NASH independent of insulin resistance. Preclinical models also suggest that adiponectin may counter NASH by improving fatty acid oxidation and by reducing hepatomegaly, steatosis, and liver inflammation. Proinflammatory cytokines decrease and adiponectin levels rise after gastric bypass in adolescents.[13] These findings provide intriguing possibilities for possible mechanisms by which surgery may affect NASH in teens.

In conclusion, Manco et al[6] provide clear evidence of the benefits of sleeve gastrectomy for the histopathologic spectrum represented by pediatric NAFLD. Improvements in liver histology in conjunction with major weight loss provide objective medical justification for use of metabolic surgery for NASH in severely obese adolescents. At the same time, these data also create enthusiasm for more in-depth research to identify mechanisms by which sleeve gastrectomy may modulate inflammatory pathways that are detrimental to normal organ function in youth with severe obesity. ■

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Thinking under Pressure

The prevalence of hypertension has increased in concert with the epidemic in obesity that has affected almost all age groups in the US. In school-aged children, among whom almost 1 out of 5 is either overweight or obese, the prevalence of hypertension is now above 10%.[1] This alarming statistic has direct health consequences, as children with primary hypertension have target organ damage that is similar to that seen in adults, albeit at a lower prevalence. Target organ damage includes left ventricular hypertrophy, increased carotid intima-media thickness, increased arterial stiffness as measured by pulse wave velocity, and reduced vascular endothelial function. Less is known, however, about the deleterious effects of hypertension on the brain in children and adolescents. In fact, descriptions of children and adolescents with respect to the brain were until recently limited to clinically apparent neurologic events such as facial nerve palsy, stroke, seizures, and posterior reversible encephalopathy that sometimes occur in the setting of malignant hypertension.[2]

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It is well established that adults with hypertension demonstrate decreased performance on neurocognitive testing compared with normotensive controls. A number of studies support an association between hypertension, particularly in midlife, and the development of cognitive disorders and dementia, including Alzheimer disease. The interval between the respec-

PSQ	Pediatric sleep questionnaire
SDB	Sleep disordered breathing
SRBD	Sleep-related breathing disorder

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tive manifestations of hypertension and cognitive deterioration in adults varies from a few years to several decades.[3] Accordingly, considering hypertension as a possible modifiable risk factor for cognitive decline is of great clinical interest and societal importance. Treatment of hypertension in midlife seems to promote considerable benefits regarding to cardiovascular outcomes. Longitudinal studies examining the possible benefit of antihypertensive treatments on cognitive decline have produced some promising results.[4] Nevertheless, the results from randomized controlled clinical trials on treatment of hypertension are not yet conclusive about the effect on cognitive decline and delay of dementia.

Mechanistically increased arterial stiffness of the large arteries has been hypothesized to lead to microvascular changes because of increased pulsatile flow. Triantafyllidi et al[5] studied this postulate in 110 patients without diabetes aged 40-80 years with newly diagnosed untreated stage I-II primary hypertension. Impaired cognitive function as assessed using the Mini-Mental State Examination was associated with increased large artery stiffness (increased pulse wave velocity) and albuminuria. These findings support the hypothesis that cognitive impairment induced by impaired microcirculation is linked to large artery stiffness and microvascular damage. Grant et al[6] examined adults with hypertension and normotensive controls regarding behavioral performance and hemodynamic changes in the prefrontal cortex. Fifteen stage I hypertensive and normotensive males (19-55 years) were compared on 4 tests of working memory (digit span and auditory consonant trigrams), and accompanying hemodynamic changes measured by functional near infrared spectroscopy. Investigators found significant correlations in the hypertensive group between test performance and changes in oxyhemoglobin and total hemoglobin in both the left and right prefrontal cortex. These findings suggest that functional near infrared spectroscopy combined with cognitive testing may provide important measures of cerebrovascular reserve in essential hypertension.[6]

Autoregulation is an important yet imperfect protective mechanism used by the brain and kidneys to reduce impact of change in mean arterial pressure on organ function. As for the kidney (with appearance of albumin in the urine, for example), there is mounting evidence for early subtle organ dysfunction in the brain as manifested by deleterious changes in cognition that probably become fixed over time and emerge in adult life (dementia). It remains to be better determined whether the cognitive changes are related to pressure flow alterations, circulating factors, tissue susceptibility, or some combination of these factors.

There is also recent and evolving evidence that children with hypertension also manifest neurocognitive differences when compared with normotensive controls. These findings are postulated to represent potentially early signs of hypertensive target organ damage to the brain.[7] Until recently, reports in children were limited to database and single-center studies underscoring the importance and relevance for further study of neurocognition in children with hypertension. Further studies are indeed now looking at the short-term impact of childhood hypertension on the child and adolescent's brain along with the long-term effects into adulthood. In addition, these studies will assess the degree to which any neurocognitive effects of hypertension are able to be reduced or possibly reversed. In 2006, Ditto et al[8] studied 88 French Canadian boys aged 14 years with a parental history of hypertension. Boys at greater risk of hypertension by virtue of having a parental history of high blood pressure and normatively elevated systolic blood pressure had significantly lower scores on a verbal learning, spatial learning, and memory factor scores compared with boys at lower risk. The results were not attributable to differences in family socioeconomic status. These results support previous suggestions that some of the neuropsychological characteristics displayed by individuals with hypertension may predate the development of clinically elevated blood pressure and could be associated with risk for the disorder. This is now being further evaluated in a multicenter American Heart Association supported study called the Study of High Blood Pressure In Pediatrics: Adult Hypertension Onset in Youth.[9] Ostrovskaya et al[10] evaluated executive function in 14 children with hypertension and prehypertension using Behavior Rating Inventory of Executive Functions and transcranial Doppler scan with reactivity measurement using time-averaged maximum mean velocity and end-tidal carbon dioxide during hypercapnia-rebreathing test. They found that these children when compared with controls had decreased executive function that correlated with low transcranial Doppler-reactivity slopes, again suggesting that the brain is an important target organ in children with hypertension.

To address the neurocognitive effects of primary hypertension in children, Lande et al[7] established an ongoing, prospective, multicenter study of neurocognition in children with primary hypertension. In an interim analysis, the authors looked at the association between sleep disordered breathing (SDB) and neurocognition among participants enrolled in their cohort of children with hypertension. As stated above, children who are hypertensive are often obese. This is a comorbidity that is associated with SDB and which itself is associated with cognitive problems, potentially confounding any relationship between hypertension and neurocognition. Subjects completed laboratory-based neurocognitive tests. Parents and subjects completed rating scales of executive function, mood, and behavior problems. Parents completed the sleep-related breathing disorder (SRDB) scale of the pediatric sleep questionnaire (PSQ). The group with hypertension had a higher percentage of subjects with SRBD-PSQ scores in the range suggestive of obstructive sleep apnea (26% vs 6%, $P = .03$), emphasizing the importance of using a multimethod approach in the assessment of cognition and adjusting for potential confounding effects of SDB in studies of cognition in children with hypertension.[11]

In this volume of *The Journal*, Lande et al[12] now report their prospective study of 75 children and adolescents with untreated hypertension compared with 75 matched normotensive controls between the ages of 10 and 18 years. The authors evaluated general intelligence, attention, memory, executive function, and processing speed and controlled for any SRBD.