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Hydration and Cognitive Function in Children

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Adequate fluid intake is critical for survival. While adults are at liberty to drink fluids as wanted, children and infants are dependent upon caregivers for food and fluid. Children are at greater risk for dehydration than adults due to their higher surface-to-mass ratio. Additionally, children have different thirst sensitivities and body cooling mechanisms than adults. Children differ from adults in total body water content, and boys and girls differ in body water content with maturation. Research in young adults shows that mild dehydration corresponding to only 1% to 2% of body weight loss can lead to significant impairment in cognitive function. Dehydration in infants is associated with confusion, irritability, and lethargy; in children, it may produce decrements in cognitive performance.

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INTRODUCTION

Water and fluid balance in humans is sharply regulated and complex. People drink liquids not only in response to physiological thirst, but also in response to a variety of cultural, social, and psychological factors. The type and amount of fluid consumed is dependent upon relative palatability and temperature of the fluid, meal type and size, and water safety and availability. Fluid intakes generally are considered to be adequate to maintain fluid balance in most people. Moreover, cultural patterns of fluid intake are sufficient to override a true physiological thirst. Risk for dehydration, therefore, arises under special circumstances such as illness, injury, heat stress, or physical activity, and also according to age. Indeed, fluid requirements relative to body weight are greatest during the early neonatal period and through childhood. As a consequence, children may be more susceptible to fluid losses and are therefore at greater risk for dehydration than are adults.

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WATER BALANCE

The balance between loss and gain of fluids maintains body water within relatively narrow limits.[1] The routes of water loss from the body are the urinary system, the skin, the respiratory surfaces, and the gastrointestinal tract. The primary avenues for restoration of water balance are fluid and food ingestion, with water oxidation making a minor contribution.[2] The volumes of water that individuals obtain from drinks and food are highly variable, although it is generally reported that the majority normally comes from liquids.[3]

Thirst and Water Intake Regulation

The act of drinking may not be directly involved with a physiological need for water intake, but can be initiated by habit, ritual, taste, or a desire for a warm or cooling effect.[4] A number of the sensations associated with thirst are learned, with signals such as dryness of the mouth or throat inducing drinking, while distension of the stomach can stop ingestion before a fluid deficit has been restored. However, the underlying regulation of thirst is controlled separately by the osmotic pressure and volume of the body fluids, and as such is regulated by the same mechanisms that affect water and solute reabsorption in the kidneys and control central blood pressure. Despite large variations in salt and water intake, homeostatic mechanisms maintain a normal plasma osmolality of 275 to 290 mOsm/kg and a normal sodium level between 135 and 145 mEq/L.

Water is excreted from the body through urine and by insensible losses such as respiration and evaporation from skin. Increases in plasma osmolality and activation of osmoreceptors (intracellular) and baroreceptors (extracellular) stimulate hypothalamic release of arginine vasopressin. Vasopressin acts at the kidney to decrease urine volume and promote retention of water. Increasing levels of vasopressin are associated with greater ratings of thirst and greater fluid intake. An increase of 1% to 2% plasma osmolality is sufficient to provoke the thirst reflex (Figure 1). Thirst is generated at a higher plasma osmolality than vasopressin release, resulting in first a concentration of urine and conservation of body water and then a subsequent drive to increase fluid intake. Thirst is also seen in cases of blood loss and in fluid loss following burn trauma. In general, the sensation of thirst results in an intake of fluid adequate to restore water balance. Cessation of drinking, however, occurs before cellular rehydration is achieved. Rather, oropharyngeal cues produce a decrease in vasopressin release and subsequently a decrease in drinking behavior.[5] It has been observed that most terrestrial animals are in a chronic state of fluid deficit, drinking only enough to achieve homeostatic water levels.

Hypernatremia, defined as plasma concentrations of Na above 145 mEq/L, can result from decreased fluid intake and can cause restlessness, altered mental status, confusion, and fatigue. So-called water intoxication, or hyponatremia, occurs when plasma concentrations of Na drop below 135 mEq/L. Interestingly, hyponatremia induced by ingesting large amounts of fluids results in similar somatic symptoms as dehydration: nausea, fatigue, confusion, and apathy,[6] but the effects of hyponatremic states on cognition have not been fully evaluated.

Total Body Water and Risk of Dehydration in Children

At birth, total body water (TBW) is approximately 75% of total body composition. TBW decreases to approximately 60% in boys and to approximately 50% in girls by puberty (Figure 2). The percentage of TBW is decreased relative to body mass as a function of increased proportion of body fat, as seen in post-pubertal girls and in overweight children. Recent data from the Fels Longitudinal study show that the progression of TBW changes with maturation.[8] Longitudinal TBW data from Caucasian boys and girls from 8 to 20 years of age were collected using deuterium nuclear magnetic resonance spectroscopy. In girls, %TBW increases until about age 14 (puberty) and then levels off (8 yrs: 14.8 ± 1.9 L; 14 yrs: 27.5 ± 3.7 L; 16 yrs: 28.4 ± 4.1 L; 20 yrs 29.0 ± 3.4 L). In boys, %TBW increases until about age 16, when it also levels off (8 yrs: 16.2 ± 2.0 L; 14 yrs: 32.6 ± 6.8 L; 16 yrs: 40.6 ± 7.7 L; 20 yrs 42.0 ± 5.0 L). In general, boys at all ages tend to have higher proportions of TBW than do girls.[8]

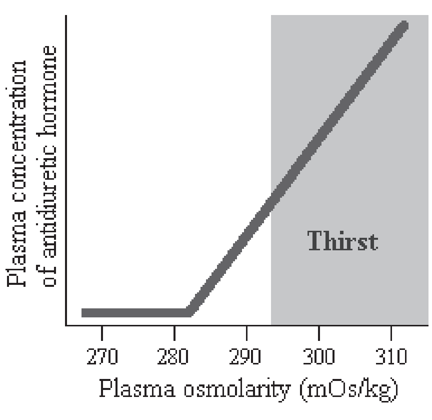

Figure 1. Comparison of osmotic threshold for vasopressin release and stimulation of the thirst reflex. (Used with permission from *Pathophysiology of the Endocrine System*.[4])

Recommended adequate water intake in children and adults under average conditions is 1 mL/kcal.[9] Measuring water intakes and, by extrapolation, hydration status, in the general population is somewhat difficult but not unfeasible. Water intakes and TBW for children are described in the Dortmund (Germany) Nutritional and Anthropometric Longitudinally Designed Study (DONALD)[9] and in the US National Health and Nutrition Examination Survey (NHANES).[3] In the DONALD study, fluid intakes from food and liquid ingestion, as well as metabolic water, averaged around 1.9 L/d for 9- to 13-year-old German boys and approximately 1.7 L/d in 9- to 13-year-old German girls. In data from NHANES III, total water intake averaged around 2.5 L/d for 9- to 13-year-old US boys and 2.2 L/d for 9- to 13-year-old US girls (see Table 1 for all reported age ranges), suggesting that children in the United States have a higher hydration level than German children. However, it is important to note that in all cases, US children consumed more calories per day compared with German children, and this is a contributing factor to the differences in fluid intakes.

Children may be at greater risk for dehydration than adults for several reasons. Young people have a greater surface-to-mass ratio, allowing for greater water losses from the skin. Fever and diarrhea result not only in a reduction in body water, but also in potentially lethal electrolyte imbalances. In developing countries, diarrheal diseases are a leading cause of death in children, resulting in approximately 1.5 to 2.5 million deaths per year.[10] Mortality in these cases can many times be prevented with appropriate oral rehydration therapy.

Children, infants in particular, are dependent upon caregivers for provision of fluids. In the case of infants, caregivers may not be aware of the extent of insensible water loss and adequate hydration may therefore not be provided.[11] As an example, inadequate breast-feeding is

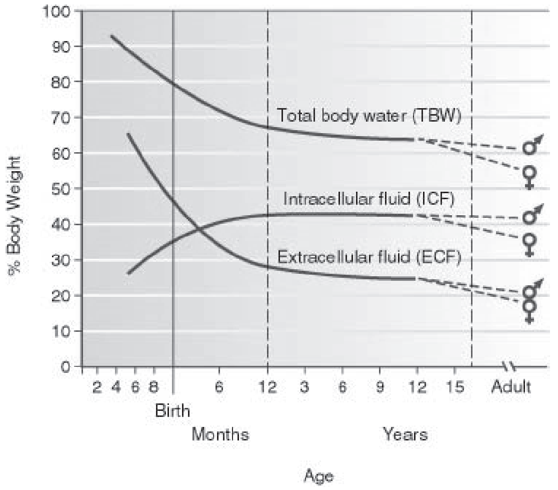

Figure 2. Total body water, intracellular fluid, and extracellular fluid as a percentage of body weight and a function of age. (Used with permission from Behrman et al., 2004.[7])

becoming more common as a risk factor for dehydration in infants.[12] Nursing mothers with insufficient milk may not recognize the signs of progressive dehydration in their infants, and parents may not recognize signs of dehydration in older children. One report suggests that although most parents understand what dehydration is, only about two-thirds could identify more than one sign of dehydration.[13]

Hydration and Physical Activity in Children

Children may also be at greater risk for "voluntary dehydration," a state of water deficit where fluids have been ingested to the point where thirst no longer provides a drive to drink, but where adequate repletion of fluids has not been achieved. Voluntary dehydration is seen most commonly in child athletes or following climatic heat stress. Children may not recognize the need to replace lost fluids, so children and coaches need specific guidelines for fluid intake.[14] Additionally, children may require longer acclimation to increases in environmental temperature than do adults. It is recommended that child athletes or children in hot climates begin athletic activities in a well-hydrated state and drink fluids over and above the thirst threshold. One study published in 1994 found that one-third of British school-aged children had nothing to drink prior to the beginning of the school day, reflecting a fluid fast of over 12 hours.[15] Since then, several programs have been instituted in the United Kingdom to promote adequate water intake in schoolchildren.[16,17]

Research suggests that, especially at the beginning of the season, young athletes are at particular risk for dehydration due to lack of acclimatization to weather conditions or suddenly increased activity levels.[18,19] Decrements in physical performance in athletes have been observed under conditions of as little as 2% dehydration, measured acutely as percent body weight loss. During exercise, children may not hydrate adequately when allowed to drink according to thirst.[20] Fluid intake during athletic events can be enhanced by presenting palatable carbohydrate-electrolyte fluids in lieu of plain water.[21] What is particularly troubling is that after periods of physical exertion, voluntary fluid intake may be inadequate to offset fluid deficits.[18,19] Mild to moderate dehydration can therefore persist for some hours after the conclusion of physical activity.

HYDRATION AND COGNITIVE FUNCTION

Cognitive function can be clustered into several main domains: memory functions, attention functions, perceptual functions, executive functions, psychomotor functions, and language skills. Each of the cognitive domains can be further divided in a number of more specified functions. Memory functions, for example, include short-term and long-term memory encoding, storage and retrieval functions, and working memory. Further differentiation is made with regard to the type of information that is processed; for example, auditory, visual, verbal, spatial, abstract, or procedures. Attention can be subdivided in selective, divided, and sustained attention functions, whereas executive functions encompass more complex processes such as reasoning, planning, concept formation, evaluation, and strategic thinking.[22]

Research in our laboratory and others supports the hypothesis that mild dehydration produces alterations in a number of important aspects of cognitive function such as concentration, alertness, and short-term memory in young adults 18 to 25 years of age[23-27] and in the oldest adults 50 to 82 years of age.[28] Most of the cited studies were randomized, controlled trials. The results vary with respect to magnitude of effect on cognition and in direction of effect. In some studies, cognitive performance was not altered by mild dehydration.[29] In others, mild dehydration produced

Table 1. Total Water Intakes of US and German Children

	US*	German†
	mean mL/d	
Boys and Girls		
Age 1–3 (US) 2–3 (G)	1420	1114
Age 4–8	1779	1363
Boys age 9–13	2535	1891
Girls age 9–13	2240	1676

*Fluid intake from food and beverages (data from Food and Nutrition Board, Institute of Medicine, 2004[3]).
†Total water from food, beverages, and metabolic water (data from Sichert-Hellert et al., 2001[9]).

modest decrements in cognitive performance[23-26] or even mild enhancement.[23] In young adults, significantly higher mood scores for anger, confusion, and fatigue were seen under conditions of mild dehydration.[23]

Mild dehydration (as small as 2% loss of body weight as water) can impair performance on tasks such as short-term memory, perceptual discrimination, arithmetic ability, visuomotor tracking, and psychomotor skills.[23-26] For example, Cian et al.[24,25] examined the effects of heat stress and dehydration on cognitive functioning in a series of studies. In these studies, participants (healthy young adults) were dehydrated (approximately 2.7%) either through heat exposure or treadmill exercise. In both studies, they found significantly decreased alertness, concentration, and tracking performance and increased tiredness and headaches; increased reaction time was also observed (the test asked the subjects to identify the color of an object), but the number of correct answers was unchanged. Gopinathan et al.[26] induced moderate levels of dehydration (2%–4%) through a combination of water restriction and exercise in a heated room, and demonstrated hydration-level-dependent decreases in short-term memory, arithmetic efficiency, attention tasks, and visuomotor tracking.

These studies demonstrate that low to moderate levels of dehydration may significantly alter cognitive performance in young adults, in whom significantly higher mood scores for anger, confusion, and fatigue were seen under conditions of mild dehydration.[23] Szinnai et al.[29] did not find an alteration of cognitive performance in healthy young adults as a result of mild dehydration. However, the authors argue that increased subjective task-related effort could suggest that healthy volunteers exhibit cognitive compensating mechanisms for increased tiredness and reduced alertness during slowly progressive moderate dehydration.

Hydration and Cognitive Function in Children

Dehydration ranges from mild to severe. Clinical signs of mild dehydration (as low as 3% body weight loss) are subtle, and include restlessness and increased alertness. Clinical signs of moderate (5%–9% body weight loss) to severe (>10% body weight loss) dehydration include dizziness, lethargy, agitation, irritability, restlessness, and confusion[7,30-32] (Table 2). Children with moderate hypernatremic dehydration may be lethargic, but then show irritability when touched.[7] Other neurological complications of dehydration include hypertonicity, hyperreflexia, seizures, myelinolysis, and brain herniation. Decreased voluntary fluid intake leads to decreased volume and increased sodium levels. In acute hypernatremia, fluid leaves the intracellular space and flows to the extracellular space. In brain, cell volume can decrease up to 10% to 15%, but then rapidly adapts.[32] In children, acute hypernatremia may have a mortality rate of up to 20%, and up to 66% of survivors experience consequent neurological symptoms.[33]

A recent examination of voluntary dehydration in 10- to 12-year-old children indicates that dehydration throughout the day may negatively impact cognitive function.[34] Israeli schoolchildren were divided into normally hydrated or dehydrated groups based on urine osmolality. Cognitive testing took place at the beginning of the school day and again at noon. Five tests were administered: 1) hidden figures (identifying a given figure in patterns that contain an additional line); 2) auditory number span (immediate memory of a sequence of dictated digits); 3) making groups (constructing conceptual categories); 4) verbal analogies; and 5) number addition. At the beginning of the day there were no significant differences in cognitive performance between the groups, although there was a trend for short-term memory scores, as measured by an auditory number span task, to be higher in hydrated students. At noon, however, students initially classified as hydrated tended to perform better on several cognitive tasks than dehydrated students. Short-term memory scores were significantly higher in hydrated children than in dehydrated children. There was a trend for hydrated students to perform better on the verbal analogy task (measuring semantic fluency) and on the making groups task (measuring semantic flexibility) relative to dehydrated children. Although there were a number of limitations with this study, including “self-selection” into hydration conditions, specific climatic conditions, and no condition for provision of fluids to dehydrated students, the data might suggest a negative influence of dehydration on children’s cogni-

Table 2. Affective Signs of Dehydration

	Degree of Dehydration		
Age Group	**None or Mild**	**Moderate**	**Severe**
Infants	Thirsty, alert, restless	Lethargic or drowsy	Limp, cold, cyanotic extremities, may be comatose
Older children	Thirsty, alert, restless	Alert, postural dizziness	Apprehensive, cold, cyanotic extremities, muscle cramps

Adapted from Gorelick et al., 1997.[30]

tion. Moreover, the authors observe that in hot climates, chronic voluntary dehydration may play a significant role in cognitive performance. To date, this study is the only one investigating the interaction between dehydration and cognitive performance in children.

Preliminary observations by schoolteachers in the United Kingdom indicate that programs encouraging water intake in students might improve student attention and concentration,[54] but at the time of this review no scientific data on these observations had been published.

Hydration and Brain Injury

As described above, cellular dehydration occurs in hypernatremia as water leaves the cell across the concentration gradient. Such cellular shrinkage is associated with neuronal lesions and brain edema.[35] Brain imaging of infants and children with hypernatremia suggests that increased plasma osmolality is associated with cerebral lesions in thalamic, cortical, hippocampal, and other regions. Furthermore, excessively fast rehydration can cause rapid influx of water into brain cells, resulting in cerebral edema, and these insults to the brain may be long-lasting or even permanent. Children develop hyponatremic encephalopathy at higher sodium concentrations than do adults. Also, children have a higher brain-to-skull ratio than adults, leaving less room for brain expansion. Evidence suggests that many of the neurological sequelae of dysnatremias are due to damage resulting from rapid changes in fluid balance across cellular concentration gradients, rather than hypo- or hypernatremic states per se. There are few studies examining either the short- or long-term influence of dehydration on cognitive functioning in these children.

Some research[36,37] suggests that repeated bouts and prolonged episodes of diarrhea in early childhood could produce long-term cognitive decrements. These decrements are independent of maternal education, parasitic infection, and many other variables. Although it is difficult to parse the effects of malnutrition and dehydration on the cognitive performance of these children, it is possible that dehydration-mediated changes in brain physiology could contribute to persistent cognitive impairments in children with early childhood diarrhea.

Potential Mechanisms Relating Hydration to Cognitive Function

Fluid is lost through the urine and feces and through respiration, sweat, and other insensible losses. Whatever the cause of loss, if fluids are not replaced, then there is shrinkage of plasma and extracellular volume that can lead to underperfusion of the brain. In older persons, urge incontinence is associated with a greater urine loss relative to other forms of incontinence. In this population, urge incontinence is positively correlated with a decrease in cognitive performance and with underperfusion of the frontal lobes of the cerebral cortex.[38,39] However, it should be noted that dehydration was not measured directly in these studies. Cerebral underperfusion is also associated with confusion, dementia, and lethargy, suggesting that changes in brain hydration levels may be partially responsible for the effects of dehydration on cognitive performance.

Dehydration is known to increase circulating levels of stress hormones such as cortisol,[40] and in humans, increased levels of cortisol have been associated with decrements in cognitive function.[41-44] It is theorized that some of the effects of dehydration are therefore related to the activation of the hypothalamic-pituitary-adrenocortical axis and the release of stress hormones. This hypothesis may be supported by observations in animals that hypothalamic-pituitary-adrenocortical axis activation induced by stress and/or pharmacological administration of glucocortocoids (stress hormones) can produce dendritic atrophy in hippocampal neurons, and that this atrophy is associated with cognitive decrements.[45]

Arginine vasopressin is released in response to fluid decrements. As described above, vasopressin released in the hypothalamus activates the thirst response and thus provokes drinking. Vasopressin may act as a neuromodulator to produce excitatory effects in neural tissue. Elevated levels of vasopressin may enhance cognitive functioning on certain tasks.[44] Specifically, elevated plasma vasopressin is associated with increased attention and arousal, and this excitatory effect may explain some of the contradictory findings on the effects of dehydration on cognition.

In animal studies, chronic dehydration increases glutamate and GABA release and augments norepinephrine-induced release of glutamate and norepinephrine-induced inhibition of GABA release.[46] Chronic dehydration may therefore produce an increase in neuronal activity and enhance the actions of both excitatory (glutamate) and inhibitory (GABA) neurotransmitters. The exact processes that these differing neurotransmitters affect are complex and well beyond the scope of this review. In brief, inhibitory and excitatory neurotransmitters may have opposing effects on behavior and cognition. However, inhibitory and excitatory neurotransmitters may also have similar effects depending on receptor subtype and localization. For example, pharmacological blockade (antagonism) of GABA-B receptors (inhibiting inhibition) augments long-term hippocampal-dependent memory.[47] In contrast, activation of GABA-A receptors (activating inhibition) enhances memory and spatial learning in rats.[48]

Table 3. Hydration and Cognitive Function in Children and Young Adults

Age (yrs)	N	Design	Effects of Hydration Status on Cognition	Study
10–12	20 boys; 31 girls	Comparison dehydrated vs. euhydrated*	No effect of initial hydration levels on cognitive performance at first test in the morning; at lunchtime, short-term memory was impaired in dehydrated children ($P = 0.024$)	Bar-David et al., 2006[34]
18–21	16 men; 15 women	Repeat testing in fluid restriction vs. ad libitum water intake	• 1.65% (women) and 2% (men) dehydration increased reaction time in the continuous performance task ($P < 0.05$) • 1.65% dehydration in women increased errors on the choice-reaction time task ($P < 0.05$) • 2% dehydration in men decreased errors on the choice-reaction time task ($P < 0.05$) • Dehydration improved short-term memory ($P < 0.05$) and intensified mood scores ($P < 0.05$)	Taylor et al., 2005[23]
20–25	11 men	Repeat testing in fluid restriction vs. ad libitum water intake	1% dehydration had no effect on cognitive performance; 2%, 3%, and 4% dehydration impaired short-term memory, arithmetic performance, and visuomotor tracking ($P < 0.001$ for all measures)	Gopinithan et al., 1988[26]
21–24	8 men	Repeat testing in fluid restriction vs. ad libitum water intake	2% and 3% dehydration impaired concentration and psychomotor performance ($P < 0.001$)	Sharma et al., 1986[55]

*Dehydrated meant that the urine had greater than 800 mosm/kg H_2O; 11/20 boys and 21/31 girls were classified as dehydrated.

Glutamate receptor antagonists are associated with memory impairments,[49] but excitotoxicity produced by chronically high levels of glutamate agonists can also induce hippocampal damage and produce cognitive decrements.[50] Dehydration is associated with a decrease in neuronal cell proliferation that is reversed by rehydration.[51] Using a model of lead exposure, Al Shuaib et al.[52] found that dehydration in combination with lead exposure significantly impairs synaptic transmission at the neuromuscular junction. Neuromuscular impairments can be reflected in decrements in psychomotor performance. Although any links between these animal studies and human cognitive performance would be speculative, the existing research suggests that dehydration produces many different physiological effects that can individually or in combination affect cognitive and psychomotor performance.

CONCLUSIONS

Although the effects of dehydration on cognitive function are now well documented in adults, there are few studies examining the relationship between hydration status and cognitive function in children (Table 3). Data reported by Bar-David et al.[34] seem to indicate negative effects on cognition induced by mild dehydration in children. However, much remains unknown about the short- and long-term effects of dehydration on cognitive function in children, so these results need to be confirmed by future research. Several countries, including the United States and the United Kingdom, are already encouraging water intake in school-age children to promote good health and improve academic performance.[16,17,53]

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