

Christopher Walsh

FROM THE  
MOUTHS OF  
PATIENTS

TO LISTEN IS TO LEARN

How do genes guide brain development and, in turn, our behavior? This question fascinates HHMI investigator and physician-scientist Christopher A. Walsh, whose Harvard lab studies the cerebral cortex, the thin layer of gray matter that controls complex thoughts and motor functions. Despite his active research program, Walsh makes time to spend with patients and their families. These interactions often guide his research—and increase his drive to do all he can to help.

*What types of patients do you see?*

In our pediatric and adult clinics, we see patients with brain abnormalities and their families. Many of these conditions are genetic. For example, in periventricular heterotopia (PH), clusters of brain cells remain near the ventricles (the fluid-filled spaces deep in the brain) instead of migrating out to the cerebral cortex. Another condition is lissencephaly, which means “smooth brain.” Instead of having a normal folding pattern, the cortex is smoother and thicker.

*You collaborate with physicians in Turkey and Arabic countries of the Persian Gulf. Why those countries in particular?*

These are rare genetic neurological diseases. Prevalence varies from about 1 in 10,000 to 1 in 100,000 people worldwide. Based on referrals from their local doctors—often, in Canada, England, and France—we usually see here in Boston only about a half-dozen patients per month. So we also visit pediatric clinics in Turkey, Dubai, and nearby countries because in these regions, people tend to have large families and about half of the marriages are between first cousins. Together, these two factors make recessive genetic disorders easier to study.

*How has talking with patients informed your research?*

The best example is in people with PH, most of whom have normal intelligence and can function well, except that many have a seizure disorder. In our clinic, one after another of these patients have told us that they suffer from dyslexia. Ten of 12 PH patients we’ve tested have reading scores remarkably lower than their general IQ scores would indicate.

Interestingly, further study has shown that they have a distinctive subtype of dyslexia. People with typical dyslexia have trouble deciphering sounds into syllables. By contrast, those with PH have a general defect that reduces the speed at which they can process information. Reading is the hardest thing the human brain does—it is the last developmental milestone that kids reach—and this probably explains why these patients will have specific reading difficulties. Now the question is, how does this form of dyslexia relate to the functional architecture of the cerebral cortex?

Another example is schizencephaly, which is a cleft or slit in the brain. Through a study of about 50 kids with this disorder, we found that a huge number of them either had very young mothers or were adopted. It’s a fact that adopted children tend to have young birth mothers too. So we think this condition is probably not genetic, because the frequency of genetic disorders increases with the age of the mother. Instead, schizencephaly may result from a blood-flow problem during pregnancy, possibly caused by exposure to infections, drugs, or toxins.

Sitting down and taking a history helps you recognize things more readily than if you just read about [a disorder]. And what we learn gives us ideas for scientific studies.

*Has working with these families affected you in other ways?*

Although some patients are almost completely normal, we also see families with severely handicapped children. Having a child with a serious brain disorder becomes the defining event for that family; it completely envelops them. As a parent with two healthy kids, I feel incredibly fortunate and blessed. It never ceases to impress me how resilient these families are, which inspires me to do everything I can to help them.

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INTERVIEW BY JULIE CORLISS. *Christopher Walsh is an HHMI investigator at Harvard Medical School, Beth Israel Deaconess Medical Center, and Children’s Hospital Boston.*