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Cerebral Blood Flow and Autoregulation after Pediatric Traumatic Brain Injury

Yuthana Udomphorn, MD¹, William M. Armstead, Ph.D², and Monica S. Vavilala, MD, FAAP^{1,3}

1Department of Anesthesiology Harborview Medical Center, University of Washington Seattle, WA

2Departments of Anesthesiology and Critical Care and Pharmacology University of Pennsylvania Philadelphia, PA

3Department of Pediatrics Harborview Medical Center, University of Washington Seattle, WA

Abstract

Traumatic brain injury is a global health concern and is the leading cause of traumatic morbidity and mortality in children. Despite a lower overall mortality than in adult traumatic brain injury, the cost to society from the sequelae of pediatric traumatic brain injury is very high. Predictors of poor outcome after traumatic brain injury include altered systemic and cerebral physiology, including altered cerebral hemodynamics. Cerebral autoregulation is often impaired following traumatic brain injury and may adversely impact poor outcome. Although altered cerebrovascular hemodynamics early after traumatic brain injury may contribute to disability in children, there is a paucity of information regarding changes in cerebral blood flow and cerebral autoregulation after pediatric traumatic brain injury. In this article, we discuss normal pediatric cerebral physiology and cerebrovascular pathophysiology following pediatric traumatic brain injury.

Introduction

Little is known about cerebral blood flow (CBF) and autoregulation in children. Most cerebrovascular data in children are derived from critically ill neonates [1-3]. The paucity of information in this area leaves clinicians without a clear understanding of how to manage hemodynamics, particularly during critical illness. Trauma accounts for 36% of deaths in U.S. children 1-14 years of age [4], and traumatic brain injury (TBI) is the leading cause of pediatric trauma [5]. Low Glasgow Coma Scale score, coagulopathy, hyperglycemia, early hypotension, and impaired cerebral autoregulation are associated with poor outcome after pediatric TBI [6-12]. In this review, we discuss what we know about CBF and cerebral autoregulation in children with and without TBI.

Please direct all correspondence to: Monica S. Vavilala, MD, FAAP Associate Professor Department of Anesthesiology and Pediatrics Harborview Medical Center Box 359724 325 Ninth Avenue Seattle, WA 98104 Email: vavilala@u.washington.edu Phone: (206) 731-3210 Fax: (206) 731-8009.

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Cerebrovascular Physiology in Healthy Children

Cerebral Blood Flow

The average brain receives about 15% of the cardiac output. In healthy adults, normal CBF is approximately 50 ml/100g/min. This represents the average blood flow to the whole brain. Blood flow to the gray matter is higher (80 ml/100g/min) than white matter (20 ml/100g/min) [13]. In the absence of primary data from children, most of the referent CBF, cerebral perfusion pressure (CPP) and cerebral autoregulation data has, until recently, been extrapolated from adults. This has been problematic because older studies did not consider the developmental and gender-related differences in cerebrovascular and physiological parameters of healthy children.

Data suggest that CBF varies by age and gender. Transcranial Doppler (TCD) ultrasonography is the more commonly used tool to estimate CBF and understand developmental cerebrovascular changes in healthy children because it is a non invasive imaging tool. Transcranial Doppler studies show that, in healthy newborns, cerebral blood flow velocity (CBFV) is approximately 24 cm/sec, thereafter increasing with age, and peaks at 6-9 years (97 cm/sec) [14]. Beyond 10 years of age, CBFV decreases, approximating adult values (approximately 50 cm/sec) [15,16]. Table 1 shows referent mean CBFV estimates for middle cerebral artery (anterior circulation) (V_{MCA}) and basilar artery (posterior circulation) (V_{BAS}) by age and gender [14,19,20]. Although the specific age at which CBF peaked in one study using perfusion computed tomography (CT) scan in children with mild neurological diseases was lower (2-4 years), what is clear is that CBF is highest during early childhood [19]. While age-related CBF changes occur in both boys and girls, there are some gender differences in CBFV. For example, although anterior circulation flow velocities are higher in both boys and girls than posterior circulation flow velocities. Girls aged 4-16 years have higher V_{MCA} and V_{BAS} than age-matched boys [20,21]. Gender differences in blood viscosity because of hematocrit, or differences in hormones, vessel size, cerebral metabolism, and/or cerebrovascular resistance may partially explain these observed gender differences [21]. Whether or not these gender differences are present at birth is unknown and the relationship between all these factors and CBF have not been examined by both age and gender. Age and gender-related changes in CBFV or CBF may correspond to change in cerebrovascular resistance (ie: young children with higher CBF have lower cerebrovascular resistance) [22].

Numerous techniques are available for examining CBF. The Kety-Schmidt technique is considered the gold standard for measurement of global CBF [23]. Regional CBF can be measured by the $^{133}\text{Xenon}$ clearance technique [24], xenon CT, single photon emission CT [25], positron emission tomography (PET) [26,27], perfusion CT [28-29], and arterial spin labeling [30-31].

Transcranial Doppler ultrasonography measures CBFV of the basal cerebral arteries. Although it is not a direct measure of CBF, changes in CBFV generally correlate well with changes in CBF [32,33], except under specific circumstances such as vasospasm. Compared to TCD, other methods used to measure CBF in children are invasive, time-consuming, and pose radiation risks. Additionally, TCD can be performed repetitively at the bedside in critically ill patients.

Cerebral Metabolism

In healthy adults, global cerebral metabolic rate for oxygen (CMRO_2) averages 3.2 ml (143 μmol)/100g/min (gray matter 6 ml/100g/min vs. white matter 2 ml/100g/min [13]. In general, there is limited information regarding CMRO_2 in children. Using modified nitrous oxide method, Kennedy, et al reported higher CMRO_2 and lower cerebrovascular resistance in healthy awake children (3-11 years) compared to young adults; CMRO_2 :5.2 ml (231 μmol)/

100g/min vs. 4.2 ml (187 μ mol)/100g/min, and cerebrovascular resistance: 0.8 mmHg/100g/min vs. 1.4 mmHg/100g/min [22]. Studies of healthy anesthetized children also suggest age-related increases in CMRO₂ after infancy: 104 μ mol/100g/min in infants [34] vs. 135 μ mol/100g/min in 3 weeks-14 years children [35]. However, one PET study of children <1 year reported lower regional CMRO₂ in young children compared to adults [36].

Similar to CMRO₂, cerebral metabolic rate for glucose (CMRglu) is lower in children at birth (13-25 μ mol/100g/min), increases during childhood, peaks by 3-4 years (49-65 μ mol/100g/min), and remains high until 9 years of age. Thereafter, CMRglu decreases, and approaches adult rates (19-33 μ mol/100g/min) [26]. The higher CMRO₂ and CMRglu in children may be related to the higher age-related changes in CBF and may be due to intact flow-metabolism coupling [22,26,37]. It appears that changes in CMRO₂, CMRglu, and CBF mirror each other and peak during early childhood; possibly reflecting maturational changes during this period. However, insufficient data regarding age-related changes in cerebral metabolic rate in healthy children and in children with TBI preclude a thorough understanding of the age and gender-related changes in these physiological parameters. Figure 1 shows age-related changes in V_{MCA}, CBF, and CMRglu [14,22,26,38,39].

Control of the Cerebral Circulation

The cerebral circulation is tightly regulated with a number of homeostatic mechanisms. The major influences of the cerebral circulation include: 1) metabolism, 2) PaCO₂, 3) PaO₂, 4) blood viscosity and 5) cerebral autoregulation.

Flow-Metabolism Coupling—Flow-metabolism coupling is perhaps the most important control of the cerebral circulation. It is a robust mechanism that is preserved during sleep [40,41] as well as during general anesthesia [42]. Under normal conditions, CBF is tightly coupled to cerebral metabolism. This occurs both at a global and a regional level. In the resting state, CBF is correlated well with CMRO₂. However, during periods of central nervous system activation, CBF increases to a greater extent than CMRO₂, resulting in a decrease in the cerebral oxygen extraction fraction [43]. Recent studies have demonstrated that the regulation of CBF during neuronal activity is independent of local tissue levels of oxygen [44].

There are few data on the relationship between metabolic substrates and CBF in healthy and ill children. Given the robust relationship between flow and metabolism, high metabolic rate probably leads to high CBF. On the other hand, low CBF limits metabolic rate. Increased metabolic demands are likely driven by enhanced excitatory neurotransmission, increased numbers of synapses and/or synaptic activity, higher levels of protein synthesis or changes in metabolic substrates but the exact nature of the interaction between these processes is unclear and speculative. There are no specific data regarding flow-metabolism coupling in children.

CO₂ Vasoreactivity—The cerebral circulation is exquisitely sensitive to changes in PaCO₂. In healthy adults, CBF increases linearly by 2-4% per mmHg PaCO₂ within the range of 25-75 mmHg, making PaCO₂ the most potent physiologic cerebral vasodilator. The change in CBF occurs within seconds after PaCO₂ is increased or decreased, and complete equilibration occurs within 2 minutes [45]. There are no studies of age-related changes in CO₂ vasoreactivity in healthy awake children. Data from healthy anesthetized children suggests that CO₂ vasoreactivity is higher in children than in adults (13.8% and 10.3% change in mean CBFV per 1mmHg change in end-tidal CO₂) with propofol [46], and doses up to 1.0 MAC of volatile anesthetics [47-49].

Hypoxic/Hyperoxic Control of CBF—Compared to PaCO₂, the influence of PaO₂ on the cerebral circulation is of much less clinical significance. There are minimal changes in CBF

with changes in PaO₂ above 50 mmHg [50]. Below a threshold of PaO₂ of 50 mmHg, CBF increases to maintain adequate cerebral oxygen delivery. Unlike CO₂ vasoreactivity, the equilibration of CBF is longer and takes approximately 6 minutes after the establishment of hypoxemia [51,52].

While hypoxemia produces cerebrovasodilation, the influence of increases in PaO₂ (hyperoxia) at normal atmospheric pressure is less well characterized and somewhat controversial. Previous reports have documented both decrease in CBF [53,54] and no change in CBF [55] during hyperoxia. Animal studies demonstrate that hyperoxia elicits pial artery vasoconstriction during normocapnia and that vasoconstrictor peptide endothelin-1 (ET-1) contributes to that vascular response [56].

Effects of Viscosity on CBF—Viscosity of blood is primarily a function of hematocrit, and decrease in viscosity is usually secondary to hemodilution. During anemia, CBF increases as a result of improved rheology of the blood flow in the cerebral vessels and as a compensatory response to decreased oxygen delivery [57]. While some data suggests that hematocrit < 30% is associated with worse discharge Glasgow Outcome Scale scores in adults with severe TBI [58], neither the optimal duration for maintaining a specific hemoglobin level, nor the relationship between target transfusion and neurological outcome are fully known [59]. A recent study of critically ill children demonstrated that maintaining hemoglobin of 7 g/dl rather than 9.5 g/dl can reduce requirements for blood transfusion, but none of these subjects had TBI [60].

Cerebral Autoregulation

Cerebral autoregulation is a homeostatic process where arterioles dilate and constrict to maintain CBF nearly constant over a range of blood pressures. In healthy adults, changes in mean arterial pressure (MAP) between 60-160 mmHg or CPP between 50-150 mmHg produces little or no change in CBF (Fig 2a) [61,62]. This homeostatic mechanism ensures that as MAP/ CPP increase, resistance increases in the small cerebral arteries and arterioles. Conversely, this adaptive mechanism maintains constant (adequate) CBF by decreasing cerebrovascular resistance or vasodilation when MAP/ CPP decreases. Beyond these limits of autoregulation, CBF depends on MAP/ CPP; hypotension results in cerebral ischemia, and hypertension causes cerebral hyperemia. Hypotension after pediatric TBI is associated with poor outcome [10-12].

There are only a few studies of cerebral autoregulation in healthy children, and clinicians have generally assumed that there are no age-related and/or gender differences in this process. Data from healthy children anesthetized with low dose sevoflurane show no age-related differences in autoregulatory capacity [63]. However, counter to the assumption that the lower limit of cerebral autoregulation in younger children is lower, we documented no age-related differences in the lower limit of cerebral autoregulation. We reported children 6 months – 2 years to have a lower limit of cerebral autoregulation of 60 ± 9 mmHg [64]. This is important because tolerating lower blood pressure and therapeutic techniques such as deliberate hypotension in young children may not be appropriate and, in fact, result in cerebral ischemia. Additionally, like adult women who have higher CBF than men [65], there may be gender differences in pediatric cerebral autoregulation [16,20], but this has not been well studied. There may also be some quantitative differences in the latency of cerebral autoregulation between children and adults. One study observed that, compared to adults, adolescents have a slightly delayed return of CBF in response to transient hypotension [16]. Despite these clinical observations, the mechanisms of normal cerebral autoregulation in healthy children are not completely understood and may involve a combination of myogenic, neurogenic, and metabolic processes that regulate cerebrovascular resistance to maintain CBF during hypotension. Finally, like

changes in CBF, both anatomic and physiological maturation might play a role in the development of a fully developed autoregulatory response.

Cerebrovascular Physiology after TBI

Altered Cerebral Blood Flow and Metabolism

Traumatic brain injury can cause flow-metabolism uncoupling, resulting in cerebral ischemia (CBF less than cerebral metabolic demand) or cerebral hyperemia (CBF in excess of CMRO₂) [66,67]. Adult TBI studies demonstrate that CBF reduction early after injury increases regional cerebral ischemia [68,69]. However, decrease in CBF may not be problematic if, following TBI, baseline CMRO₂ is low and there is a compensatory increase in oxygen extraction fraction [70]. Regional alterations of brain metabolism, reduction in metabolic rates and energy crisis have been demonstrated in adult patients after TBI [71-73]. Although the incidence of cerebral ischemia was reported to be low (1% when using oxygen extraction fraction and cerebral venous oxygen content, and 2.4% when using microdialysis technique), the incidence of metabolic crisis (elevated lactate/pyruvate ratio) following TBI was high (25%) [74].

Recent evidence suggests that compared to children without TBI, children with TBI have lower V_{MCA} (surrogate for CBF) [75] and that following pediatric TBI, cerebral hypoperfusion (CBF < 25ml/100g/min) is the dominant derangement [76]. This is important because cerebral hypoperfusion has been associated with cerebral ischemia and poor outcome [76-78]. However after severe pediatric TBI, CBF may also be normal or high [79] and may result in cerebral hyperemia and cerebral hemorrhage. Potentially preventable derangements leading to cerebral hyperemia may include hypoventilation, fever, agitation, or acidosis.

Three phases of change in CBF following TBI have been documented [80]: in the first 6–12 hours after injury, the brain may suffer poor perfusion and cerebral ischemia. A second phase of hyperemia often follows which is notable for “luxury perfusion” and increased intracranial pressure (ICP). Finally, vasospasm and poor perfusion may occur although the incidence of vasospasm after pediatric TBI is low [81]. However it is difficult to know which patient will be at risk for either hyperemia or ischemia unless point of care examination of the relationship between CBF and CMRO₂ occurs. Examination of CBF after pediatric TBI during the 1980s concluded that cerebral hyperemia was responsible for the frequently observed diffuse brain swelling [66,82,83]. However, recent studies suggest age and gender differences in CBFV. Younger children have higher V_{MCA} and V_{BAS} than boys (Table 1) [20,21]. Studies also indicate that the incidence of cerebral hyperemia exceeds the incidence of vasospasm and may only approximate 20% [75].

In the clinical setting, CPP is used as a surrogate for CBF and in 2003, the Pediatric Guidelines recommended that CPP < 40 mmHg be avoided after severe TBI to prevent cerebral hypoperfusion leading to cerebral ischemia [84]. However, there is likely an age dependent CPP threshold, with older children with TBI requiring higher CPP (85,86), although this has not yet been well elucidated. Data from Chambers' study were obtained during the first 6 hours of monitoring which might have been many more hours after admission. More data are needed to fully understand the age-related relationship between CPP, CBF and outcome in pediatric TBI.

Altered CO₂ Vasoreactivity

During the early period after TBI, CO₂ vasoreactivity can be transiently impaired, but generally recovers after 4 to 7 days [87,88]. Impaired CO₂ vasoreactivity following TBI may be associated with cerebral hyperemia, cerebral ischemia, or intracranial hypertension [89]. Studies of CO₂ vasoreactivity in adult TBI patients show that CBF changes about 3% for every

1 mmHg change in PaCO₂ but that CO₂ vasoreactivity is less in patients with lower baseline CBF [87]. In one study of 30 infants and young children with severe TBI, CO₂ vasoreactivity changes < 2% were associated with poor outcome [76]. Since CO₂ vasoreactivity is not routinely examined in individual patients, hyperventilation to induce cerebral vasoconstriction and reduce CBF, ICP and cerebral blood volume may unintentionally lead to secondary ischemic damage after TBI [90,91]. Alternatively, hyperventilation may not be effective in TBI if CO₂ vasoreactivity is decreased.

Secondary Insults and Injuries

Whereas trauma prevention is paramount to decreasing the incidence of primary TBI, avoidance of secondary insults and minimization of secondary TBI after injury decreases TBI burden [92]. Secondary insults, representing discrete events that may be monitored for and intervened upon, are predictable, potentially avoidable, and include systemic causes such as hypotension [93,94], hypocarbia, hypercarbia [78,79,95], hypoxia [11,96], hyperthermia [97], and hyperglycemia [98,99]. These insults result in secondary injuries which signify underlying neurological processes related to cellular and molecular mechanisms of injury/death, including inflammatory responses, impairment of cerebral autoregulation, excitotoxicity, delayed cell death, and BBB breakdown [92]. Data elucidating their roles and mechanism of injury in pediatric TBI are largely lacking.

Impaired Cerebral Pressure Autoregulation

In adults, the incidence of impaired cerebral autoregulation depends on the severity of injury: 28% after moderate and 67% after severe TBI [100,101]. Studies of children with TBI also demonstrate that cerebral autoregulation is impaired and similarly more so after severe (42%) compared to mild (17%) TBI [75,102-104]. Additionally, cerebral autoregulation may be more severely affected in children with inflicted TBI than in children with noninflicted TBI [104]. Autoregulatory disturbances can be unilateral or bilateral and can range from minimal impairment to completely absent autoregulation (unpublished data). Our study of moderate to severe pediatric TBI shows that hemispheric differences in cerebral autoregulation are common (40%) after focal TBI, and that, cerebral autoregulation may be impaired in those hemispheres without radiographic evidence of TBI (unpublished data). Furthermore, a recent study of severe pediatric TBI reported that cerebral autoregulation often changed and worsened during the first 9 days after injury, and that worsening cerebral autoregulation may mirror worsening TBI [105].

In patients with impaired cerebral autoregulation, lower blood pressure may passively result in diminished CPP and CBF (Fig 2b). Patients with intact autoregulation but reduced intracranial compliance may also be at risk of cerebral ischemia. Decrease in MAP causes cerebral vasodilation, increase in cerebral blood volume, and thus an increase in ICP. Increase in ICP further decreases CPP, leading to more cerebral vasodilation. The vicious cycle that ensues is called the vasodilator cascade. Autoregulation is not an all-or-none phenomenon but represents a continuous spectrum of adaptive response in cerebrovascular resistance to a change in CPP. Additionally, cerebral autoregulation is not a static condition and may deteriorate in patients with initially intact autoregulatory capacity. Since, theoretically, augmenting MAP in the hyperemic brain could result in cerebral hemorrhage [66,81,106], these data question whether empirically increasing MAP to prevent cerebral ischemia in the presence of unilaterally impaired cerebral autoregulation and cerebral hyperemia may potentially be harmful.

Clinical reports of the relationship between cerebral autoregulation and outcome in adults are inconsistent [107,108]. Adult studies report poor outcomes with permanent but variable outcomes with transient loss of autoregulation [109]. Impaired cerebral autoregulation has been

associated with poor outcome after pediatric TBI [104,110], but there is a paucity of information in children. While the relationship between cerebral autoregulation and outcome is complex and incompletely understood, it is clinically important. Loss of autoregulation with poor outcome may reflect the severity of TBI in patients with impaired cerebral autoregulation, or impaired cerebral autoregulation may directly impact outcome.

Fluid percussion brain injury is thought to be a good mimic of TBI [111]. Age dependent cerebral autoregulatory mechanisms have been well studied in piglets using fluid percussion injury [112,113]. Impairment of several vasodilator systems has implicated in the genesis of impaired cerebral autoregulation after fluid percussion injury and TBI. For example, in piglets after fluid percussion injury, decrements in nitric oxide (NO), cGMP, cAMP, and prostanoids have been reported [114,115]. Cerebrospinal fluid (CSF) concentration of the ET-1 is increased to a greater level and for a longer period of time in the newborn versus juvenile pig after fluid percussion injury [116]. Impaired NMDA receptor mediated vasodilation after fluid percussion injury is also more pronounced in the immature brain [117]. In humans after TBI, loss of NO and decreased sensitivity to NO is thought to contribute to impaired cerebral autoregulation [118]. Although adenosine and procalcitonin [119], which mediate vasodilation in response to ischemia, have been found in CSF after pediatric TBI, increased CSF ET-1 levels suggest that the effect of high vasoconstrictor levels may override endogenous vasodilators and cause cerebral ischemia during hypotension. Using fluid percussion injury, ATP-sensitive K^+ (K_{ATP}) channel activation is blunted to a greater degree and for a longer time in newborn versus juvenile piglets [120], suggesting that an important pathway leading to cerebral vasodilation during hypotension is more compromised in the immature brain. Activation of K^+ channels, principally K_{ATP} , and calcium-sensitive channel, is an important mechanism for cerebral vasodilation and increases K^+ efflux, producing hyperpolarization of vascular muscle. Hyperpolarization then decreases the probability of opening of voltage dependent calcium channels, and relaxes smooth muscle [121]. Calcitonin gene related peptides (CGRP) activate K_{ATP} channels, and nerve fibers containing CGRP which innervate pial arteries [122]. In-vitro, CGRP produces hyperpolarization of cerebral vessels [123]. Although unlike age dependent mechanisms, sex has not been well examined. A recent study found that adrenomedullin produced gender-dependent impaired cerebral autoregulation in newborn pigs and involved in K^+ channel-mediated vasodilatation [124].

Future Directions for Research

So little is known about developmental changes in cerebrovascular physiology in children with and without neurological disease. Studies examining age and gender-related differences in CBF, cerebral autoregulation, and $CMRO_2$ of the anterior and posterior cerebral circulations in healthy children are needed as reference for us to better understand derangements in illness, particularly when systemic and cerebral hemodynamics such as CPP and ICP are abnormal. In pediatric TBI, data are needed to better understand the age-related relationships between $CMRO_2$, CBF, CPP and outcome. Changes in CBF and cerebral autoregulation following TBI need description, and finally, the role of cerebral autoregulation testing in the hemodynamic management of children with TBI merits investigation.

Summary

The acute care determinants of outcome in children after TBI are at best incompletely understood. In particular, changes in cerebrovascular physiology, including CBF and cerebral autoregulation after pediatric TBI, are not well known. These gaps in knowledge are problematic and preclude us from deriving therapies needed to optimize CBF, $CMRO_2$, and cerebral autoregulation needed to improve outcome after pediatric TBI.

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Figure 1.

Age-related changes in mean flow velocity of middle cerebral artery (V_{MCA}) in both genders, cerebral blood flow (CBF), cerebral metabolic rate of glucose (CMRglu) [14,22,26,38,39]. (Adult values: $V_{MCA} \sim 50$ cm/sec [15,16], CBF 50 ml/100g/min [13], CMRglu 19-33 $\mu\text{mol}/100\text{g}/\text{min}$) [26])

(2a) Intact Cerebral Autoregulation

(2b) Impaired Cerebral Autoregulation

Figure 2.

Intact (2a) and impaired (2b) cerebral autoregulation by transcranial Doppler ultrasonography from 2 children with traumatic brain injury. Vmca scales are different in Figures 2a and 2b. MABP = mean arterial blood pressure. Lt = left; Rt = right; Vmca = middle cerebral artery flow velocity [110].

Table 1
Age and gender differences in mean flow velocity values (cm/sec) of middle cerebral (V_{MCA} , anterior circulation) and basilar arteries (V_{BAS} , posterior circulation)

Age	V_{MCA}			V_{BAS}		
	Boys ^{a,b}	Girls ^{a,b}	Both ^c	Boys ^{a,b}	Girls ^{a,b}	Both ^c
0-10 days	-	-	24 ± 7	-	-	-
11-90 days	-	-	42 ± 10	-	-	-
3-11.9 months	-	-	74 ± 14	-	-	-
1-2.9 years	-	-	85 ± 10	-	-	-
3-5.9 years	92 ± 13 *	99 ± 11 *	94 ± 10	61 ± 9 #	70 ± 10 #	51 ± 6
6-9.9 years	-	-	97 ± 9	-	-	58 ± 6
10-16.9 years	75 ± 16 †	89 ± 16 †	81 ± 11	51 ± 12 ‡	59 ± 11 ‡	58 ± 9
						46 ± 8

^a*Vavilala, et al* [21]

^b*Tontisirin, et al* [22]

^c*Bode* [19]

* $p < 0.05$ (Adult values: $V_{MCA} \sim 50$ cm/sec [15,16] and $V_{BAS} \sim 40$ cm/sec [17,18])

$p < 0.05$ (Adult values: $V_{MCA} \sim 50$ cm/sec [15,16] and $V_{BAS} \sim 40$ cm/sec [17,18])

† $p < 0.05$ (Adult values: $V_{MCA} \sim 50$ cm/sec [15,16] and $V_{BAS} \sim 40$ cm/sec [17,18])

‡ $p < 0.05$ (Adult values: $V_{MCA} \sim 50$ cm/sec [15,16] and $V_{BAS} \sim 40$ cm/sec [17,18])