Explaining a genetic disorder's unique shift

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Findings reported in this week's *PLoS Biology* give insight into the unique characteristics of the birth defect known as Prader-Willi Syndrome (PWS), and at the same time, may help explain the way that a certain type of gene is expressed in all humans.

The research by University of Tennessee, Knoxville, professor Francisco Ubeda finds that the amount of care a father gives to his child may cause a shift in the syndrome in which its symptoms, in essence, reverse themselves.

At birth, children with PWS experience great difficulty suckling and have very low weight. After they are weaned from their mothers, though, their appetites become voracious, and they become obese.

Ubeda believes that this shift results from PWS' genetic roots on what is known as a group of imprinted genes. Humans typically get two copies of every gene—one from their mother and one from their father. Imprinted genes are prevented from working in one of the two copies, so that only the mother's gene or father's gene is expressed. This can be problematic when the working gene is somehow damaged.

Until now, scientists assumed that those genes and their level of expression—how much their effect was felt on the individual who carried them—was based on how the offspring drew resources from their mother. In this case, resources can mean anything from basic nourishment to less-tangible resources such as affection and attention.

Ubeda's work, however, seems to show that as more of an offspring's resources are provided by its father, that shift can also trigger a change in how those imprinted genes are expressed.

Ubeda said that PWS, which results from a deleted portion of the father's copy of a group of imprinted genes, provides a clear example.

"Before weaning, the mother has the monopoly on providing resources directly to her offspring," said Ubeda, an assistant professor of ecology and evolutionary biology at UT Knoxville. "After weaning, the father directly provides a greater share of resources to his offspring."

Ubeda found that as the share of the father's contribution of resources increases, there is a shift in which copies of the PWS group of imprinted genes is expressed, leading to the marked change in how PWS itself affects the child.

While Ubeda notes that this finding is unlikely to have an immediate effect on how PWS is treated, it provides implications for how diseases and conditions that are a result of imprinted genes are viewed.

"I don't have any sense that this will somehow lead to a cure for PWS, but it does present a new area for those interested in the disease to study and hopefully a new understanding of how the disease functions," said Ubeda.

According to Ubeda, perhaps the larger implication of the research lies in his finding that a small contribution of resources by the father may influence how imprinted genes are expressed and trigger a change of expression during development.

It's a new finding, he said, and one that fills in a blank caused by conditions like PWS that seem to be influenced by more than just the

mother's contribution. It exemplifies how social structure may have shaped the symptoms of some diseases over the course of human evolution.

According to the Prader-Willi Syndrome Association of the United States, the syndrome is found in one out of every 12 to 15 thousand children, and while rare, is considered the most common genetic cause of obesity.

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