Vascular Feature Quantification on the exploration of cerebral blood flow, cognitive function and more

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Abstract

The brain requires a continuous supply of oxygen and glucose, which are delivered through the complex network of blood vessels. Disruptions to this network can affect cognitive function. Vascular feature quantification provides a means of analyzing the structure and function of blood vessels in the brain, allowing researchers to better understand the mechanisms that underlie cognitive impairment. IntraCranial Artery Feature Extraction (iCafe) is an innovative method for quantitatively assessing the intracranial vasculature developed by Dr. Li Chen at the University of Washington. iCafe allows for the extraction of quantitative vascular features that can be used as biomarkers for brain blood flow and cognitive function. This review summarizes the current research direction in Vascular Imaging Lab on how quantitative vascular analysis by iCafe is helping the exploration of cerebral blood flow, cognitive function, and more.

Keywords: Vascular feature quantification, Cognitive function, Cerebral blood flow, iCafe, Brain imaging

Introduction

The brain requires a continuous supply of oxygen and glucose, which are delivered through the complex network of blood vessels. Any disruption to this network can have significant implications on cognitive function, including memory, attention, and decision-making. Vascular feature quantification provides a means of analyzing the structure and function of blood vessels in the brain, allowing researchers to gain a better understanding of the mechanisms that underlie cognitive impairment.

Vascular features, such as length, tortuosity, and vasculature density, can indicate blood flow change because the structure of blood vessels directly affects the resistance of blood flow. For instance, if a blood vessel is longer or more tortuous, it can increase the resistance of blood flow, which can lead to a decrease in blood flow to the tissues that the vessel supplies. Conversely, if the vasculature density is higher, it can indicate increased blood flow to the region. Moreover, vascular features can also reflect changes in the vascular network's architecture, which can affect blood flow distribution. For example, changes in vessel branching patterns can alter blood flow distribution within the vasculature, leading to changes in regional blood supply. Therefore, by quantifying vascular features using techniques such as 3D time-of-flight magnetic resonance angiography and iCafe, researchers can obtain objective measures of vascular morphology and better understand blood flow changes associated with various conditions, including brain development and vascular diseases.

There has been an increasing amount of research conducted on the topic of vascular feature quantification and its relationship with cerebral blood flow and cognitive function. One such study by Liu et al. (2019) used machine learning algorithms to predict cognitive decline based on vascular features extracted from magnetic resonance imaging (MRI) scans of the brain. The study found that vascular features such as vessel tortuosity and branching angle were significant predictors of cognitive decline. Another study by Ma et al. (2020) investigated the relationship between cerebral blood flow and cognitive impairment in patients with Alzheimer's disease using perfusion-weighted MRI. The study found that decreased cerebral blood flow in specific regions of the brain was associated with cognitive impairment. Additionally, the study showed that vascular feature quantification, such as arterial transit time and mean transit time, could be used as potential biomarkers for cognitive impairment in Alzheimer's disease. These studies demonstrate the potential applications of vascular feature quantification in the exploration of cerebral blood flow and cognitive function, and highlight the importance of further research in this area.

IntraCranial Artery Feature Extraction (iCafe) is an innovative method for quantitatively assessing the intracranial vasculature using imaging techniques (L. Chen, Mossa-Basha, et al., 2018, 2019; L. Chen, Dager, et al., 2020) developed by Dr. Li Chen during his stay in Vascular Imaging Lab (VIL), University of Washington. Since its initial publication in Magnetic Resonance in Medicine in 2018 as Editor's Pick (L. Chen, Mossa-Basha, et al., 2018), iCafe has been validated (Balu et al., 2021; L. Chen, Mossa-basha, et al., 2018; L. Chen, Mossa-Basha, et al., 2019) and iteratively updated with new features and automations (L. Chen, Wang, et al., 2019; L. Chen, Dager, et al., 2020; L. Chen, Hatsukami, et al., 2020; L. Chen, Liu, et al., 2021; L. Chen, Shaw, et al., 2021). As a tool for quantitative analysis of vasculature, it has been widely used in the academic society for various research projects. iCafe allows for the extraction of quantitative vascular features, such as vessel length, branch number, and vessel diameter, which can be used as biomarkers for brain blood flow and cognitive function.

In this review, we will delve deeper into the importance of vascular feature quantification and its potential applications in studying cerebral blood flow and cognitive function. Here, using iCafe's research applications from Vascular Imaging Lab as examples, we review and summarize the current research direction in VIL on how quantitative vascular analysis by iCafe is helping the exploration on cerebral blood flow, cognitive function and more.

Validity of using vascular features to quantify blood flow

There are several existing imaging methods used to quantify cerebral blood flow, including arterial spin labeling (ASL) perfusion imaging and 3D phase contrast (PC) quantitative flow imaging.

Using these two imaging methods as reference, the VIL authors evaluate and compare the vascular features quantified by iCafe in the paper "Vessel length on SNAP MRA and TOF MRA is a potential imaging biomarker for brain blood flow,"(Gould et al., 2021). This study aims to investigate if vessel length on time-of-flight (TOF) or simultaneous non-contrast angiography and intraplaque hemorrhage (SNAP) magnetic resonance angiography (MRA) can be used as a marker for blood flow in the brain. The researchers analyzed data from 30 subjects with carotid atherosclerotic disease and compared the vessel length on TOF and SNAP with arterial spin labeling (ASL) perfusion imaging and 3D phase contrast (PC) quantitative flow imaging as references. The results showed that vessel length on both TOF and SNAP MRA correlated with whole-brain and hemispheric ASL and 3D PC blood flow measurements, with a higher correlation coefficient observed for SNAP vessel length. This suggests that the visible intracranial arteries' length on TOF or SNAP MRA can potentially serve as an imaging marker for cerebral blood flow.

In the paper of "Intracranial vascular feature changes in time of flight MR angiography in patients undergoing carotid revascularization surgery,"(Z. Chen, Chen, et al., 2020, 2021; Shirakawa et al., 2019), VIL team further validated iCafe vascular feature quantification technique with blood flow changes before and after carotid revascularization surgeries. This study aimed to explore the feasibility of using brain time-of-flight (TOF) magnetic resonance angiography (MRA) imaging to quantify intracranial blood flow and compare it to arterial spin labeling (ASL) cerebral blood flow (CBF) measurements. The study analyzed TOF and ASL images of 99 subjects who underwent carotid revascularization, and used iCafe to quantify the vasculature features such as total vessel length on the TOF images. The results showed that the TOF-iCafe vasculature parameters increased from baseline to postsurgery and then returned to a level slightly higher than the baseline, similar to ASL CBF measurements. Significant correlation between the interhemisphere asymmetry of ASL CBF and TOF-iCafe parameters at baseline was observed. The study suggests that TOF-iCafe vasculature parameters can be used as robust surrogate image markers of intracranial blood flow. investigated changes in intracranial vascular features in patients undergoing carotid revascularization surgery. The study found that vessel diameter and curvature were significantly altered following surgery, suggesting that iCafe could be used to monitor changes in the intracranial vasculature over time.

With these validation studies, iCafe was then used for multiple research topics by VIL researchers.

Vascular development during healthy aging

One direction of exploring vascular feature change is on natural aging of healthy subjects. This helps us understand vascular development from infants to the elderly.

In the paper "Quantitative Assessment of the Intracranial Vasculature in an Older Adult Population using iCafe," (L. Chen, Yuan, et al., 2018; L. Chen, Sun, Hippe, et al., 2019) VIL authors demonstrated the feasibility of using iCafe to extract quantitative features of the intracranial vasculature in an older adult population. This paper discusses a study that looks at how the blood vessels in the brain change as we age. The researchers used a technique called three-dimensional time-of-flight magnetic resonance angiography to capture images of the blood vessels in the brains of 163 participants aged 56 to 85 years. They then used a new technique called the IntraCranial artery feature extraction technique to measure the different aspects of the blood vessels. The study found that as people age, their blood vessels become more twisted and turn more. However, they also found that the number of branches and average order of the blood vessels decreased with age. These changes were consistent across different regions of the brain. The results of this study suggest that the combination of time-of-flight magnetic resonance angiography and the IntraCranial artery feature extraction technique could be a useful tool for studying changes in the blood vessels of the aging brain. By understanding how the blood vessels change as we age, we can gain insight into the development of vascular diseases and potentially develop new treatments. This is the first study of using iCafe on quantitative analysis of MRA data, suggesting that iCafe can be used to study age-related changes in the intracranial vasculature.

In the following up paper, "Quantitative Assessment of the Intracranial Vasculature of Infants and Adults Using iCafe (Intracranial Artery Feature Extraction),"(L. Chen, Shaw, et al., 2021) authors demonstrated the feasibility of using iCafe to extract quantitative features of the intracranial vasculature in infants and adults. This paper presents a study that investigates the age-related differences in intracranial vasculature features of healthy individuals, with a focus on the developmental changes in infants. The study analyzed the vasculature features of 27 healthy infants during natural sleep, 13 infants at 7 months, 14 infants at 12 months, and 13 older healthy adults. 3D time-of-flight magnetic resonance angiography acquisitions were processed using a technique called iCafe to quantify arterial features and characterize intracranial vasculature. The results showed that adult subjects had increased ACA length, tortuosity, and vasculature density compared to both 7-month-old and 12-month-old infants, as well as MCA length compared to 7-month-old infants. No brain laterality differences were observed for any vascular measures in either infant or adult age groups. The study also observed reduced skull and brain sharpness in infants, which may indicate increased head motion and brain/vascular pulsation, but this was not correlated with length, tortuosity or vasculature density measures. The paper concludes that quantitative analysis of TOF MRA using iCafe may provide an objective approach for systematic study of infant brain vascular development and for clinical assessment of adult and pediatric brain vascular diseases. Overall, this study provides valuable insights into the regional variations of blood supply during early brain development and aging.

Quantify vascular flow and rarefaction

In the paper of "Uncontrolled hypertension associates with subclinical cerebrovascular health globally: a multimodal imaging study" (Liu, Huang, et al., 2020), VIL authors investigates the association between hypertension control and subclinical cerebrovascular health using a multimodal imaging approach. The study involved 200 hypertensive older males without previous cardiovascular diseases, and magnetic resonance imaging was used to evaluate their cerebrovascular health in four aspects: intracranial atherosclerosis, vascular rarefaction (use of iCafe for vascular rarefaction analysis), cerebral blood flow, and white matter hyperintensity. The results showed that uncontrolled hypertension was associated with subclinical cerebrovascular injury globally, affecting both small and medium-to-large arteries. Furthermore, the study revealed that uncontrolled diastolic blood pressure, but not uncontrolled systolic blood pressure, was associated with increased white matter hyperintensity volume.

In the paper of "Arterial elasticity, endothelial function and intracranial vascular health: A multimodal MRI study," (Liu, Chen, et al., 2020), VIL authors investigated the relationship between arterial elasticity, endothelial function, and intracranial vascular health using multimodal MRI. This paper reports on a study that investigates the relationship between vascular dysfunctions such as arterial stiffness and endothelial dysfunction and subclinical intracranial vascular health in hypertensive subjects. The study involved 200 older hypertensive males without overt cardiovascular or cerebrovascular diseases. The researchers measured arterial elasticity as carotid-femoral pulse wave velocity (cfPWV) and endothelial function as digital reactive hyperemia index (RHI), and evaluated cerebrovascular health using MRI in four aspects: intracranial atherosclerosis, brain perfusion as cerebral blood flow (CBF), vascular rarefaction analyzed as visible arterial branches on angiography using iCafe, and small vessel disease measured as white matter hyperintensity (WMH). The results showed a negative association between cfPWV and CBF, suggesting a link between arterial stiffness and CBF decline. Higher cfPWV was also associated with the presence of intracranial stenotic plaque and greater WMH volume. RHI was positively related to CBF, indicating that endothelial dysfunction was associated with reduced CBF. The study concludes that arterial stiffness and endothelial dysfunction are associated with reduced brain perfusion in older hypertensive males, and that arterial stiffness is also associated with global cerebral vascular injury, affecting both small and medium-to-large arteries.

The paper "Urinary Sodium and Potassium Excretion and Cerebrovascular Health: A Multimodal Imaging Study" (Liu et al., 2021) investigates the association between dietary sodium and potassium intake and subclinical cerebrovascular health in hypertensive older males using multimodal magnetic resonance imaging (MRI). The study included 189 hypertensive male subjects without previous cardiovascular or cerebrovascular disease. Daily urinary sodium and potassium excretion were estimated from a fasting spot urine sample. A dedicated cerebrovascular health imaging protocol was performed to study intracranial atherosclerosis, vascular rarefaction (use of iCafe for vascular rarefaction analysis), brain perfusion, and small vessel disease. The results showed that increased urinary sodium excretion was associated with decreased cerebral blood flow, and elevated urinary potassium excretion was associated with reduced prevalence of intracranial plaque. The study concluded that in hypertensive older males without overt cardiovascular disease, increased sodium intake and reduced potassium intake are associated with impaired subclinical cerebrovascular health.

The paper “Effects of Levodopa Therapy on Cerebral Arteries and Brain Tissue Perfusion in Parkinson’s Disease Patients” (Xiong et al., 2018, 2022) investigates the effects of levodopa, the most commonly used therapy for Parkinson's Disease (PD), on cerebral arteries and blood flow in PD patients. The study included 57 PD patients and 17 age-matched healthy controls who were scanned for artery morphology (quantified by iCafe) and cerebral perfusion imaging at baseline, then re-scanned 50 minutes after taking levodopa. The results indicated that levodopa elevated blood perfusion levels in the brains of PD patients to normal levels and dilated proximal arteries. Additionally, the study found a correlation between blood perfusion and motor syndrome scale post-levodopa. The findings suggest that levodopa may have a regulatory effect on cerebrovascular abnormalities in PD patients.

Relation of vascular features with cognitive impairment

The paper "Associations of intracranial artery length and branch number on non-contrast enhanced MRA with cognitive impairment in individuals with carotid atherosclerosis,"(Z. Chen et al., 2022) investigated the association between quantitative features of the intracranial vasculature and cognitive impairment in individuals with carotid atherosclerosis. This study aimed to find new ways to identify and understand the role of vascular factors in cognitive impairment and dementia. The researchers used non-contrast enhanced magnetic resonance angiography (NCE-MRA) images to extract three features of intracranial distal arteries (A2, M2, P2 and more distal) in 29 subjects aged 40-90 years with carotid atherosclerotic disease. They also measured cerebral blood flow using arterial spin labeling (ASL) and phase contrast (PC) as references. The study found that the length and number of branches of intracranial arteries on NCE-MRA were positively associated with global cognition measured by the Montreal Cognitive Assessment (MoCA) scores. These findings suggest that intracranial vascular features on NCE-MRA could be useful markers for cerebrovascular health and provide additional information beyond conventional brain blood flow measurements in people with cognitive impairment.

The paper "Alterations in cerebral distal vascular features and effect on cognition in a high cardiovascular risk population: A prospective longitudinal study" (Zhang et al., 2022, 2023) further explore the longitudinal alterations of vascular feature changes on cognition in a high cardiovascular risk population. While previous studies have mainly focused on proximal large arteries and small vessels, this study specifically examines medium-to-large intracranial arteries. The authors use two types of non-contrast enhanced magnetic resonance angiography (NCE-MRA) techniques to measure vascular morphologic features and arterial spin labeling (ASL) MRI to assess grey matter tissue level perfusion. They found that alterations in the vascular features of distal medium-to-large arteries, as measured by simultaneous non-contrast angiography and intraplaque hemorrhage (SNAP) MRA, were significantly associated with changes in cognitive function as measured by the Montreal Cognitive Assessment (MoCA) scores. In contrast, there were no significant associations between MoCA scores and vascular features on 3D Time-of-flight (TOF) MRA or ASL GM CBF. The findings suggest that hemodynamic information from distal medium-to-large arteries provides an additional tool to advance understanding of the vascular contributions to cognitive function.

iCafe application of flow quantification on other vascular beds

In addition to cerebral arteries, VIL team has also documented interests on analyzing other vascular beds, including carotid arteries (L. Chen, Sun, Canton, et al., 2019; L. Chen, Sun, et al., 2018, 2020; L. Chen, Zhao, Balu, et al., 2019; L. Chen, Zhao, et al., 2021; Geleri et al., 2022; Guo et al., 2021; Jiang et al., 2020), popliteal arteries (Canton et al., 2021; L. Chen, Canton, et al., 2020; L. Chen, Liu, et al., 2020; Hippe et al., 2020) and peripheral arteries (Balu et al., 2019; L. Chen, Benyakorn, Canton, et al., 2019). iCafe, after minor editions (L. Chen, Benyakorn, Canton, et al., 2019), can also be applied on other vascular beds to quantify their vascular flow.

For example, the paper "Quantitative measurements of decreased arterial collateralization and branching in peripheral artery disease." (Balu et al., 2019) reports on the development and use of automated quantitative measurements of lower limb vascular morphology (modified iCafe version) to assess the extent of collateralization/branching (CB) in patients undergoing revascularization for peripheral artery disease (PAD). The study found that CB was increased in cases of occlusion compared to stenosis, indicating compensatory CB development. The findings suggest that pCafe metrics could be useful for informing risk of ischemia and response to revascularization in patients with severe PAD.

Conclusion

In conclusion, iCafe is a promising method for quantitatively assessing the intracranial vasculature using imaging techniques. These studies suggest that non-invasive imaging techniques can provide valuable insights into the underlying mechanisms of cerebrovascular disease and cognitive impairment. By studying the relationships between vascular dysfunctions and intracranial vascular health, we can identify potential biomarkers for early detection and prevention of cerebrovascular disease and cognitive decline. Further research is needed to validate these findings and to explore the full potential of iCafe in clinical practice.

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