

Functional TCD

Background:

Functional transcranial Doppler sonography (fTCD) constitutes a complementary neuroimaging tool measuring cerebral perfusion changes due to neural activation. Functional TCD utilizes pulse-wave Doppler technology to record blood flow velocities in the anterior, middle, and posterior cerebral arteries. Comparable to other perfusion-sensitive neuroimaging techniques like functional magnetic resonance imaging or positron emission tomography, fTCD is based on a close coupling between regional cerebral blood flow changes and neural activation.

Presurgical determination of language lateralization is important for planning and outcome estimation of neurosurgical interventions in patients with drug-refractory epilepsy.

Literature:

Is vasomotor reactivity impaired in idiopathic Parkinson's disease?

Author	<p><i>M. F. Hanby, R. Panerai, T. Robinson and V. Haunton</i></p> <p>Department of Cardiovascular Sciences, University Hospitals of Leicester, Leicester, United Kingdom</p>
Content/Summary	<p>Diameter of a cerebral blood vessel is regulated by a combination of myogenic, metabolic and neurogenic influences. The ability of a blood vessel to change diameter in response to a change in [CO₂] is often referred to as vasomotor reactivity (VMR).</p> <p>The autonomic neurogenic influences originate from both noradrenergic neurons and dopaminergic neurons. In addition to its local effects, a change in [CO₂] affects activation of the autonomic nervous system.</p> <p>Methods: Transcranial Doppler was used to measure cerebral blood flow velocity (CBFV) in the middle cerebral artery in forty patients with IPD and fifty HC. End-tidal CO₂; heart rate and arterial blood pressure were continuously monitored. Subjects breathed room air for 60 seconds, hyperventilated for 90 seconds and returned to breathing room air for a further 120 seconds. VMR ($\Delta\text{CBFV}/\Delta\text{ETCO}_2$) was calculated under normocapnic and hypocapnic conditions</p>
Comment	<p>Neither baseline CBFV or VMR was found to significantly differ in patients with IPD in comparison to HC.</p>

Doppler-device	Not known
Quantification	

Association between carotid stenosis and cerebral vasomotor reactivity measured by breath holding index

Author	<i>M. Mijajlovic, M. Stojanovic, T. Pekmezovic, N. Sternic</i> Neurology Clinic of the Clinical Center of Serbia and School of Medicine University of Belgrade, Belgrade, Serbia
Content/Summary	<p>Many extrinsic and intrinsic factors influence cerebral vasomotor reactivity (VMR), which is a reliable marker of cerebral small vessels functional status, including morphological and functional parameters of large and small brain blood vessels.</p> <p>The aim of our study was to investigate correlation between VMR, and morphological and hemodynamic parameters of carotid arteries.</p> <p>Methods: In retrospective cross sectional study we included 285 patients. Cerebral VMR was evaluated measuring breath holding test (BHI), while morphological and hemodynamic parameters of carotid arteries were measured using ultrasonic methods (intima-media thickness-IMK, peak systolic velocity-PSV, end diastolic velocity-EDV). We also noted middle cerebral artery (MCA) hemodynamic parameters: mean flow velocity (MFV) and pulsatility index (PI). From medical records we collected information about age, gender, and vascular risk factors: hypertension, diabetes mellitus, atrial fibrillation, cardiomyopathy, dyslipidemia and smoking.</p>
Comment	Our investigation shows correlation between cerebral VMR, and morphological as well as hemodynamic parameters in carotid arteries. Our results also show higher influence of morphological than hemodynamic parameters on VMR.
Doppler-device	Not known
Quantification	

Transcranial Doppler ultrasonography CO₂ reactivity does not predict recurrent ischaemic stroke in patients with symptomatic carotid artery occlusion.

Author	Jolink WM ¹ , Heinen R, Persoon S, van der Zwan A, Kappelle LJ, Klijn CJ.
Content/Summary Abstract	<p>BACKGROUND:</p> <p>Patients with transient ischaemic attacks (TIAs) or minor disabling ischaemic stroke associated with an internal carotid artery (ICA) occlusion have a high risk of recurrent stroke in case of compromised cerebral blood flow. Recent studies showed that increased oxygen extraction fraction measured by positron emission tomography (PET) is still an independent predictor of subsequent stroke under current medical treatment, but PET facilities are not widely available. Transcranial Doppler (TCD) ultrasonography CO₂ reactivity is a cheap and non-invasive alternative to measure haemodynamic compromise. The aim of our study was to investigate whether TCD CO₂ reactivity is an independent predictor of recurrent ischaemic stroke in a large cohort of patients with symptomatic ICA occlusion in a time where rigorous control of vascular risk factors has been widely implemented in clinical practice.</p> <p>METHODS:</p> <p>Between July 1995 and December 2009, we included consecutive patients with TIAs or minor disabling ischaemic stroke (modified Rankin Scale ≤3) associated with ICA occlusion who were referred to the University Medical Centre Utrecht, The Netherlands. All patients were treated with antiplatelet therapy and received rigorous control of vascular risk factors, including statins, treatment for diabetes and hypertension and lifestyle advices. CO₂ reactivity was measured with TCD within 3 months after presentation. We determined the predictive value of TCD CO₂ reactivity for recurrent ischaemic stroke using Cox proportional hazard analysis.</p> <p>RESULTS:</p> <p>We included 201 patients with a median follow-up time of 7.1 years. Mean CO₂ reactivity was 15% (±20 standard deviation). The annual rate for ipsilateral ischaemic stroke was 2.2% [95% confidence interval (CI) 1.4-3.2] and for any recurrent stroke 3.2% (95% CI 2.3-4.4). We did not find a significant relationship between CO₂ reactivity and the risk of ipsilateral [hazard ratio (HR) for every increase in percentage point 1.01, 95% CI 0.99-1.02] or any recurrent ischaemic stroke (HR 1.01, 95% CI 0.998-1.02). Multivariable analysis showed a significant relationship with history of stroke (HR 4.0, 95% CI 1.8-9.0) for ipsilateral recurrent stroke, and age (HR for increase per year 1.05, 95% CI 1.01-1.09) and a history of stroke (HR 3.4, 95% CI 1.7-6.6) for any recurrent stroke.</p> <p>CONCLUSIONS:</p> <p>In patients with TIAs or non-disabling stroke associated with occlusion of</p>

	the carotid artery, the long-term annual risk of stroke is generally low with careful control of vascular risk factors. Impaired CO ₂ reactivity measured within 3 months after presentation does not identify the subgroup of patients at high risk of recurrent ischaemic stroke.
Comment	TCD with CO ₂ reactivity test failed to identify high risk for stroke after TIA in patients with ICA occlusion. The strengths of the study are the long term follow-up and high number of patients.
Doppler-device	Multi-Dop X device, DWL
Quantification	Authors believe that TCD with CO ₂ reactivity failed to identify high risk for stroke after TIA in patients with ICA occlusion.

Cerebrovascular reactivity predicts stroke in high-grade carotid artery disease.

Author	Reinhard M ¹ , Schwarzer G ² , Briel M ² , Altamura C ² , Palazzo P ² , King A ² , Bornstein NM ² , Petersen N ² , Motschall E ² , Hetzel A ² , Marshall RS ² , Klijn CJ ² , Silvestrini M ² , Markus HS ² , Vernieri F ² .
Content/Summary Abstract	<p>OBJECTIVE:</p> <p>To assess the usefulness of transcranial Doppler CO₂ reactivity (CO₂R) for prediction of ipsilateral ischemic stroke in carotid artery stenosis and occlusion with a meta-analysis of prospective studies based on individual patient data.</p> <p>METHODS:</p> <p>We searched Medline, Biosis Previews, Science Citation Index, The Cochrane Library, and EMBASE for studies in which patients with severe carotid artery stenosis or occlusion underwent Doppler CO₂R testing (inhalation of CO₂ or breath-holding) and were prospectively followed for ipsilateral ischemic stroke. Individual data from 754 patients from 9 studies were included. We used percentage cerebral blood flow velocity increase (pCi) during hypercapnia as the primary CO₂R measure, and defined impaired reactivity as pCi <20% increase.</p> <p>RESULTS:</p> <p>In a multiple regression model, impaired CO₂R was independently associated with an increased risk of ipsilateral ischemic stroke (hazard ratio [HR] 3.69; confidence interval [CI] 2.01, 6.77; p < 0.0001). Risk prediction was similar for recently symptomatic vs asymptomatic patients. Using continuous values of pCi, a significant association between decreasing pCi and increasing risk of ipsilateral stroke was found: HR of 1.64 (95% CI 1.33, 2.02; p < 0.0001) per 10% decrease in pCi. For patients with asymptomatic internal carotid artery stenosis only (n = 330), a comparable stroke risk prediction was found: increasing HR 1.95 (95% CI 1.26, 3.04; p = 0.003) per 10% decrease in pCi.</p>
Comment	This analysis supports the usefulness of CO ₂ R in risk prediction for patients with severe carotid artery stenosis or occlusion, both in recently symptomatic and asymptomatic patients. Further studies should evaluate whether treatment strategies in asymptomatic patients based on CO ₂ R could improve patient outcomes.
Doppler-device	Not known
Quantification	A review on the usefulness of CO ₂ reactivity tests in prediction of stroke for patients with severe carotid stenosis or occlusion which suggests that the results of selected studies confirm its application in both symptomatic and asymptomatic patients.

Cerebrovascular reactivity assessed by transcranial Doppler ultrasound in sport-related concussion: a systematic review.

Author	Gardner AJ¹ , Tan CO² , Ainslie PN³ , van Donkelaar P⁴ , Stanwell P⁵ , Levi CR¹ , Iverson GL⁶ .
Content/Summary Abstract	<p>BACKGROUND: Traumatic brain injury influences regulation of cerebral blood flow in animal models and in human studies. We reviewed the use of transcranial Doppler ultrasound (US) to monitor cerebrovascular reactivity following sport-related concussion.</p> <p>REVIEW METHOD: A narrative and systematic review of articles published in the English language, from December 1982 to October 2013.</p> <p>DATA SOURCES: Articles were retrieved via numerous databases using relevant key terms. Observational, cohort, correlational, cross-sectional and longitudinal studies were included.</p>
Comment	Three publications met the criteria for inclusion; these provided data from 42 athletes and 33 controls. All three studies reported reductions in cerebrovascular reactivity via transcranial Doppler US.
Doppler-device	Not known
Quantification	These initial results support the use of cerebrovascular reactivity as a research tool for identifying altered neurophysiology and monitoring recovery in adult athletes. Larger cross-sectional, prospective and longitudinal studies are required to understand the sensitivity and prognostic value of cerebrovascular reactivity in sport-related concussion.

Functional TCD: regulation of cerebral hemodynamics--cerebral autoregulation, vasomotor reactivity, and neurovascular coupling.

Author	<u>Wolf ME¹</u> .
Content/Summary Abstract	Three main mechanisms influence cerebral hemodynamics, with the aim of adapting the cerebral blood flow to the metabolic demand of the brain. Cerebral autoregulation ensures stable perfusion of the brain, independent of the systemic blood pressure. Vasomotor reactivity reflects the hemodynamic responses to modifications of the arterial pCO ₂ /pH of the brain tissue. Neurovascular coupling adapts the perfusion to increased metabolic demand as a consequence of enhanced brain activity to permit reasonable functioning of cells. Different methods using transcranial Dopplersonography have been developed to characterize these mechanisms in healthy subjects and under pathologic conditions. The most established applications in clinical settings are described, and the results of specific research studies are briefly reported.
Comment	
Doppler-device	Not known
Quantification	

Assessment of cerebrovascular reactivity during resting state breathing and its correlation with cognitive function in hypertension.

Author	Hajjar I¹ , Marmorelis V , Shin DC , Chui H .
Content/Summary Abstract	BACKGROUND: Hypertension is associated with cognitive deficits, particularly executive function, and decreased cerebral microvascular responsiveness to CO ₂ (CO ₂ vasoreactivity). The relation between CO ₂ vasoreactivity and executive function is not known. Protocols to assess CO ₂ vasoreactivity are cumbersome and require inhaling a CO ₂ -enriched gas. We explored the ability to measure CO ₂ vasoreactivity using end-tidal CO ₂ fluctuations during normal breathing and the association of this measure with cognitive function in hypertension.
Comment	Data were collected from 41 individuals with hypertension (mean age 71 years, 24% African Americans, 61% women, off antihypertensive therapy). Lower CO ₂ vasoreactivity was associated with a worse executive function test score using both calculation methods: p value using the hyper/hypoventilation data was 0.04 and from the PDM analysis was 0.009. PDM calculations showed a stronger correlation with executive function (0.41 vs. 0.21 using the hyper/hypoventilation data). There were no associations with memory or attention measures. There was a weak but statistically significant correlation between the two calculation methods of CO ₂ vasoreactivity ($R(2) = 14\%$, $p = 0.02$).
Doppler-device	Not known
Quantification	This study suggests that the decrease in CO ₂ vasoreactivity in hypertension is associated with lower executive function. This may offer new insight into the vascular underpinning of cognitive decline in hypertension. We demonstrate that calculating CO ₂ vasoreactivity is possible during normal breathing. If replicated in future studies, this may offer a more convenient clinical way to assess CO ₂ vasoreactivity in hypertension and cognitive disorders.

Hemodynamic monitoring of middle cerebral arteries during cognitive tasks performance.

Author	Boban M¹ , Črnac P. , Junaković A. , Malojčić B.
Content/Summary Abstract	<p>AIM: The aim of this study was to obtain temporal pattern and hemispheric dominance of blood flow velocity (BFV) changes and to assess suitability of different cognitive tasks for monitoring of BFV changes in the middle cerebral arteries (MCA).</p> <p>METHODS: BFV were recorded simultaneously in MCA during performance of phonemic verbal fluency test (pVFT), Trail Making Tests A and B (TMTA and TMTB) and Stroop tests in 14 healthy, right-handed volunteers aged 20-26 years.</p>
Comment	A significant increase of BFV in both MCA was obtained during performance of all cognitive tasks. Statistically significant lateralization was found during performance of Stroop test with incongruent stimuli, while TMTB was found to have the best activation potential for MCA.
Doppler-device	DWL Doppler Boxx
Quantification	<p>Author findings specify TMTB as the most suitable cognitive test for monitoring of BFV in MCA.</p> <p>© 2014 The Authors. Psychiatry and Clinical Neurosciences © 2014 Japanese Society of Psychiatry and Neurology.</p>

Autonomic dysfunction affects dynamic cerebral autoregulation during Valsalva maneuver: comparison between healthy and autonomic dysfunction subjects.

Author	<u>Castro PM¹, Santos R², Freitas J³, Panerai RB⁴, Azevedo E².</u>
Content/Summary Abstract	<p>The role of autonomic nervous system (ANS) in adapting cerebral blood flow (CBF) to arterial blood pressure (ABP) fluctuations [cerebral autoregulation (CA)] is still controversial. We aimed to study the repercussion of autonomic failure (AF) on dynamic CA during the Valsalva maneuver (VM). Eight AF subjects with familial amyloidotic polyneuropathy (FAP) were compared with eight healthy controls. ABP and CBF velocity (CBFV) were measured continuously with Finapres and transcranial Doppler, respectively. Cerebrovascular response was evaluated by cerebrovascular resistance index (CVRI), critical closing pressure (CrCP), and resistance-area product (RAP) changes. Dynamic CA was derived from continuous estimates of autoregulatory index (ARI) [ARI(t)]. During phase II of VM, FAP subjects showed a more pronounced decrease in normalized CBFV (78 ± 19 and $111 \pm 16\%$; $P = 0.002$), ABP (78 ± 19 and $124 \pm 12\%$; $P = 0.0003$), and RAP (67 ± 17 and $89 \pm 17\%$; $P = 0.019$) compared with controls. CrCP and CVRI increased similarly in both groups during strain. ARI(t) showed a biphasic variation in controls with initial increase followed by a decrease during phase II but in FAP this response was blunted (5.4 ± 3.0 and 2.0 ± 2.9; $P = 0.033$). Our data suggest that dynamic cerebral autoregulatory response is a time-varying phenomena during VM and that it is disturbed by autonomic dysfunction. This study also emphasizes the fact that RAP + CrCP model allowed additional insights into understanding of cerebral hemodynamics, showing a higher vasodilatory response expressed by RAP in AF and an equal CrCP response in both groups during the increased intracranial and intrathoracic pressure, while classical CVRI paradoxically suggests a cerebral vasoconstriction.</p>
Comment	
Doppler-device	Not known
Quantification	

Inferring common cognitive mechanisms from brain blood-flow lateralization data: a new methodology for fTCDanalysis.

Author	<u>Meyer GF¹, Spray A², Fairlie JE³, Uomini NT³.</u>
Content/Summary Abstract	The aim of this paper is to show how a time-locked correlation-analysis of cerebral blood flow velocity (CBFV) lateralization data, obtained with functional TransCranial Doppler (fTCD) ultrasound, can be used to infer cerebral activation patterns across tasks. In a first experiment we demonstrate that the proposed analysis method results in data that are comparable with the standard Lateralization Index (LI) for within-task comparisons of CBFV patterns, recorded during cued word generation (CWG) at two difficulty levels. In the main experiment we demonstrate that the proposed analysis method shows correlated blood-flow patterns for two different cognitive tasks that are known to draw on common brain areas, CWG, and Music Synthesis. We show that CBFV patterns for Music and CWG are correlated only for participants with prior musical training. CBFV patterns for tasks that draw on distinct brain areas, the Tower of London and CWG, are not correlated.
Comment	Current neuroimaging techniques with high spatial resolution constrain participant motion so that many natural tasks cannot be carried out.
Doppler-device	Not known
Quantification	The proposed methodology extends conventional fTCD analysis by including temporal information in the analysis of cerebral blood-flow patterns to provide a robust, non-invasive method to infer whether common brain areas are used in different cognitive tasks. It complements conventional high resolution imaging techniques.

dopOSCCI: A functional transcranial Doppler ultrasonography summary suite for the assessment of cerebral lateralization of cognitive function.

Author	(Badcock, Holt, u. a., 2011)
Content/Summary	New software package, 'dopOSCCI', which summarises data from experimental studies where functional transcranial Doppler ultrasonography (fTCD) is used to compare hemispheric rates of blood flow in order to assess lateralization of a cognitive process.
Comment	
Doppler-device	Multi-Dop Doppler Ultrasound devices (DWL Multidop T2: manufacturer, DWL Elektronische Systeme, Singen, Germany)
Quantification	The unique aspects of dopOSCCI allow multi-file processing, multi-event marker processing, behavioural and multi-session summaries, image file data visualization, and tab-delimited output files which includes split-half, single-trial summaries and data quality variables.

Presurgical functional transcranial Doppler sonography (fTCD) with intravenous echo enhancing agent SonoVue enables determination of language lateralization in epilepsy patients with poor temporal bone windows.

Author	(House u. a., 2011)
Content/Summary	Here, we established stable and sufficient CBFV signals in both MCAs using continuous intravenous application of echo-enhancing agent SonoVue in 7 of 10 patients with poor temporal bone windows and were thus able to determine language lateralization.
Comment	10 native German-speaking adults (3 female, 7 male) with a mean age of 49.6 years [standard deviation (SD) 10.78; range 29–68 years] with drug-refractory temporal lobe epilepsy.
Doppler-device	Multi-Dop- L1 (Compumedics Germany GmbH, Singen, Germany)
Quantification	We conclude that the application of SonoVue can solve one principal disadvantage of fTCD and improves the applicability of the technique as a pre-surgical functional language lateralization procedure.

Assessment of cerebral lateralization in children using functional transcranial Doppler ultrasound (fTCD).

Author	(Bishop, Badcock, u. a., 2010)
Content/Summary	Compared with other brain imaging methods, fTCD is relatively unaffected by movement artefacts from speaking, and so we are able to get a reliable result from tasks that involve describing pictures aloud.
Comment	Other methods, such as fMRI, are expensive for large-scale studies, and not always feasible with children. Here we will describe the use of functional transcranial Doppler ultrasound (fTCD) as a cost-effective, non-invasive and reliable method for assessing cerebral lateralization.
Doppler-device	Not known
Quantification	Accordingly, we have developed a child-friendly task that involves looking at video-clips that tell a story, and then describing what was seen.

An efficient and reliable method for measuring cerebral lateralization during speech with functional transcranial Doppler ultrasound.

Author	(Bishop u. a., 2009)
Content/Summary	Animation Description gave valid results, and we subsequently demonstrated its reliability in a group of 21 4-year-old children.
Comment	fTCD to compare indices of language lateralization in 33 adults in three different paradigms: Word Generation, Picture Description and a shorter Animation Description task.
Doppler-device	Not known
Quantification	Cerebral lateralization during spoken language generation can be assessed reliably and cheaply using fTCD with a paradigm that is less taxing than the traditional word generation paradigm, does not require literacy skills and can be completed in 15min or less.

Transcranial Doppler monitoring during language tasks in stroke patients with aphasia.

Author	(Treger u. a., 2007)
Content/Summary	Delta mean flow velocity (MFV) in the left Middle Cerebral Artery (MCA) was found to be much lower in aphasia patients as compared to healthy subjects. Negative statistical correlation was found between the improvement of language ability and the blood flow velocity parameters in the left hemisphere. Aphasia patients with good language ability showed much higher MFV in the right MCA during the first test. Left hemispheric blood flow velocity shift was found to be higher during speech tasks in the patients with poor language ability.
Comment	Prospective study investigating results of TCD monitoring during language naming and recognition tasks in ischemic stroke patients (n = 32) with and without aphasia and 5 control subjects.
Doppler-device	Not known
Quantification	Our study suggests that the performance of language tasks in aphasia patients during early recovery after stroke is associated with relatively high right hemisphere activation. High blood flow velocity in the right MCA of aphasia patients was found to be a good prognostic sign for better language ability. Arterial blood flow that shifted towards the left hemisphere during speech tasks was associated with poor language ability.

Functional transcranial Doppler sonography.

Author	(Lohmann u. a., 2006)
Content/Summary	fTCD is predestinated for follow-up investigations, especially in individuals with diminished ability to cooperate, like patients or children. Since its introduction the technique has contributed substantially to the elucidation of the hemispheric organization of cognitive, motor, and sensory functions in adults and children.
Comment	Review
Doppler-device	Smart Lite Rimed TCD device (Rimed LTD., 7 Hayezira Street, PO Box 2402, Ra'anana, Israel 43000)
Quantification	The technique is noninvasive and easy to apply. Blood flow measurements are robust against movement artifacts.

Summary:

TCD technique is noninvasive and easy to apply. Blood flow measurements are robust against movement artifacts. Absent TCD signals due to poor bone windows can be enhanced due to use of US contrast agents.

In stroke patients high blood flow velocity in the right MCA of aphasia patients was found to be a good prognostic sign for better language ability. Arterial blood flow that shifted towards the left hemisphere during speech tasks was associated with poor language ability.

Experts:

Bishop

Literature

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