**EFFECT OF AGE AND SEX IN CBF**

**Title**

**Cerebral Blood Flow and Core Mood Symptoms in Youth Bipolar Disorder: Evidence for Region–Symptom Specificity**

**Author/ Year**

Mikaela K.Dimick, Simina Toma, Bradley J.MacIntosh, Anahit Grigorian, Lisa Fiksenbaum, Eric A.Youngstrom, Andrew D.Robertson, Benjamin I.Goldstein/ 2019

**Study population**

youths with BD (13-20 years old)

**Study purpose**

This study investigated regional cerebral blood flow (CBF) in relation to DSM-5 criterion A symptoms of depression and mania in youth with bipolar disorder (BD)

**Methods (Study Design)**

The study recruited 81 youths with BD and 75 healthy controls 13-20 years old. CBF was ascertained using pseudocontinuous arterial spin labeling magnetic resonance imaging. ROI analyses examined the amygdala, anterior cingulate cortex (ACC), middle frontal gyrus, and global gray matter CBF. The association of criterion A depression and mania symptoms with CBF was examined dimensionally in youth with BD in regression analyses with continuous symptom severity scores. Age and sex were included as covariates.

**Main findings**

* Lower CBF was associated with greater depressive symptoms, both with regional specificity and globally.
* In individual symptom analyses, **ACC CBF and global CBF** were inversely correlated with depressed mood and anhedonia. These results did not remain significant following correction for multiple comparisons.
* Depression-related irritability, fatigue, and mania symptoms were not associated with regional or global CBF.
* In multivariate analyses, the depression symptom factor was **inversely correlated with ACC, Middle Frontal Gyrus, and global CBF**; no significant relationship was observed between the mania symptom factor and CBF.
* Comparing BD and HC, they found increased amygdala CBF in the BD group, which was no longer significant after correction for multiple comparisons.

**Title**

Altered Cerebral Perfusion in Executive, Affective, and Motor Networks During Adolescent Depression

**Author/ Year**

Tiffany C.Ho, Jing Wu, David D.Shin, Thomas T.Liu, Susan, F.Tapert, Guang Yang, Colm G.Connolly, Guido K.W. Frank, Jeffrey E.Max, Owen Wolkowitz, Stuart Eisendrath, Fumiko Hoeft, Dipavo Banerjee, Korey Hood, Robert L. Hendren, Martin P.Paulus, Alan N.Simmons, Tony T.Yang/ 2013

**Study population**

medication-naive adolescents (13–17 years of age) diagnosed with major depressive disorder

**Study purpose**

The aim of this study was to examine baseline cerebral perfusion in adolescent depression using a newly developed ASL technique: pseudocontinuous arterial spin labeling (PCASL).

**Methods (Study Design)**

A total of 25 medication-naive adolescents (13–17 years of age) diagnosed with major depressive disorder (MDD) and 26 well-matched control subjects underwent functional magnetic resonance imaging. Baseline rCBF was measured via a novel PCASL method that optimizes tagging efficiency.

**Main findings**

* Significant **hypoperfusion in the MDD relative to the HCL group within frontal, amygdalar, insular, cingular, and cerebellar region**s
* Significant **hyperperfusion in the MDD compared to the HCL adolescents within the subcallosal cingulate, putamen, and fusiform gyri**
* These results did not qualitatively change even when controlled for comorbid anxiety disorders in brain analyses

**Title**

Developmental changes in resting and functional cerebral blood flow and their relationship to the BOLD response

**Author/ Year**

Pamela Moses, Mishaela DiNino, Leanna Hernandez, Thomas T. Liu/ 2013

**Study population**

three age groups, 8 year olds, 12 year olds, and adults

**Study purpose**

The goal of this study was to measure CBF in typically developing, nonsedated children to examine possible age-related changes during both rest and in response to sensory stimulation. Further, this study examined the CBF stimulus response in direct relationship to the BOLD response to determine whether or not elevated CBF in childhood corresponds to greater amplitude in the BOLD response.

**Methods (Study Design)**

This study used noninvasive arterial spin labeling magnetic resonance imaging to compare resting state and stimulus-driven CBF between typically developing children 8 years of age, 12 years of age, and adults. They further acquired functional CBF and BOLD images simultaneously to examine their relationship during sensory stimulation.

**Main findings**

* Noninvasive arterial spin labeling reveals age-related differences in CBF in typically developing volunteer children.
* Greater CBF in children than in adults is evident during resting state.
* During stimulation of the auditory cortex, younger children also showed a greater absolute increase in CBF than adults. However, the magnitude of CBF response above baseline was comparable between groups.
* The combination of the 8 year olds' elevated CBF, both at rest and in response to stimulation, without elevation in the BOLD response suggests that additional physiological factors that also play a role in the BOLD effect, such as metabolic processes that are also elevated in this period, may offset the increased CBF in these children.
* The elevated rates in the younger child group compared to young teens and adults suggest that a decline to adult levels occurs in preteen and adolescent years.

**Title**

Age dependence of cerebral perfusion assessed by magnetic resonance continuous arterial spin labeling

**Author/ Year**

Laura Biagi, Arturo Abbruzzese, Maria Cristina Bianchi, David C. Alsop, Alberto Del Guerra, Michela Tosetti

**Study population**

children, teenagers, and adults

**Study purpose**

To study the normal dependence of cerebral perfusion changes on age, to measure values of perfusion early in life, and to create a reference dataset.

**Methods (Study Design)**

Perfusion maps were collected from a total of 44 healthy subjects (from four to 78 years old) using the arterial spin labeling (ASL) technique. The population was retrospectively divided into three age groups: children, teenagers, and adults. For each group, mean values of cerebral blood flow (CBF) were calculated in gray matter (GM) and white matter (WM). Results were compared across the three different age groups.

**Main findings**

* CBF values decreased with age (97 ± 5 mL/100 g/minute in GM and 26 ± 1 mL/100 g/minute in WM for the children, GM 79 ± 3 mL/100 g/minute and WM 22 ± 1 mL/100 g/minute for the teenagers, and GM 58 ± 4 mL/100 g/minute, WM 20 ± 1 mL/100 g/minute for the adults).
* The quantitative results suggest a rapid drop, rather than a gradual decrease, in cerebral perfusion between children and adult subjects, especially in the GM. This step in CBF occurs during adolescence, at approximately the 16th year of age.

**Title**

Arterial spin labeling magnetic resonance perfusion study to evaluate the effects of age and gender on normal cerebral blood flow

**Author/ Year**

Neetu Soni, Anshul Jain, Sunil Kumar, Chandra M Pandey, Ashish Awasthi/ 2016

**Study population**

normal individuals (age range: 6-72 years, 95 male and 65 female subjects) with no history of any neurological disease, substance abuse, injury, and nonspecific headache

**Study purpose**

The aim of this study was to obtain a reference set of normal values of cerebral blood flow (CBF) in different age groups using three-dimensional pseudocontinuous ASL (3D PCASL) technique to quantify age-related changes in the whole and regional CBF and have also investigated the effect of gender in influencing CBF.

**Methods (Study Design)**

One hundred and sixty normal volunteers of varying age (6-72 years), arranged in 4 age groups, underwent MR perfusion imaging using 3D PCASL technique at 3 Tesla (T). The mean values of GM and WM CBF in frontal GM, frontal WM (FGM, FWM), parietal GM, parietal WM (PGM, PWM), temporal GM, temporal WM (TGM, TWM), and occipital GM, and occipital WM (OGM, OWM) regions were extracted by averaging the data obtained in 10 manually selected regions of interest (ROI)

**Main findings**

* On regression analysis, a significant negative correlation was found between age and GM and WM CBF
* Significant age-associated regional CBF reduction was widely observed throughout the cortex, and the current findings may indicate a distinct pattern characteristic of the normal aging process.
* Global GM CBF and WM CBF showed disparities between the genders, with women being associated with relative higher CBF values.

**Title**

Using arterial spin labeling to examine mood states in youth

**Author/ Year**

Nina Mikita, Mitul A. Mehta, Fernando O. Zelaya, Argyris Stringaris/ 2015

**Study population**

adolescents aged 16 to 18 (10 males, 12 females)

**Study purpose**

The aim of this study was to investigate the neural correlates of mood states and the specific physiological changes associated with their valence and duration in young people.

**Methods (Study Design)**

They investigated brain perfusion patterns involved in mood changes in a sample of healthy adolescents. They used film clips combined with mood elaboration instructions and compared sad and happy mood conditions against the neutral. They also used unbiased, voxel-wise, whole-brain analyses as well as predefined, bilateral regions of interest (ROIs): the amygdala, subgenual anterior cingulate cortex (sgACC), dorsolateral prefrontal cortex (dlPFC), ventromedial prefrontal cortex (vmPFC), and the ventral striatum.

**Main findings**

* The main finding in the sad versus neutral contrast was a **change in perfusion in the middle frontal gyrus** (BA 6), with increased rCBF on the left, and decreased rCBF on the right side following sad mood induction.
* decreased rCBF in the inferior parietal lobule following sad versus neutral mood induction is consistent with this region's role as a component of the default mode network (DMN), a network of brain regions that are active during wakeful rest
* **decreased rCBF in the inferior parietal lobule** following happy mood induction, suggesting that the DMN activity was suppressed when participants actively engaged in mood elaboration regardless of mood valence.
* There is a correlation between the intensity of self-reported sadness and increased rCBF in the precuneus during sad mood elaboration, consistent with the role of precuneus in the recall of episodic and self-referential memory
* increased rCBF in the limbic regions (including the ventral striatum and a marginally not significant finding in the amygdala) following happy mood induction procedures.
* a positive correlation between the self-reported increase in happiness and rCBF change in the left amygdala and left dlPFC
* These results are consistent with the role of the frontolimbic circuitry in emotional processing, with the amygdala involved in determining the emotional content of stimuli and frontal regions modulating emotional responses. This is in keeping with mood induction fMRI findings in patients with depression, who show an opposite direction of effects compared with healthy controls.
* an increase in sgACC perfusion following happy, rather than sad mood induction

**Title**

Depressive Disorders: Focally Altered Cerebral Perfusion Measured with Arterial Spin-labeling MR Imaging

**Author/ Year**

Su Lui, Laura M. Parkes, Xiaoqi Huang, Ke Zou, Raymond C. K. Chan, Hong Yang, Ling Zou, Dongming Li, Hehan Tang, Tijiang Zhang, Xiuli Li, Yi Wei, Long Chen, Xueli Sun, Graham J. Kemp, Qi-Yong Gong/ 2009

**Study population**

patients with RDD, patients with NDD, and healthy control subjects

**Study purpose**

To assess focal cerebral perfusion in patients with refractory depressive disorder (RDD), patients with nonrefractory depressive disorder (NDD), and healthy control subjects by using arterial spin-labeling (ASL) magnetic resonance (MR) imaging

**Methods (Study Design)**

All participants were imaged with a 3-T MR system. ASL and echo-planar images were subtracted and averaged to give perfusion-weighted images. Voxel-based analysis was performed. Region-of-interest analysis was applied to the bilateral hippocampi, thalami, and lentiform nuclei

**Main findings**

* Patients with NDD showed **reduced perfusion in the left prefrontal cortex** versus control subjects and increased perfusion mainly in the limbic-striatal areas
* patients with RDD had **decreased perfusion predominantly in the bilateral frontal and bilateral thalamic regions**
* Compared with patients with RDD, patients with NDD showed **higher perfusion mainly in the limbic-striatal areas**
* In region-of-interest analysis, the NDD group showed higher regional cerebral blood flow than both RDD and control groups in the **left hippocampus, right hippocampus and right lentiform nucleus**

**Title**

Occipital Brain Perfusion Deficits in Children with Major Depressive Disorder

**Author/ Year**

Frederick J. Bonte, Madhukar H. Trivedi, Michael D. Devous, Thomas S. Harris, J. Kelly Payne, Warren A. Weinberg and Robert W. Haley/ 2001

**Study population**

a group of children who were drug naive and had clinically diagnosed MDD and a group of healthy children

**Study purpose**

The aim of this study was to investigate the occipital lobe perfusion defects that have been identified on regional cerebral blood flow (rCBF) SPECT scans of adolescent children and young adults with major depressive disorder (MDD).

**Methods (Study Design)**

To test whether visually apparent abnormalities in rCBF constitute statistically significant differences between patients, given the relatively small sample sizes, they applied the technique of statistical parametric mapping (SPM).

**Main findings**

* Two groups of patients were identified: 8 with significant **posterior flow deficits in the occipital cortex** (Brodmann’s areas 18 and 19), usually symmetric, and best visualized on paramedian sagittal sections, and 13 without obvious occipital perfusion deficits but with anterior rCBF deficits in a pattern often described in the literature, attaining statistical significance in the right frontal region.
* Other localizations in the left frontal and bilateral prefrontal regions did not attain significance