out of the posterior cerebral branch. This is the dead point, the place where the opposing streams from the carotid and vertebral arteries (through the basilar) meet, and, the pressure being equal, the streams do not mix.

EXPLANATION OF PLATES.

PLATE 52.

The photographs are colored to show the distribution of the stain.

FIG. 1. The brain of a dog after the injection of methylene blue (intra vitam) into the right carotid artery.

FIG. 2. A horizontal section of the brain of a monkey (*Macacus sinicus*) after the injection of methylene blue (intra vitam) into the right carotid artery.

FIG. 3. The brain of a *Macacus sinicus* monkey (basal aspect) after the injection of methylene blue (intra vitam) into the right carotid artery.

FIG. 4. The brain of a dog after the injection of methylene blue (intra vitam) into the right vertebral artery.

FIG. 1.



FIG. 2.



FIG. 3.



FIG. 4.

PLATE 53.

In all the tracings, the upper line indicates the time in seconds; the second line indicates the blood pressure in the femoral artery (central); the third line, respiration. The up-stroke represents expiration, and the down-stroke inspiration; the lowest line indicates the time of injection.

FIGS. 5, 6, and 7. Tracings obtained from experiments made to show the difference in action between injection into the carotid and vertebral arteries. The vertebral injection is followed by a marked interference in respiration, and vagus irritation with fall in blood pressure. If the dosage is large enough, the respiration ceases and begins again only after artificial respiration.

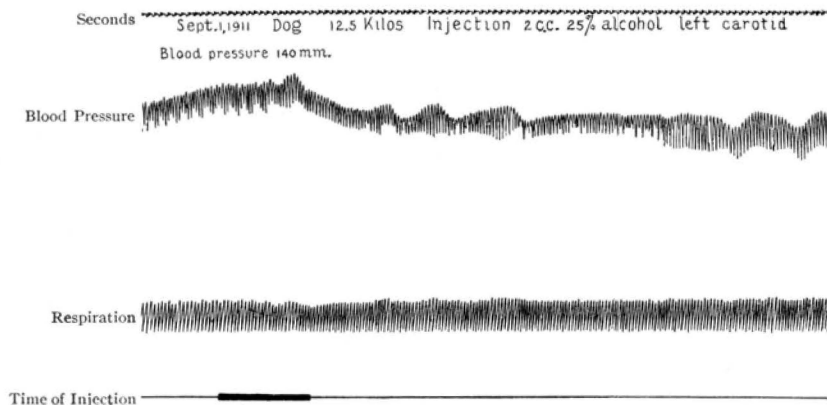


FIG. 5.

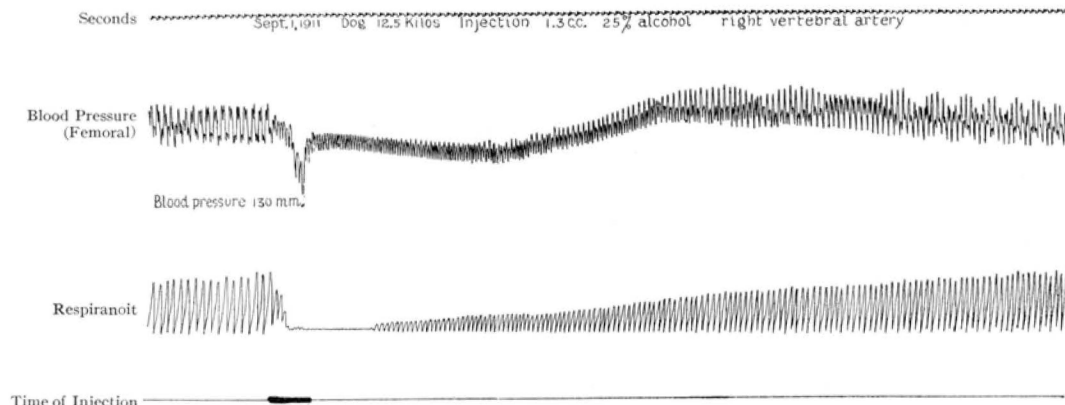


FIG. 6.

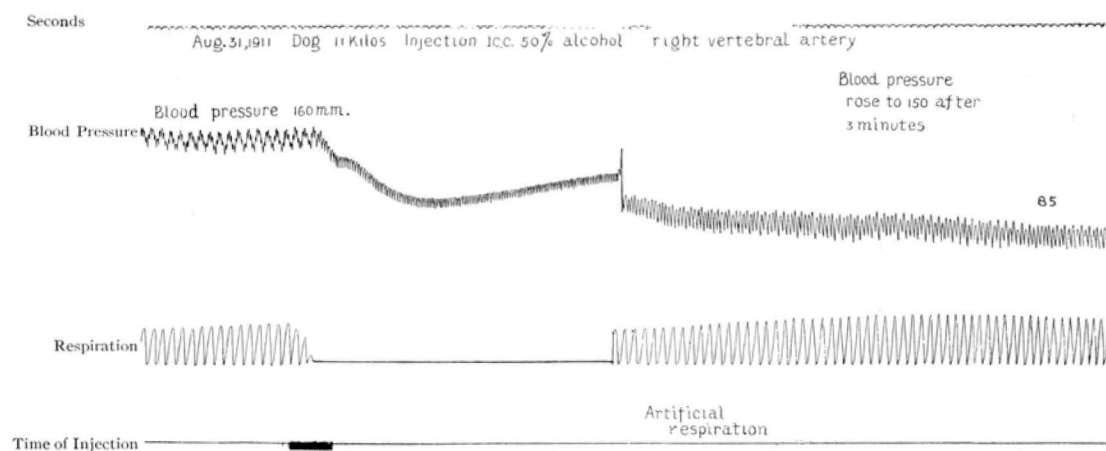


FIG. 7.

PLATE 54.

FIGS. 8, 9, and 10. These tracings show the action of ether after injection into the carotid and vertebral arteries. The injection into the carotid of small doses is without effect. After vertebral injection, there follows stoppage of respiration, vagal irritation, and a fall in blood pressure. In the experiment from which figure 10 was obtained, cessation of respiration was permanent, in spite of the fact that artificial respiration was continued for ten minutes.

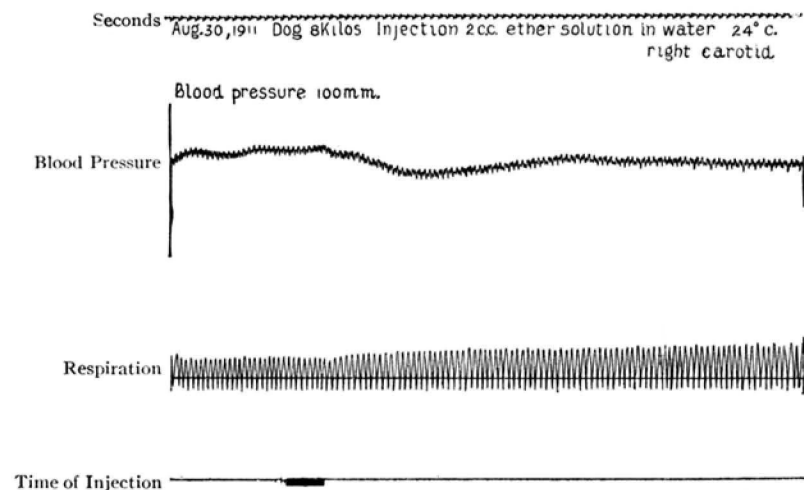


FIG. 8.

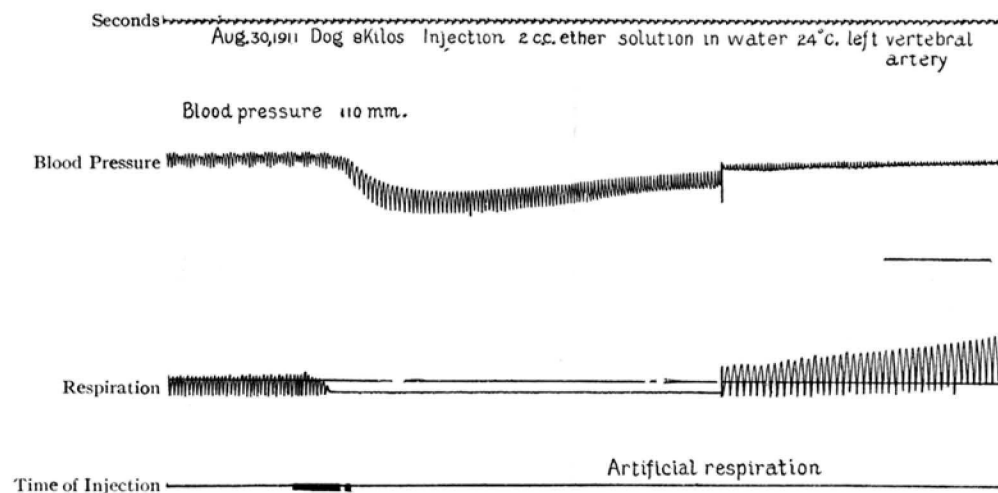


FIG. 9.

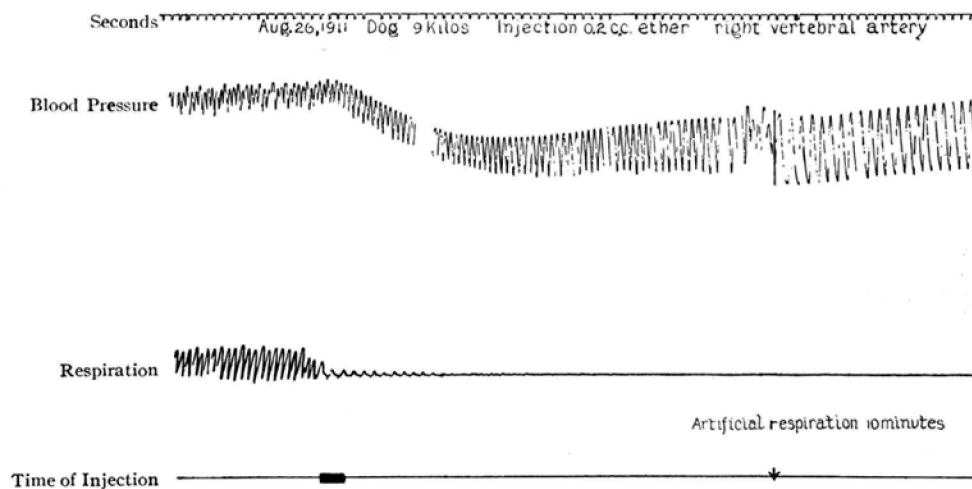


FIG. 10.

PLATE 55.

FIGS. 11, 12, 13, and 14. Tracings showing the action of chloroform after injection into the carotid and vertebral arteries. The action is similar to that of alcohol and ether.

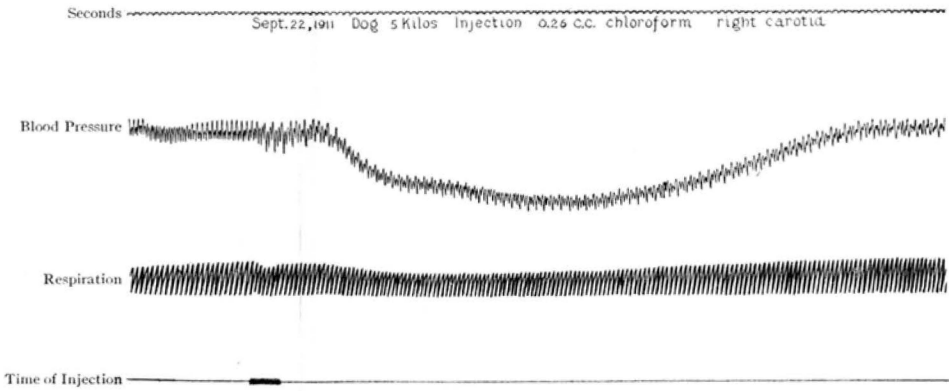
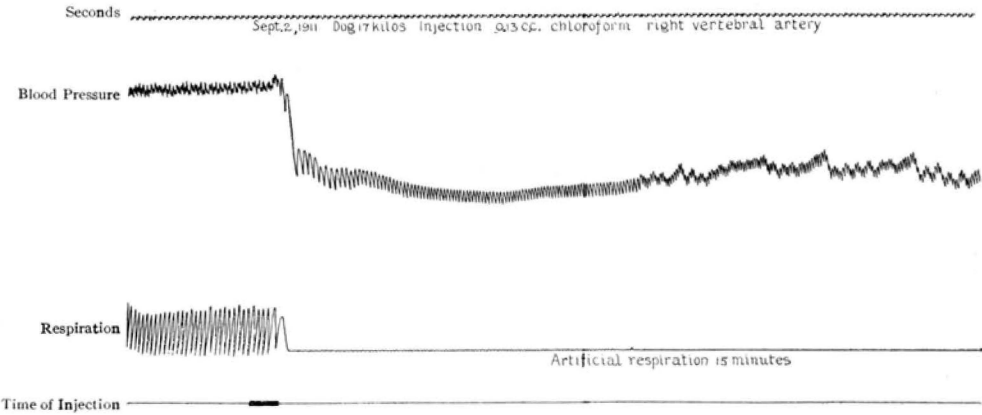
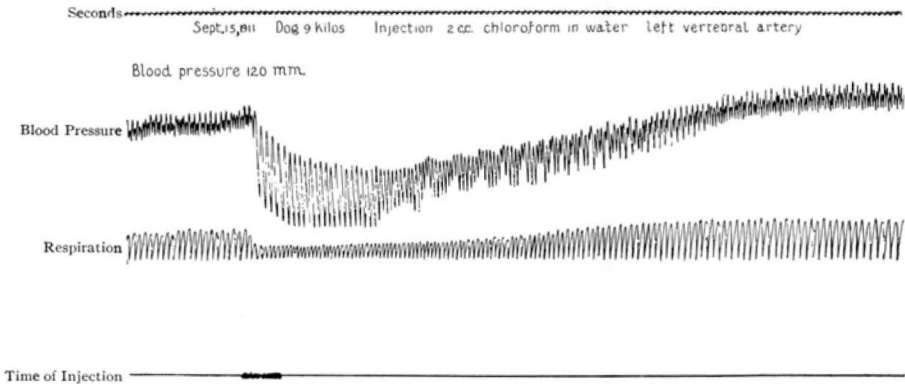
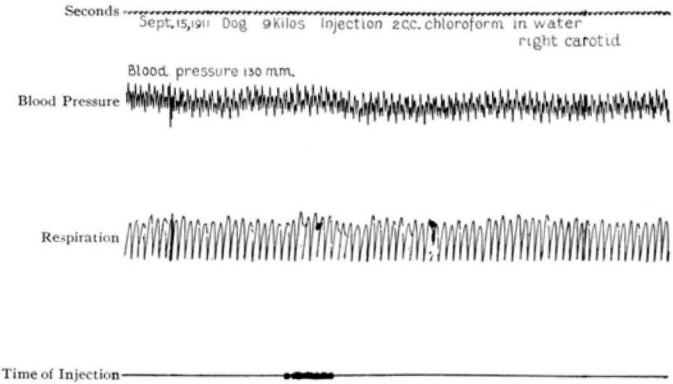


PLATE 56.

FIG. 15. Tracing obtained from an experiment in which chloroform was injected into the carotid artery before and after ligation of both vertebral arteries. When both vertebral arteries are closed, the chloroform is partly carried directly to the centers in the medulla, and an effect similar to that which follows vertebral injection, as shown in figure 13, is produced.

FIG. 16. Model of the circle of Willis. A and A' represent the anterior cerebral branches; M and M', the middle cerebral branches; P and P', the posterior cerebral branches; V and V', two vertebral tubes uniting to form the basilar, B; C and C', the carotid tubes. A hypodermic needle is inserted into one carotid. The arrows indicate the anterior and posterior limits of the blue stain when injected as indicated.

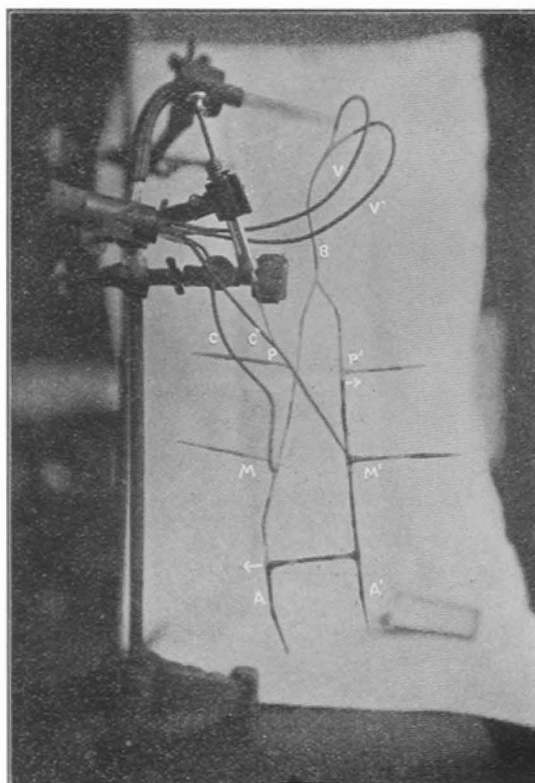
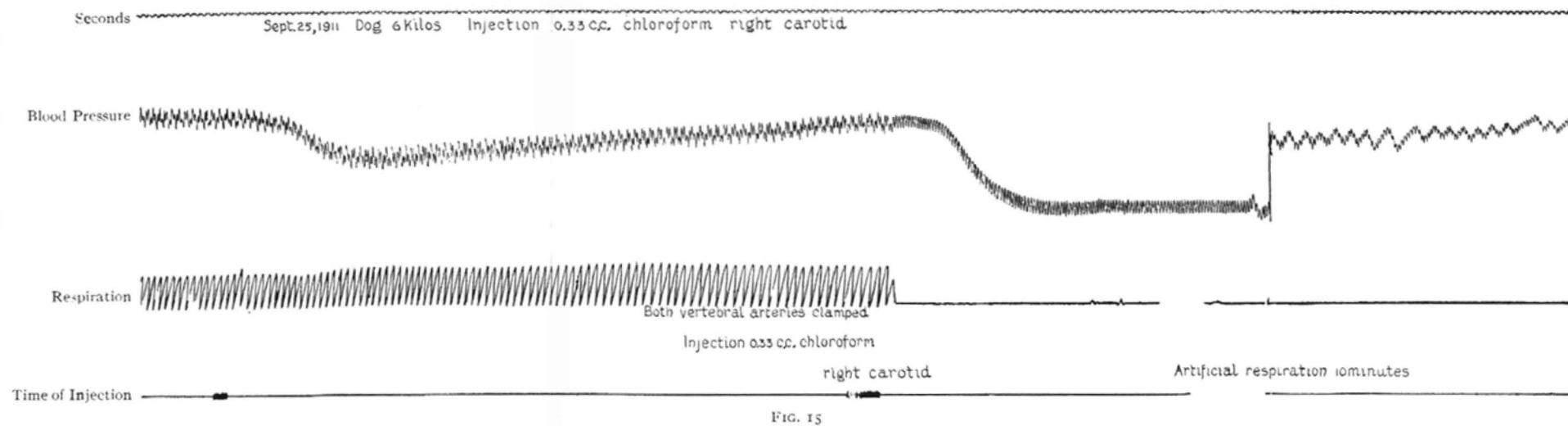


FIG. 16.

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Increase in cerebral blood flow indicated by increased cerebral arterial area and pixel intensity on brain magnetic resonance angiogram following correction of cervical lordosis

Evan A Katz, Seana B Katz, Curtis A Fedorchuk¹, Douglas F Lightstone¹, Chris J Banach, Jessica D Podoll²

Abstract:

CONTEXT: Loss of cervical lordosis is associated with decreased vertebral artery hemodynamics.

AIM: The aim of this study is to evaluate cerebral blood flow changes on brain magnetic resonance angiogram (MRA) in patients with loss of cervical lordosis before and following correction of cervical lordosis.

SETTINGS AND DESIGN: This study is a retrospective consecutive case series of patients in a private practice.

MATERIALS AND METHODS: Cervical lordosis of seven patients (five females and two males, 28–58 years) was measured on lateral cervical radiographs ranging from -13.1° to 19.0° (ideal is -42.0°). Brain MRAs were analyzed for pixel intensities representing blood flow. Pixel intensity of the cerebral vasculature was quantified, and percentage change was determined.

STATISTICAL ANALYSIS USED: A Student's *t*-test established significance of the percentage change in cerebral blood flow between pre- and postcervical lordosis adjustment images. Regression analysis was performed. An *a priori* analysis determined correlation between cervical lordosis and change in MRA pixel intensity. The statistician was blinded to the cervical lordosis.

RESULTS: Pixel intensity increased 23.0%–225.9%, and a Student's *t*-test determined that the increase was significant ($P < 0.001$). Regression analysis of the change in pixel intensity versus the cervical lordosis showed that as the deviation from a normal cervical lordosis increases, percentage change in pixel intensity on MRA decreases.

CONCLUSION: These results indicate that correction of cervical lordosis may be associated with an immediate increase in cerebral blood flow. Further studies are needed to confirm these findings and understand clinical implications.

Keywords:

Brain magnetic resonance angiogram, cerebral artery, cerebral blood flow, Cervical Denneroll™, cervical lordosis

Introduction

Loss of lordosis of the cervical spine is associated with decreased vertebral

artery hemodynamics.^[1] “Vertebral arteries proceed superiorly, in the transverse foramen of each cervical vertebra and merge to form the single midline basilar artery”^[1] which continues to the circle of Willis and cerebral arteries. Based on this

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close anatomical relationship between the cervical spine, the vertebral arteries, and cerebral vasculature, we hypothesized that improvement in cervical hypolordosis increases collateral cerebral artery hemodynamics and circulation. This retrospective consecutive case series evaluates brain magnetic resonance angiogram (MRA) in patients with cervical hypolordosis before and following correction of cervical lordosis.

Materials and Methods

All procedures performed in this case series involving the seven human participants were in accordance with the ethical standards of the Declaration of Helsinki 1964 and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the case series. Additional informed consent was obtained from all individual participants for whom identifying information is included in this article. The participants were patients in a private chiropractic practice, clinically evaluated by a doctor of chiropractic with 18 years of experience, and provided informed consent for publication of the results of this case.

The seven patients were made up of five females and two males with an age range of 28–58 years and a mean age of 42 years. Cervical lordosis was measured on neutral lateral cervical radiographs using PostureRay® X-ray analysis electronic medical record (EMR) software (PostureCo, Inc., Trinity, FL, USA) according to the Harrison posterior tangent method.^[2] The posterior tangent method has established high intraclass and interclass reliabilities with a “smaller standard error of measurement than the four-line Cobb methods.”^[3] Cervical lordosis is defined as the angle between the lines tangent to the posterior aspect of C2 and C7 vertebral bodies.^[2] Inclusion criteria were cervical lordosis $< -25^\circ$ as this is one standard deviation below the mean value reported by Harrison *et al.*^[4,5] Research has shown that the range of normal cervical lordosis, measured at the posterior of C2 and C7 vertebrae, is from -16.5° to -66.0° , with a mean of -34.0° ^[6] and an ideal normal of -42° .^[7] The negative sign indicates the normal direction of curvature for cervical lordosis. A positive angle indicates a cervical kyphosis or reversal of cervical curve. In this study, precervical lordosis adjustment measurements ranged from 19.0° to -20.4° with a mean of -1.8° [Table 1 and Figure 1]. Postcervical lordosis adjustment measurements ranged from -22.1° to -44.7° with a mean of -37.3° [Table 1 and Figure 2]. Exclusion criteria were presence of hypoplastic vertebral artery, unresolved head trauma, psychiatric disorders (i.e., depression and anxiety), age younger than 18 or older than 60 years, cervical spondylosis, cervical rib, block vertebra, cardiovascular disorders (i.e., valvular heart disease), acute or chronic infections, rheumatic diseases, or any other systemic disorders.^[1]

Table 1: Cervical lordosis and cerebral blood flow quantifications of participants for pre- and postcervical lordosis adjustment magnetic resonance angiogram

Participants	Normal ARA C2-C7 (°)	Precervical ARA C2-C7 adjustment (°)	Deviation from ideal ARA C2-C7 (°)	Postcervical ARA C2-C7 adjustment (°)	Difference between pre to post-ARA C2-C7 (°)	Preadjustment MRA area over threshold (in ²)	Postadjustment MRA area over threshold (in ²)	Preadjustment MRA total pixel intensity	Postadjustment MRA total pixel intensity	Percentage change in total pixel intensity (%)	Preadjustment MRA threshold
1	-42.0	19.0	61	-34.7	53.7	0.444	0.525	453,094	557,461	23.0	76
2	-42.0	6.7	48.7	-42.2	48.9	0.257	0.311	190,537	240,016	26.0	60
3	-42.0	3.7	45.7	-39.8	43.5	0.104	0.273	84,668	249,567	194.8	70
4	-42.0	3.0	45	-44.4	47.4	0.304	0.427	300,480	444,834	48.0	79
5	-42.0	-11.8	30.2	-22.1	10.3	0.190	0.256	170,810	256,071	49.9	70
6	-42.0	-13.1	28.9	-44.7	31.6	0.333	0.655	386,883	841,061	117.4	90
7	-42.0	-20.4	21.6	-33.1	13.1	0.235	0.607	176,260	574,491	225.9	65
Mean	-42.0	-1.8	40.2	-37.3	35.5	1.721	2.815	251,819	451,929	97.9	73

ARA C2-C7: Absolute rotational angle or cervical lordosis from C2 to C7 vertebrae, MRA: Magnetic resonance angiogram



Figure 1: Precervical lordosis adjustment radiograph. Lateral cervical images were analyzed using PostureRay® EMR software. Preradiographs show patients without the Cervical Denneroll™ Spinal Orthotic. Each image was analyzed for cervical lordosis measurements using the Harrison posterior tangent method. Red indicates the posterior aspect of the cervical vertebrae from C2 to C7. Green indicates ideal cervical lordosis from C2 to C7

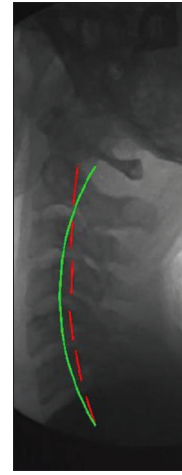


Figure 2: Postcervical lordosis adjustment radiograph. Lateral cervical images were analyzed using PostureRay® EMR software. Postradiographs show the patients with the Cervical Denneroll™ Spinal Orthotic applied as a fulcrum to the cervical spine yielding an increase in cervical lordosis. Each image was analyzed for cervical lordosis measurements using the Harrison posterior tangent method. Red indicates the posterior aspect of the cervical vertebrae from C2 to C7. Green indicates ideal cervical lordosis from C2 to C7

Brain MRA was obtained before and following cervical lordosis adjustment which was made using the Cervical Denneroll™ Spinal Orthotic (Denneroll Pty Ltd, New South Wales, Australia). As such, the findings from the MRAs before the cervical spine adjustment were served as control data compared to the findings of the MRAs following cervical lordosis adjustment. The MRAs were performed at a private medical imaging facility by a radiologic technologist certified by the American Registry of Radiologic Technologists with 8 years of experience. The Cervical Denneroll™ was used to correct loss of cervical lordosis via Mirror Image® cervical extension.^[8] Precervical lordosis adjustment MRA was performed with the patient lying flat, supine, and with their arms at their sides. The timing of the intervention was controlled. The Cervical Denneroll™ was applied to all patients immediately following the preadjustment MRA. The Cervical Denneroll™ was placed posterior to the middle-to-lower cervical spine providing a fulcrum and creating the desired cervical spine extension, and a postcervical lordosis adjustment MRA was performed with the patient lying flat, supine, and with their arms at their sides.

The circle of Willis and cerebral artery values were measured on brain MRA. Regions of interest (ROIs) were defined by the same area within each patient, and measurements taken therein were normalized internally. The ROI was the same per patient to measure pixel intensity pre- and postcervical lordosis adjustments. These measurements were then normalized internally, and the fold increase in blood flow to the area was reported. To compare images for each patient pre- and postcervical lordosis adjustments, pixel thresholds were determined for the image set and the pixel intensity

above the threshold was measured. This method ensured that the background for the image set was constant. The fold change in pixel intensity was determined for each image set based on the two images. Each set was normalized internally so that only the fold change from the initial measurement would be compared to the initial measurement. Images were analyzed using FIJI/ImageJ.^[9] Each image set was converted to an 8-bit TIF format, and appropriate pixel thresholds were set for each image pair using the threshold tool [Figures 3–6]. Pixel intensity of the cerebral vasculature was quantified by first selecting the ROI using the oval tool and quantifying the pixel intensity above the threshold using the analysis tool [Figures 4 and 6]. Pixel intensity is a gray scale depending on the degree of white or black in each pixel. Images were converted to an 8-bit format which has a gray scale from 0 (black) to 255 (white). The threshold for the images was set so that the brighter pixels, indicating blood flow, were compared. The program measured every pixel above the threshold (0–255) to give the total intensity based on the gray scale. The evaluation parameters included initial pixel intensity (I_i), final pixel intensity (I_f), and percentage change in pixel intensity ($\% \Delta I$). For each image set, the percentage change in pixel intensity was determined before and after cervical adjustment. $\% \Delta I$ is the ratio of the difference between the I_f and the I_i divided by the I_i and multiplied by 100: $\% \Delta I = (I_f - I_i) / I_i \times 100$ and provides information about cerebral blood flow (CBF). Pixel intensity analyses were done by the same PhD researcher who was blinded to the status of cervical lordosis and has 7 years of experience with the FIJI/ImageJ.

A Student's *t*-test was used to establish the significance of the percentage change in pixel intensity between

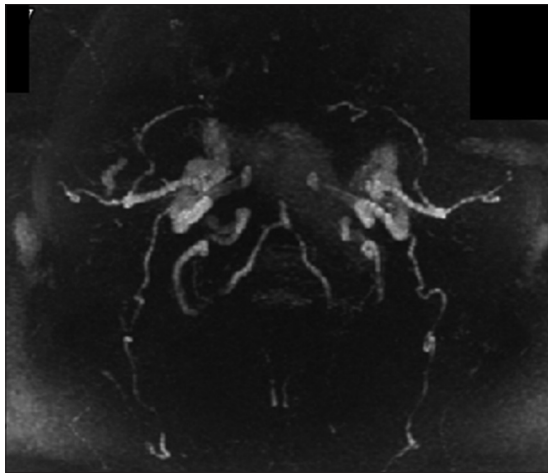


Figure 3: Precervical lordosis adjustment magnetic resonance angiogram. Brain magnetic resonance angiogram images were analyzed using FIJI/ImageJ. Each image set was converted to an 8-bit TIF format and appropriate pixel thresholds were set for each image pair using the threshold tool. White indicates blood in cerebral vasculature

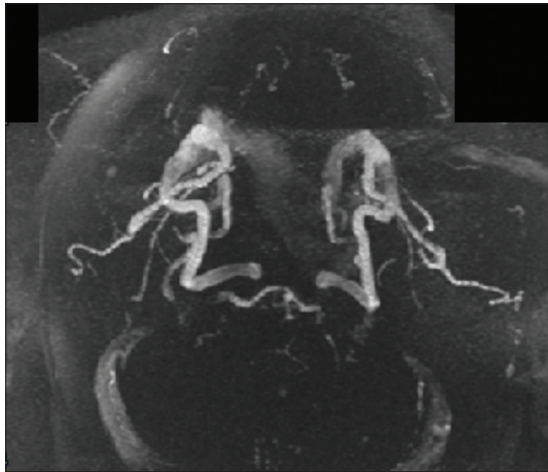


Figure 5: Postcervical lordosis adjustment magnetic resonance angiogram. Brain magnetic resonance angiogram images were analyzed using FIJI/ImageJ. Each image set was converted to an 8-bit TIF format, and appropriate pixel thresholds were set for each image pair using the threshold tool. White indicates blood in cerebral vasculature

the pre- and postadjustment image sets using the Data Analysis Plugin in Microsoft Excel. A regression analysis of the change in pixel intensity versus the cervical lordosis was performed. An *a priori* analysis was performed using G*Power 3 software to calculate the required sample size to produce a significant correlation between measured cervical lordosis and change in MRA pixel intensity. The statistician was blinded to the status of cervical lordosis.

Results

Still MRA images were analyzed using FIJI/ImageJ and their pixel intensities representing the fold change in measured blood flow were quantified [Table 1].^[9] Pixel intensities for each image following the cervical adjustment were normalized to the image taken before the adjustment

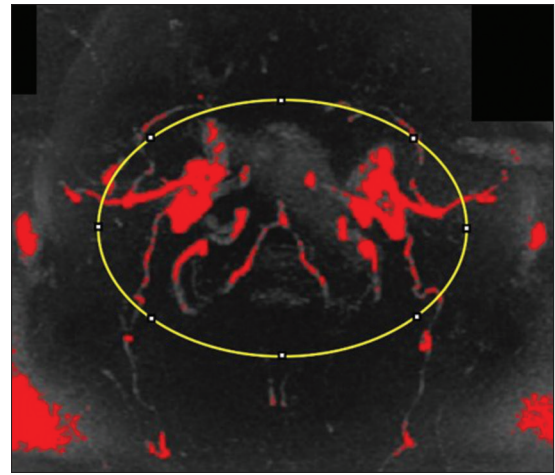


Figure 4: Precervical lordosis adjustment magnetic resonance angiogram pixel intensity analysis using FIJI/ImageJ. Pixel intensity of the cerebral vasculature was quantified by selecting the region of interest and quantifying pixel intensity. The threshold for the images was set so that the pixels indicating blood flow were compared. The quantity of red in the precervical lordosis adjustment magnetic resonance angiogram serves as a baseline for this patient. Red indicates pixels above threshold quantifying blood in cerebral vasculature. Yellow indicates the region of interest selected using the oval tool

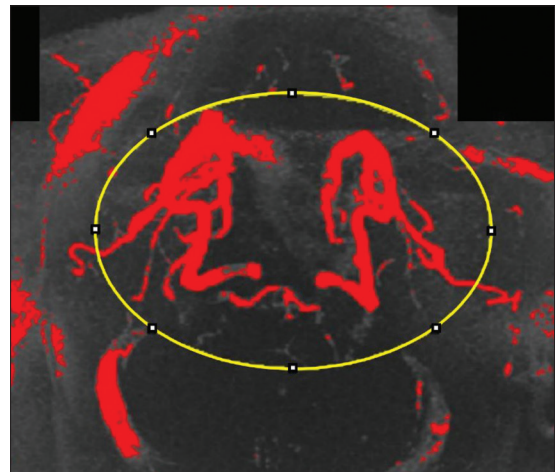


Figure 6: Postcervical lordosis adjustment magnetic resonance angiogram pixel intensity analysis using FIJI/ImageJ. Pixel intensity of the cerebral vasculature was quantified by selecting the region of interest and quantifying pixel intensity. The threshold for the images was set so that the pixels indicating blood flow were compared. The increased quantity of red in the postcervical lordosis adjustment magnetic resonance angiogram indicates increased blood volume after correction of cervical lordosis. Red indicates pixels above threshold quantifying blood in cerebral vasculature. Yellow indicates the region of interest selected using the oval tool

to calculate the percentage or fold change in pixel intensity. In each case, an increase in pixel intensity was observed ranging from 23.0% to 225.9%, and a Student's *t*-test showed that the observed increase was statistically significant within the population tested ($P = 0.001$) [Table 2]. These data indicate that correction of cervical lordosis may result in an immediate increase in the amount of CBF of the brain.

A regression analysis of the change in pixel intensity versus the cervical lordosis (absolute rotational angle [ARA])

C2–C7) was performed [Table 3].^[10] This analysis showed that as the deviation from a normal ARA increases, the percentage change in pixel intensity observed by MRA decreases [Table 3 and Figure 7]. The R-squared value for this interaction is 0.3382, indicating that 33.8% of the possible changes in observed pixel intensity can be attributed to the initial measured cervical lordosis [Table 3]. When there is a statistically significant correlation, a less than perfect linear regression is still notable.^[11] A larger sample size may allow for increased statistical significance.

An *a priori* analysis was performed using G*Power 3 software to calculate the required sample size to produce a significant correlation between measured ARA C2–C7 and change in MRA pixel intensity.^[12] If the effect size and variance remain the same, a sample size of $n = 16$ would give an 80% chance of achieving $P < 0.05$ ($r = 0.8$ and $P < 0.05$) [Table 4].

Discussion

This retrospective consecutive case series was performed to test the hypothesis that loss of cervical lordosis may be associated with the circle of Willis and cerebral artery hemodynamics. The results of this case series revealed that the circle of Willis and cerebral artery parameters were significantly different between pre- and postcervical adjustments with preadjustment values showing lower values in comparison to postadjustment values. To the best of our knowledge, there are no published data investigating the effect of loss of cervical lordosis on cerebral artery parameters. Our findings demonstrate preliminary evidence that loss of cervical lordosis may play a role in the development of changes related to the circle of Willis and cerebral artery hemodynamics and decreased blood flow in the brain.

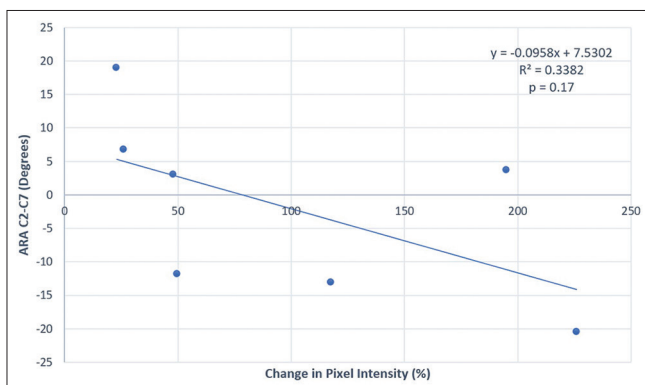


Figure 7: Change in pixel intensity versus absolute rotational angle (cervical lordosis) from C2 to C7 vertebrae. This linear regression analysis shows that as a deviation from a normal ARA increases, the percentage change in pixel intensity observed by magnetic resonance angiogram decreases. The R-squared value for this interaction is 0.3382, indicating that 33.8% of the possible change in observed pixel intensity can be attributed to the initial measured cervical lordosis. ARA C2–C7 is the absolute rotational angle measurement of cervical lordosis from C2 to C7 vertebrae (normal is 34° and ideal is 42°)

One strength of this case series is that the patients are consecutive which eliminates selection bias. One limitation of our study is that the sample size is small in total as well as within narrowed age ranges and sexes. Another limitation is that our results cannot be generalized to pediatric or geriatric populations as the participants' ages ranged from 28 to 58 years. Another limitation is that the cervical spinal orthotic changes the angle of the head and affects the angulation of the brain vasculature on the MRA.

A normal sagittal cervical spine has a lordotic curve.^[6] Loss of lordosis or cervical kyphosis is associated with increased spinal cord and nerve root tension, pain, disability, and poor health and quality of life.^[13,14] The poor health outcomes and disease processes related to loss of cervical curve originate from prolonged biomechanical stresses and strains in the neural elements.^[6] Loss of cervical lordosis leads to very large altered stresses to the vertebrae providing the basis for vertebral compression, osteoarthritis, and osteophyte formation consistent with Wolff's law.^[15] In addition to these skeletal changes in the cervical spine, the muscles and soft tissue that support

Table 2: Student's *t*-test of two sample means assuming unequal variances

Parameter	Variable 1	Variable 2
Mean	1	1.9771
Variance	0	0.6919
Observations	7	7
Parameter	Value	
Hypothesized MD	0	
df	6	
<i>t</i> statistic	-3.108	
<i>P</i> (<i>T</i> <) one-tail	0.00104	
<i>t</i> critical one-tail	1.9432	
<i>P</i> (<i>T</i> < <i>t</i>) two-tail	0.02090	
<i>t</i> critical two-tail	2.4469	

MD: Mean difference

Table 3: Regression analysis

Parameter	Value
Multiple <i>R</i>	0.581585445
<i>R</i> ²	0.33824163
Adjusted <i>R</i> ²	0.205889956
SE	12.23919497
Observations	7
SE: Standard error	

Table 4: *A priori* analysis

Parameter	Value
Input	
Tail (s)	1
Effect size <i>r</i>	0.5813777
α error probability	0.05
Power	0.8
Output	
Sample size	16
Actual power	0.802301

the neck work harder to compensate for biomechanical instability creating soft-tissue weakness and damage.^[16,17] As such, since the basilar artery is formed by the anterior spinal artery which courses through the spinal cord and the vertebral arteries which course cephalad through the transverse foramina of the first six vertebrae, prolonged aberrant stresses and strains applied to the spine will be applied to the vasculature within the spine.^[18-20]

Clinical trials have shown that correction of cervical lordosis improves neuromusculoskeletal conditions such as cervical spondylotic radiculopathy, neck pain, segmental motion, lumbosacral radiculopathy, discogenic cervical radiculopathy, cervicocephalic kinesthetic sensibility, and central conduction time and neuroplasticity,^[8,21-24] and visceral conditions such as dizziness and cervicogenic headaches.^[8] The spinal correction technique applied throughout these clinical trials employs imaging before care to determine the physiological effects of the technique protocol to ensure effective spinal care. Considering the research showing decreased cervical hemodynamics with loss of cervical lordosis and well-established spinal correction technique, MRA imaging was performed before and following cervical spine adjustments.

In this case series, data indicate that correction of cervical lordosis results in an immediate increase in the amount of CBF of the brain [Table 1] consistent with the notion that biomechanics influence physiology. Furthermore, the analysis shows that as the deviation from a normal cervical lordosis increases, the percentage change in pixel intensity observed by MRA decreases [Table 3 and Figure 7]. This may be due to the viscoelastic response of the vertebral arteries under prolonged stresses and strains due to a straightening or reversal of curve in the cervical spine. Arteries under prolonged stresses and strains become stiffer and less elastic.^[25,26] As such, restoration of normal cervical lordosis may result in a slower response from arteries that were stressed and strained the most and a faster response from arteries that were stressed and strained the least.

Loss of cervical lordosis has been associated with decreased vertebral artery hemodynamics.^[1] A relationship between loss of cervical lordosis and the vasculature that follows the vertebral arteries is an expected and logical finding. However, the possible effects of loss of cervical lordosis on cerebral hemodynamics and their clinical implications are completely unknown. Because the cerebral arteries are a major source of blood supply to the brain,^[27] the possible factors affecting these vasculatures justify investigation.

The circle of Willis and cerebral artery hemodynamics have not been studied in patients with loss of cervical lordosis. However, patients with instability of the cervical spine of >3 mm of vertebral dislocation caused

cerebral circulation dysfunction in 80% of cases,^[28] showing an association of biomechanical stress and strain in the cervical spine with cerebral circulation. We restricted our sample to individuals aged 18–60 years of age, and we included the participants without instability of the cervical spine of >3 mm of vertebral dislocation to eliminate the effects on cerebral vasculature.

While the clinical impact of loss of cervical lordosis on various health measures is well-documented,^[6,13,29] there are not many studies measuring the clinical impact of cervical lordosis on cerebral vasculature and addressing pathophysiologic mechanisms. Our results may be helpful in addressing pathophysiological mechanisms to help create a better understanding of potential clinical implications. “Substantial evidence suggests that the neurodegenerative process (for dementia and Alzheimer’s disease [AD]) is initiated by chronic cerebral hypoperfusion.”^[30] “Cervicogenic headache is a relatively common and still controversial form of headache arising from the structures in the neck.”^[31] “A control group did not show any changes in CBF between two time points, but concussed athletes demonstrated a significant decrease in CBF at 8 days relative to within 24 h.”^[32] In addition, CBF has been linked to sports-related concussion outcomes and recovery. As CBF increased in athletes following sports-related concussion, the magnitude of initial psychiatric symptoms decreased, “suggesting a potential prognostic indication for CBF as a biomarker.”^[33]

The methods or results of this case series are not being compared to studies cited in this paper. The studies cited show potential clinical significance and relevance in healthcare providing that future studies determine that correction of cervical lordosis is associated with increase in cerebral blood flow. Studying and identifying the relationship between vascular and extraspinal changes and cervical alignment may be important for considerations for spinal care. Further studies are needed to determine clinical implications of this, including rates and predisposition to transient ischemic attack or strokes. A study on how correction of cervical lordosis affects cerebral perfusion using perfusion-weighted magnetic resonance imaging or a computed tomography perfusion scan would be warranted for dementia, AD, cervicogenic headaches, and traumatic brain injury.

The results of this case series show that correction of loss of cervical lordosis was associated with increased cerebral artery parameters indicating an immediate increase in blood flow in the brain. Evidence hierarchies reflect the relative value of different types of research, providing levels of evidence. There is neither study nor level of evidence which provides unequivocal statements. Studies are always confined to their inclusion criteria as well as time, location, environment, etc., Case studies and

case series help to document remarkable or noteworthy findings and explain their relevance. This case series shows a significant increase in the cerebral vascular area indicating an increase in blood flow through the brain with improvement in cervical spinal curvature. This study follows another study which shows that decreased hemodynamics in the cervical region is associated with loss of cervical curvature. Various studies show how AD, dementia, headaches, and postconcussion and postmild traumatic brain injury symptoms are affected by CBF. This manuscript reports on remarkable and noteworthy findings that provide evidence supporting the need for further investigation. This study opens the door for future studies and clinical trials to confirm or deny these findings helping us to understand better human physiology and health which is of the utmost value. Further studies and clinical trials must include more participants and need to be done to confirm these findings and to understand their possible clinical implications. It would help to show MRA data of the patients before loss of cervical lordosis to compare with data following loss of cervical lordosis and correction thereof. However, loss of cervical lordosis can occur slowly, over years or decades due to poor posture and ergonomics, or more quickly with a trauma such as whiplash. One limitation with measuring CBF before loss of cervical lordosis and following loss of cervical lordosis due to poor posture and ergonomics over years or decades is that the data would compare a person to their much younger selves. There would be many variables to consider in comparing MRA data that were years apart such as vascular elasticity. A difficulty with measuring CBF before loss of cervical lordosis and following loss of cervical lordosis due to trauma such as whiplash is that we do not know when a whiplash-inducing trauma event may occur and the Institutional Review Board approval for inducing cervical trauma via whiplash is not feasible. Furthermore, it is unrealistic that patients who suffer from whiplash trauma would have MRA data just before the trauma. Further, the trauma has the potential to damage internal structures which add another variable. It would be valuable to compare a matched control group with a healthy cervical lordosis to one with loss in cervical lordosis (with long-term follow-up analyses), and this will be considered for future studies. In addition, to exclude the effect of the correction procedure itself, future studies need to include long-term follow-up analyses to determine whether improvement of CBF is conserved.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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