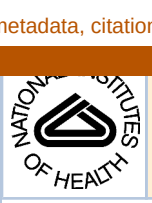

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A Place for Genetic Uncertainty: Parents Valuing an Unknown in the Meaning of Disease

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Abstract

Klinefelter, Turner, and fragile X syndromes are conditions defined by a genetic or chromosomal variant. The timing of diagnosis, tests employed, specialists involved, symptoms evident, and prognoses available vary considerably within and across these syndromes, but all three share in common a diagnosis verified through a molecular or cytogenetic test. The genetic or chromosomal variant identified designates a syndrome, even when symptoms associated with the particular syndrome are absent. This article analyzes interviews conducted with parents and grandparents of children with these syndromes from across the US to explore how they interpret a confirmed genetic diagnosis that is associated with a range of possible symptoms that may never be exhibited. Parents' responses indicate that they see the genetic aspects of the syndrome as stable, permanent and authoritative. But they allow, and even embrace, uncertainty about the condition by focusing on variation between diagnosed siblings, the individuality of their diagnosed child, his or her accomplishments, and other positive aspects that go beyond the genetic diagnosis. Some families counter the genetic diagnosis by arguing that in the absence of symptoms, the syndrome does not exist. They use their own expertise to question the perceived certainty of the genetic diagnosis and to employ the diagnosis strategically. These multiple and often conflicting evaluations of the diagnostic label reveal the rich ways families make meaning of the authority attributed to genetic diagnosis.

Keywords

USA; uncertainty; sex chromosome anomaly; fragile X syndrome; Klinefelter syndrome; Turner syndrome; genetic diagnosis

Introduction

The Human Genome Project and related genetic research have rapidly expanded the identification of genetic variants with unknown or probabilistic effects. As genetic predispositions for more conditions are explored, an increasing number of patients and medical providers encounter genetic test results with unknown or uncertain implications. This paper examines family perspectives on confirmed genetic diagnoses of three syndromes: Klinefelter, Turner, and fragile X (FXS), all of which have a broad range of possible symptoms. In

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interviews, parents of children with these syndromes made meaning of these genetic conditions by inserting a level of uncertainty into the diagnosis or prognosis.

As genetic conditions, Klinefelter, Turner, and FXS are particular kinds of syndromes. Their diagnosis differs from syndromes identified solely through a clinical evaluation that associates a combination of physical signs and symptoms with a named condition, such as adult respiratory distress syndrome. They also differ from more recent iterations of syndrome that include an explicit uncertainty, where patient advocacy groups allied with medical practitioners and researchers collect and label an otherwise disaggregated set symptoms (e.g., repetitive strain injury or chronic fatigue syndrome [see Dumit, 2006; Nettleton, 2006]).

Klinefelter, Turner, and fragile X syndromes are defined by a chromosomal or genetic variant. They each vary in the timing of diagnosis, specialists involved, and symptoms and prognoses, but in the U.S. their diagnosis is confirmed by a molecular or cytogenetic test. An individual whose cytogenetic test result is negative is not diagnosed with Turner or Klinefelter, regardless of mental or physical difficulties present. If the test result is positive, the individual is diagnosed with the condition, even if physical or mental characteristics are absent. The same consequences apply to the molecular test for FXS. For these syndromes, patient presentation and symptoms are not the basis for a confirmed diagnosis: a definitive diagnosis can occur in the absence of symptoms. These syndromes are indicative of the increasing number of conditions in the U.S. in which the presence or absence of a genetic or chromosomal variant alone confirms the diagnosis and therefore becomes the basis for medical advice, monitoring, and intervention.

Locating Uncertainty

Medical uncertainty has been thoroughly analyzed by sociologists and anthropologists (see particularly, Fox, 2000). Some authors have focused on uncertainty inherent to medical uses of experimental or new technologies (Brown & Webster, 2004; Christakis, 1999). Others have examined the ways in which medical practitioners, patients, and the public approach uncertainty in diagnosis, symptoms, and prognosis: how practitioners manage it; how patients cope with it; how it is minimized, ignored, controlled, or made acceptable practice (Babrow & Kline, 2000; Bosk, 2000; Brookes-Howell, 2006; Griffiths, Green, & Bendelow, 2006; Williams, 2006). Several studies have explored how individuals contend with “uncertain” syndromes or those not given medical legitimacy (Dumit, 2006; Lillrank, 2003; Nettleton, 2006; Petersen, 2006; Ware, 1992; Whitehead, 2006). This literature demonstrates how medical practice normalizes ambiguity and risk and how patients contend with uncertainty in diagnoses as a problem to be reckoned with.

In contrast, we explore an uncertainty that is valued. We focus on the ways parents open a space for uncertainty in the diagnosis, symptoms, and prognosis of genetic syndromes. With this comes a flexibility and resistance to a biomedical perspective that links a positive test result with diagnostic certainty. In interviews, families talked about their children as more than the diagnostic label, as achieving things that doctors told them would not be possible, as being “atypical” Turner or Klinefelter or not having “true fragile X.” They saw their children’s future as open-ended, emphasizing possibilities beyond the limitations of a diagnosis that translates a genetic or chromosomal variant into the permanence of a syndrome. Their counterdiscourse, underemphasized in the medical literature, is an alternative to the widely noted desire of patients for more detailed prognoses of their conditions (see Forrest, Simpson, Wilson, van Teijlingen, McKee, Haites et al., 2003).

The Medical Genetic Description of the Conditions

When clinicians and families use “Klinefelter,” “Turner,” and “fragile X,” they are not simply referring to a genetic or chromosomal variant, but to a medical label with a set of diagnostic implications that include possible symptoms, outcomes, and treatments. According to parents’ accounts, clinicians also often inserted a kind of uncertainty in their representations of the syndromes as having a spectrum of symptoms and phenotypic outcomes varying from mild to severe. These representations are given as probabilities, offering a kind of certainty in that the child receives the syndrome label whether or not symptoms are present. Statistical representations of the range of certainties are a way of closing spaces—they have the effect of making an unknown knowable, of excluding a fundamental uncertainty by placing it within the realms of certainty (Fox, 2000) with a range of variability.

Klinefelter and Turner are sex chromosome anomalies or variations, which are not inherited. Klinefelter occurs in approximately 1/800 males and is characterized by an extra X chromosome (in addition to variant forms of additional sex chromosomes: 48, XXYY, 48, XXXY, etc.) (Linden, Bender, & Robinson, 1996). Males with Klinefelter most commonly exhibit androgen deficiency and infertility, and may exhibit behavioral problems and learning disabilities (Lanfranco, 2004). Other symptoms may include decreased truncal muscle tone, speech delay, and motor problems (Simpson, de La Cruz, Swerdloff, Samango-Sprouse, Skakkebaek, Graham et al., 2003). However, aside from infertility, none of these symptoms is shared by all males who have an extra X chromosome (Lanfranco, 2004). The timing of and route to diagnosis vary, but commonly include: prenatally through amniocentesis or chorionic villus sampling (CVS); in early childhood due to behavior issues; during adolescence or adulthood due to small testes and lack of other signs of puberty; and in adulthood due to inability to conceive (Wattendorf & Muenke, 2005). An estimated 10% are diagnosed prenatally, 25% in childhood or adulthood, and 65% are estimated to be undiagnosed (Simpson et al., 2003). Confirmation occurs through a cytogenetic test (karyotype). Treatment recommendations include testosterone treatment for sexual functioning, bone mineral density, body hair, and other aspects associated with puberty (Lanfranco, 2004). Early intervention for learning disabilities is also recommended (Simpson et al., 2003).

Turner occurs in 1/2,000–5,000 females and is characterized by the loss or inactivation of all or part of an X chromosome (Frias, Davenport, & the Committee on Genetics and the Section on Endocrinology, 2003; Sybert & McCauley, 2004). Almost all females with Turner exhibit short stature and gonadal dysgenesis; 30–40% have lymphedema, resulting in puffy hands and feet and redundant nuchal skin (Sybert & McCauley, 2004); 20–40% have a heart structure anomaly (Frias et al., 2003); and 70% have nonverbal learning disabilities (Sybert & McCauley, 2004). Other symptoms may include kidney conditions, hearing loss, hypothyroidism, increased risk of heart disease, and eye or vision problems. As with Klinefelter, the timing of and route to diagnosis vary, but commonly include: prenatally through amniocentesis or CVS, often in response to an obstetrician finding anomalous heart readings; at birth when a pediatrician or obstetrician observes puffy hands and feet, or extra skin around the neck; in childhood when a pediatrician or parent notices short stature, hearing loss, or developmental delays; in adolescence by a pediatrician or occasionally an endocrinologist when pubertal changes do not occur; or in adulthood due to an inability to conceive. Some remain undiagnosed. Like Klinefelter, Turner is confirmed by a karyotype. Although there is disagreement about when growth hormone treatment should be started (Wasniewska, De Luca, Bergamaschi, Guarneri, Mazzanti, Matarazzo et al., 2004), the standard regimen is a course of recombinant growth hormone over several years, with additional treatment of symptoms as they arise (Frias et al., 2003). Other treatments include heart surgery for heart structure anomalies and estrogen to initiate puberty.

Fragile X syndrome, caused by a mutation on the X chromosome, is the leading hereditary cause of intellectual disability, occurring in approximately 1/4,000 males and 1/8,000 females (Crawford, Acuña, & Sherman, 2001). FXS results in significant impairments in development and adaptive function (Bailey, Hatton, & Skinner, 1998; Mazzocco, 2000). Males with the full mutation usually exhibit moderate to severe intellectual impairment, a range of language disorders, and social and behavioral difficulties, including problems with attention, impulsivity, anxiety, and arousal (Hagerman & Cronister, 2002). As many as 25–35% also meet the diagnostic criteria for autism (Bailey, Mesibov, Hatton, Clark, Roberts, & Mayhew, 1998; Rogers, Hehner, & Hagerman, 2001). Females are usually less severely affected. They may display milder but characteristic patterns of social anxiety and challenges in executive function (Lachiewicz, 1995). Diagnosis typically occurs in childhood at age three or older as an outcome of testing for developmental delays. Parents often visit numerous specialists before this referral is made (Bailey, Skinner, & Sparkman, 2003). Some individuals with the mutation are never diagnosed. FXS is typically confirmed by a Southern blot test indicating a FMR1 gene with greater than 200 CGG trinucleotide repeats. Polymerase chain reaction (PCR) may be used to find the exact repeat size, often in order to determine if a smaller but significant repeat number (premutation) is present. Both full and premutation status have reproductive implications for males and females. There is no medical treatment for FXS, but the child may benefit from early intervention with therapeutic and educational services (Bailey, 2004).

No genetic disorder is simple, and this complexity introduces ambiguity in prognosis (Feetham, Thomson, & Hinshaw 2005). In the case of Klinefelter, karyotypes with more than one additional X chromosome are considered to result in more severe symptoms than a 47XXY karyotype (Wattendorf & Muenke, 2005). With Turner, the amount of inactivation of the X chromosome appears related to symptomology (Frias et al., 2003). With FXS, the number of CGG repeats is not simply correlated with severity; individuals with CGG repeats in the premutation range may be at risk for some mental and physical conditions (Hagerman & Hagerman, 2002). Each syndrome also includes cases of mosaicism, where some cells are ‘normal’ and some have the chromosomal variation, resulting in a milder phenotype. For many genetic syndromes, such ambiguity may lead clinicians to doubt a genetic test result on the basis of their clinical judgments (Shaw, Latimer, Atkinson & Featherstone, 2003). Our research with families and medical geneticists indicates that test results for Turner, Klinefelter, and fragile X are taken to confirm or rule out the condition (Raspberry and Skinner, in press). This research is specific to the U.S., and the process of diagnosis and authority given genetic information may differ elsewhere. In our studies, parents describe receiving the diagnostic label independent of mosaicism or level of gene or chromosome inactivation. In this sense, these syndromes differ from those diagnosed by clinical observation alone. We focus here on parents’ interpretations of such confirmation based on genetic testing. This focus is significant given the increasing moments in the U.S. when a genetic diagnosis is made independent of symptoms, e.g., by prenatal amniocentesis due to maternal age; karyotype for an unrelated condition; or in expanding newborn screening programs.

The Study

We interviewed mothers, fathers, and grandparents of children diagnosed with Klinefelter or Turner and mothers of children with FXS. Semi-structured interviews about Turner and Klinefelter were conducted between March 2006 and June 2006. Families were recruited when clinicians agreed to forward our recruitment letter to parents of children at a university-based genetic clinic and a pediatric clinic in a southeastern state in the U.S. The researchers were unaware of any information about the individuals until parents responded to the letter, allowing researchers to contact interested families, explain the study in detail, and obtain informed consent. All individuals who responded to the contact letter agreed to participate: six families (six mothers, three fathers, one grandmother) of a child with Klinefelter, and eight families

(eight mothers, seven fathers) of a child with Turner. Parents ranged in age from their thirties to their fifties. Children ranged in age from 1 year to 16 years. The diagnosis for all children had been confirmed by a cytogenetic test.

Our analysis also includes 108 families of children diagnosed with fragile X syndrome. Researchers conducted semi-structured interviews with mothers between April 2003 and April 2005 as part of a larger, mixed methods, longitudinal study of family adaptation to fragile X. Families were recruited across the U.S. from genetic clinics, pediatricians' offices, developmental clinics, FXS family support groups, and a FXS parent listerv. Inclusion criteria included having at least one child below the age of 14 with the full mutation of FXS. The diagnoses for all children had been confirmed by a Southern blot or PCR test.

Confidentiality issues preclude reporting individuals' exact age or age at time of diagnosis, but when introducing families below, we report this information in terms of the following categories: prenatal; infant (0–11 months); toddler (1–4 years); young child (5–8 years); pre-teenager (9–12); and teenager (13–19 years).

In both studies, interviewers, including the first and third author, met the parent or parents at their home or other place of their choice. Interviews were designed to elicit in-depth narratives of parents' experiences of receiving the diagnosis, evaluations of the information and services they received, and their understanding of the syndrome and significance of the diagnosis. Interviews lasted 1–2 hours, and were digitally recorded and transcribed. The authors examined all transcriptions for segments pertaining to the ways in which parents understand their children and their condition relative to a genetic diagnosis. All such segments were collated and analyzed for cross-cutting themes.

The two studies differed in scope and number of participants. They are combined because of the cross-cutting themes evident in the ways parents made sense of the genetic basis for the syndromes. The small number of Turner and Klinefelter parents caution against considering these families representative of parents of children diagnosed with Turner and Klinefelter generally. Instead, we include these narratives along with those of parents of children with FXS to reveal particular forms that parents use to question the perceived certainty of a diagnosis.

The process of getting a confirmed diagnosis varied broadly in our sample. Parents of girls with Turner described diagnosis occurring through prenatal ultrasound or amniocentesis; an obstetrician or pediatrician noticing physical features in infancy; or a pediatrician noticing short stature in childhood. For Klinefelter, parents described the diagnosis occurring through prenatal amniocentesis or a pediatrician noticing physical features or responding to behavior issues in childhood. For FXS, someone, usually a parent, first became concerned about the child's development between 9 and 13 months of age. Often there ensued a series of visits to a pediatrician or specialist to determine if development was delayed, a fact that was typically confirmed by 22–25 months of age. On average, the diagnosis of FXS did not occur until 30–35 months of age when the child was referred for a test for FXS (see also Bailey et al., 2000; 2003). For the diagnoses of all three conditions that involved a pediatrician, he or she either sent a blood sample for analysis or referred the child to a clinic where the genetic test was conducted.

Receipt of the genetic test result reveals the multiple and negotiated process of reaching a genetic diagnosis, as the decision of whether to conduct a genetic test for Turner, Klinefelter, or FXS involves various kinds of expertise (e.g., psychology, dysmorphology, cardiology). An ethnographic study of a genetic clinic (Featherstone, Latimer, Atkinson, Pilz, & Clarke, 2005; Latimer, Featherstone, Atkinson, Clarke, Pilz, & Shaw, 2006; Shaw et al., 2003) demonstrates that the decision to look for chromosomal or genetic variants via a cytogenetic

or molecular test is a negotiated process that exists in tandem with other more traditional means of diagnosis (see also Brookes-Howell, 2006; Kerr, 2000). These means include clinical observations, adherence to standards of clinical practice, expertise in distinguishing competing conditions, assessments of test utility, evaluations of resources, and explorations of the potential social consequences for the patient. In the U.S., the specialist or general physician may note physical features, behaviors, and developmental signs of Turner, Klinefelter, and FXS that distinguish the syndromes from other genetic and non-genetic conditions, including autism and ADHD. Because FXS is an inherited condition, family histories and photographs may also be used to suggest a diagnosis, but in current U.S. practice, the diagnosis is not made definitively without performing the genetic test.

Certain Genetics, Uncertain Significance

For the majority of parents, genetics is an arcane field. When asked what they had learned from genetic counseling, most referred in general to the X chromosome or mutations, but expressed doubt about the details or significance of the genetic information. For many, even years after knowing the diagnosis, doing their own research, and interacting with medical practitioners, the genetics of the condition remained an abstract aspect.

While parents may view the science of genetics as arcane, they also consider it to be very precise. From their perspective, genetic or chromosomal variants are either present or absent, the genetic test result is reproducible, and crucially, once the genetic diagnosis is made, it will never change (see also Raspberry & Skinner, in press). When parents first learned the results of a genetic test, they viewed the syndrome associated with the test as both present and permanent, even if the manifestation of symptoms was uncertain.

Jeremy (all proper names are pseudonyms), whose teenage daughter was diagnosed with Turner as a toddler, indicated the unequivocal and stable aspects of the diagnosis when asked what he understood best about Turner:

> I know that she's missing a chromosome. I know that she was born with it, that she didn't develop it. I know that she'll always have it.

This theme of permanence pervades parents' understandings. Penny and Mark have a teenage son diagnosed with Klinefelter as a teenager. Mark distinguished Klinefelter from a diagnosis of cancer on the basis of permanence:

> **Mark::** …it's not like having cancer where okay, I've got 47 possible things that I can do and lots of-
>
> **Penny::** Options?
>
> **Mark::** Options and variations to get rid of this cancer. I mean he's got this Klinefelter's and you know, short of a miracle, he's going to have it when he dies. There's not anything you can do about changing the disorder. What is it called? It's not a disease, right? What is it?
>
> **Penny::** Syndrome.
>
> **Mark::** A syndrome, you know, so-
>
> **Penny::** Condition.
>
> **Mark::** You can't fix it you just have to learn how to deal with it.

In this exchange, ambiguity about the meaning of the diagnosis (e.g., a disease, syndrome, or condition) reveals the lack of certainty about what precisely Klinefelter is. But the genetic basis of the diagnosis is considered unchangeable.

In families' accounts, the karyotype and molecular test results reveal a stable and authoritative diagnosis. Parents described how genetic counselors explained the genetic condition to them by talking about flaws, inborn errors, and abnormality—terms that describe set conditions. Evelyn had two toddler daughters each diagnosed with FXS as infants. Evelyn talked about her relatives believing that there was nothing wrong with her children. She used the authority of the genetics of FXS to counter their perspective, emphasizing genetics as "true": "But I know. And the doctors know. Blood don't lie when they take it. And genetics doesn't lie when they take blood. So, it's either there or it's not there. And it's there."

The specificity, certainty, and stability of the genetics in these accounts contrast sharply with the uncertainty of symptoms, prognosis, and variation among affected individuals. Many families explicitly talked about this discrepancy (as have genetic counselors; see Miller, Ahern, Ogilvie, Giacomini, & Schwartz, 2005). Lisa, whose pre-teenage daughter was diagnosed as having Turner as an infant, spoke about the clarity of the karyotype and genetic expertise in her acceptance of the diagnosis. As the conversation continued, this clarity contrasted with what the syndrome meant:

> The ones who did the explanation were basically geneticists, this is what they dealt with, this diagnostic, the diagnosis of disease that affects the genes, the chromosomes and that type of thing. I can't remember everyone who was there when we had the conference about…what this means for Jennifer… Yeah it's so vague. I mean their descriptions of, I mean it's not like, okay they will have difficulty doing multiplication, they will have difficulty doing this. It's so varied and kind of vague as to where it's actually going to affect them that even now you have kind of a hard way of being able to put an actual handle on what to expect… it's still kind of, it's very fuzzy about, you know, is this exactly Turner's, what is this kind of thing?

Lisa and other families are sometimes frustrated with the discrepancy they experience in the clinic between the definitive diagnosis and the indefiniteness of the syndrome. Cynthia, whose pre-teenage son was diagnosed with Klinefelter as a young child, remarked, "Well you find out and then you don't know any more than you did before you found out… It's just, you just know that he has an extra chromosome and that's as far as it goes."

When parents feel they encounter an automatic link between a genetic test result and a confirmed diagnosis of an uncertain syndrome, the frustration is not simply a wish for a more certain prognosis. Instead parents are perplexed by the vague and uncertain significance of what they take as an unequivocal diagnosis. Frustration with the uncertainty of the prognosis and symptoms only occurs in the context of the perceived certainty of the genetic diagnosis.

Evaluating Medical Representations of the Diagnosis

Parents draw on various resources to make sense of a diagnosis for their child and family. Novas and Rose (2000) point out that an individual with a genetic diagnosis is expected to optimize health by gaining knowledge about what the diagnosis implies. In the U.S., when children are diagnosed with Klinefelter, Turner, or FXS, parents, especially mothers, hold responsibility for locating medical information and services (see Rapp, 1999; Rapp & Ginsberg, 2001). They may search for other kinds of knowledge about the condition beyond what is available in the health practitioner's office, such as Internet searches, discussions with family members, and conversations with other families of children with the same diagnosis (see also Raspberry & Skinner, in press; Schaffer, Kuczynski, & Skinner, in press; Skinner &

Schaffer, 2006). Searches are particularly intense directly after hearing the possible diagnosis. Parents described looking for any information available in the time between their physician's first mentioning the condition and receiving the confirmatory test result.

In their searches, parents may come across information that is misleading and often alarming, particularly in relation to Turner and to Klinefelter (Linden, Bender, & Robinson, 2002). As Lisa related:

> It was Kansas where we were living and I looked up everything I could find on the Internet and in books, which was maybe not the best thing to do because we ran into some old misleading information that got me really scared. I remember going back out to the car and using the car phone and just kind of crying to my husband over the phone about this because a lot of the information I found was a bit outdated. It talked about mental retardation and that type of thing associated with it.

Misinformation about disorders can also come directly from medical practitioners. Most families received diagnoses and learned about Klinefelter and Turner from pediatricians who must convey genetic information regarding sex chromosome variations that is difficult to interpret (see Hall, Abramsky, & Marteau, 2003). Many families said that their pediatrician portrayed the condition as excessively negative or that health care providers presented misinformation. As Gunther and colleagues (2004) point out in the case of Turner, the large number of undiagnosed persons creates a bias in the medical literature toward those who have been diagnosed and, therefore, have increased severity. These persons are more likely to be involved in national organizations, medical care, and therefore medical studies, resulting in a possibly overly severe depiction in the medical literature. In the case of Klinefelter, parents described medical practitioners drawing on studies conducted in the 1970s, now discredited, linking the condition with prison populations (see Linden, Bender, & Robinson, 2002). Virginia, whose teenage son was diagnosed with Klinefelter as a toddler, talked about such negative depictions:

> It paints a pretty grim picture. It's not the truth, in any way, shape or form, it's not the truth… Doctors paint such a grim picture and it's so inaccurate. ….[The doctors say]: "They may not speak, they may not talk and if they do it's going to be very limited and they are going to have a very decreased IQ." And you know they'll throw around words like "mentally retarded" or "mildly mentally retarded," and they don't understand the power of those words to people who don't have the training.

The authority accorded a genetic diagnosis makes misinformation about symptoms particularly powerful for families. In the case of Turner and Klinefelter, on the basis of the information received from the Internet or the clinic, parents may still consider their child as potentially having mental retardation or becoming violent even in the absence of any symptoms (on such creation of the pre-symptomatic person, see Konrad, 2003; 2005). Families draw on their experiences and research over time to correct overly negative misrepresentations.

Parental Expertise

Families open up a space for uncertainty and close spaces for misinformation based on their experiences. They use their child's individuality and unexpected accomplishments, variation between affected siblings, and similarities to unaffected siblings to gain confidence in questioning the certainty accorded the genetic label.

In narratives, parents draw on their children's accomplishments and characteristics to distance them from the implications of the diagnosis (see also Landsman, 2005). Some families achieve this by questioning the limitations presumed by the diagnosis, as did Rachel, whose young son was diagnosed with FXS as a toddler:

> Because even with him having fragile X. And the label that – I don't know who gives that label. But the label that's there, I try to let him know that he's just the same as [his siblings], me, you, and everybody else. Because, I mean I try to tell him, "You're no different than anybody else. And you can do exactly what they do. It may take you a little time. But we'll work with you until you get it."… But other than that, I know that he can do more than what fragile X or whatever says that he can do. Because he's shown me so many times.

Often parents questioned the label by contrasting the individuality of their child with the reductionism of the genetic label and criticized medical practitioners who saw their child simply as a reflection of the diagnosis (see also McKeever & Miller, 2004). Virginia talked about her approach with doctors: "I'll educate you, you know, but don't you ever pretend to look at my son and see him for a genetic disorder."

In these accounts, parents expressed frustration with the simplicity of the diagnosis in contrast to the individuality and multiplicity of their child. Similar to other parents of children with disabilities, many talked about positive aspects related to the condition, in contrast to what they saw as a clinical focus on negative aspects (see Hastings, Koyshoff, Ward, degli Espinosa, Brown, & Remington, 2005; King, Zwaigenbaum, King, Baxter, Rosenbaum, & Bates, 2006; Landsman, 2005; Skotko, 2005). Kelly has a young son diagnosed with FXS as a toddler and a toddler diagnosed with FXS as an infant. She talked about the positive aspects of FXS: "I think any kids I've seen with disabilities or fragile X specifically are very, very loving. Gives them a big heart." Other parents of children with FXS noted their sense of humor. Parents of children with Klinefelter talked about their sons being "sweet" and having a "nurturing personality."

In treasuring these characteristics, parents offer a counterview of valued personhood in the negativity they sometimes otherwise encounter. This view may come at a price, as mothers who focus on positive aspects are frequently considered by medical practice to be in denial (Landsman, 2005; McKeever & Miller, 2004), or holding unreasonable expectations that need correction. These interpretations may be dismissive of parental knowledge and preclude the possibility of multiple valid perspectives of the condition.

Families also separate their child's individuality from the diagnosis by contrasting syndrome language with their child's needs. Cheryl, whose toddler son and daughter were both diagnosed with FXS as infants, provided an example:

> That even though like two kids can have fragile X that you don't put a label on it… You don't say, "He's got fragile X." It's, "What is he lacking?" Like, "Where is he falling short." … I think that is the most important thing to understand about fragile X.

This language of needs differs from representations of their children as a set of symptom probabilities.

The diagnostic label may be most significant for parents within the medical setting as a site where genetic information is created and valued in particular ways. This can be especially true for families of children with syndromes where symptoms can be particularly mild or non-existent. Kathleen and Richard, parents of a toddler daughter diagnosed with Turner prenatally, talked about this limited relevance:

> **Kathleen::** Kathleen: We don't even, it's so funny because we don't think about it at all. You know, other than when she has her appointment with her cardiologist or we need to go see Dr. Barrett.

> **Richard::** Richard: Well, we do think about it but I think what Kathleen's trying to say is there's nothing about her that makes us think Turner's syndrome at all. Looking at her, living day to day with her, I mean it's so easy to forget that she even has that because there's no outward signs.

Evelyn similarly contrasted the medical aspect of FXS with her daughter's condition, distancing her child from the medical arena and the genetic diagnosis by framing her child's symptoms as developmental delays not requiring medicine:

> When people ask me about her condition or whatever, they always try to put a label on her or myself or whatever. And the way I see it is, don't put a label on that. Even though that is a condition that you have. But we don't take any medicine or anything. We don't have to take any medicine. It's nothing like that. It's just that when you have a developmental delay, that's all that it really is. And that you… just learn different than others.

Amid the medical expertise associated with the genetic diagnosis, families value their own experiences as revealing the limitations of the label, the open-endedness of their children's lives, and the valued characteristics in contrast to clinical images. As Landsman (2003; 2005) describes, mothers are involved over time in negotiating understandings of their children with disabilities in and against physicians' representations. Disassociating the collection of various symptoms from the diagnosis and then from the child takes time and work on the part of parents. The initial certainty of the diagnosis makes the symptoms and their child's future all seem unequivocal. Only through later experiences with the child do parents build confidence to create a space for change and reflection on how their child refutes aspects of the diagnosis. These lively and multiple ways of describing and understanding their children; of talking about changes, possibilities, frustrations and joys; and of giving their children complex subjectivities are important ways of valuing an unknown that is often considered problematic in the context of genetic diagnosis.

Difference in the Diagnosis

Parents' emphasis on their children's experiences as contradicting diagnoses and prognoses introduces difference as integral to the conditions. Families talked extensively about variations among those diagnosed. Tracey, mother of Conrad, a young child diagnosed with FXS as a toddler, and Maureen, a pre-teenager found as a toddler to be a carrier, remarked, "But my understanding is that I know it's different between Conrad and Maureen. I know that it's different in me. I know that it does things differently in all three of us." Kelly talked similarly about her two sons with FXS: "When people see Marcus, they think Marcus is so quote unquote normal. And so, I'm like 'Marcus has the same thing Luke has. And it affects different kids differently.'" Natalie, grandmother of a teenager diagnosed prenatally with Klinefelter, talked about how he differed from others:

> He's really not a full blown Klinefelter, he's just a borderline because I see things that when I look on the website or people have described to me like the facial hair, the hair you know, I'm just amazed at how much hair he has. …I go you know, he's just a little Klinefelter's, he's not a lot Klinefelter's.

In these accounts, parents' explanations go beyond a view of the syndromes as representing a spectrum. They speak of difference, of contradictions, of their child as unlike other diagnosed children, as having characteristics typical of non-diagnosed children. Fundamental uncertainty is part of the diagnostic category. For example, Georgia, whose young son and pre-teenage son were both diagnosed with FXS as infants, indicated a basic unknown when asked what she understood most about the syndrome:

> Um, just that you can't predict what somebody who has a diagnosis is going to be like… there's the lab component where you measure the sequence…but basically that's not an indication of how affected somebody is, that the variations could be very great. My own children have basically the same sequence number, repeat number, but they're so different.

For parents, distinguishing their child from "normal" FXS, or Turner, or Klinefelter, can be another way of leaving the future unknown, even if they also acknowledge that their child's future may include more characteristics of the condition.

Some families argue that in the absence of symptoms, the syndrome does not exist. Lisa explained, "I don't think Turner's exists without some of the physical aspects of it." Janis, whose teenage son was diagnosed prenatally with Klinefelter, believed that babies can have 47XXY but not the syndrome: "I think of men as having Klinefelter's, I don't think of children as having Klinefelter's." For these parents, complexities of the variations and their uneasy link to symptoms call the diagnostic label into question. They shift its identity from the genetic result to the symptoms that comprise the syndrome.

Interpreting the Label

Many parents reflected on this ambiguity in the significance of the diagnosis. Melissa whose toddler son was diagnosed with FXS as a toddler, proposed the possibility of her own overuse of the diagnosis:

> Okay, what do I understand the most? (Pauses) The black and the white. The genetic, the numbers… Yeah, the actual facts of the genetic reproduction and that. (Pauses) I think I'm gaining an understanding on the social anxiety and hyper-arousal and how that is like the skeleton of my son. It all comes down to "was he anxious, is he anxious, is he excited, was he excited?"… I don't really understand it, but it's getting easier to see and I don't know if it's a product of knowledge, like you read about it and you see it—you know, hypochondriac syndrome—or if it's because I'm just becoming more knowledgeable of my son, you know, and saying, "Yes, this is factually an issue with him."

Wanda, mother of a young child recently diagnosed with Klinefelter, ADHD, and bipolar disorder, reflected on the relationship of these labels:

> …I would say that those are just labels or diagnoses that they have given to his behavior you know and like I said the ADHD, he was diagnosed with before he ever had the diagnosis of Klinefelter's. So they were just diagnosing the behavior he was having at the time but as an overall, like an umbrella, the Klinefelter's is the umbrella and then you have all these different diagnoses underneath with the abnormal EEG and different things that are going on and from what I understand, you know, not one specific case of Klinefelter's is going to be exactly the same for another.

These families viewed the diagnoses as labels, reflecting on the impossibility of clearly delineating diagnoses, symptoms, and experiences. Families used these labels strategically. Christina, whose teenage son was diagnosed with FXS as a young child, said:

> One time my ex says, "Is this fragile X thing the reason why you're crazy?" And I said, "Thank God it is. What's your reason?" I have a reason. I can fly it. I'm not just crazy because of no reason. So, it gives me an answer. And that means a lot. It gives me an answer when academically I can't function like other people. I hate to use it. I hate to tell people about it. But sometimes I whip it out if I have to.

Christina invoked the label of FXS to explain her behavior to others, sometimes seriously, sometimes playfully. Other parents talked about how they used the genetic diagnosis in

sociopolitical ways: to qualify the child for special services, for insurance purposes, or to explain the condition to others. Parents who said they did not think about the diagnosis at home described using it elsewhere to get resources for their child. They may hide the diagnosis to avoid problems or employ it to gain access to needed services. In these ways, parents recognized the power and authority accorded genetic labels.

Families were thus complex in their use of the diagnosis. They held multiple and often conflicting evaluations and emotions around the label: they wanted the stabilization of getting the diagnosis, of having the label, while renouncing its stability; they wanted more prognoses while considering the prognoses to be too restricted, not individualized to their child.

These multiple evaluations of the diagnosis allow negotiation. The diagnosis is used to particular effect in different contexts—at times it provides a valued explanation, at other times it poses a hindrance to deeper explanations. What families perceive as unequivocal presentation is critiqued through families' experiences of and hopes for their children. Parents' accounts reveal an ambivalent and multiple significance of the genetic diagnosis.

Conclusion

Patients' or parents' knowledge of genetic information is commonly measured for concurrence with medical knowledge, but this indicator is inadequate to the task of analyzing their understandings. We focus instead on parents' complex evaluations of genetic information, and how they draw on their own experiences to question clinical genetic expertise and the certainty that attends some disorders. Their understandings of family, kinship, procreation, and disease are not reducible to the biomedical descriptions that they learn and sometimes accept. Families treat medical knowledge as but one kind of knowledge. They can use medical labels as simultaneously positive and negative, as both restricting future possibilities and resolving confusion. Their complex uses of the diagnostic label may seem dissonant and may be misunderstood in places where ambiguity and multiple meanings are devalued.

The various ways in which parents construct meaningful representations of genetic syndromes for their own child and family raise questions as to the special significance that should or can be accorded to genetic diagnosis and information (e.g., Green & Botkin, 2003; Plantinga, Natowicz, Kass, Hull, Gostin, & Faden, 2003; Wilfond & Ravitsky, 2005). For some families, what is exceptional about genetic information may be that they feel medical practitioners treat it as exceptional. When taken as authoritative, unequivocal, and determinant, genetic information seems privileged. The special weight given to a genetic finding can turn a genetic variation, without symptoms or other findings, into an unambiguous diagnosis rather than signal a risk for a syndrome. Diagnoses confirmed by a cytogenetic or molecular test can have a fundamental certainty, even when they include only probabilities for symptoms. Part of this fixedness is in the attention focused on the power of genes in media and scientific discourses, what Fox (2000) calls "hyper-certainty."

Yet this fixedness is subjected to considerable contestation by families. Parents of children with genetic diagnoses critically appraise the scope and efficacy of medical models and the certainty they report experiencing within the medical system. Parents' pronouncements of their children as going beyond the limitations of the diagnosis/prognosis are used to place the expertise and models of medical practice into doubt, and to value other kinds of knowledge and the positive characteristics of the child. This analysis of parents' treatment of certainty reveals a valued uncertainty.

Parents' holding onto a fundamental unknown contrasts with the kinds of medical uncertainty that social researchers have analyzed. The search for more prognoses, for an unequivocal label, for more stability and certainty amid amorphous risk is here reversed. In this study, parents

drew on their experiences and knowledge produced in raising children diagnosed with Klinefelter, Turner, or fragile X syndrome to question the perceived certainty of genetic information in order to introduce a valued uncertainty. Emphasizing the uncertainty in genetic diagnoses, rather than a drive for its reduction, may make genetic information and genetic diagnoses more relevant and less deterministic for families. This emphasis may also create a productive space for medical providers and researchers to evaluate the link between genetic test results and the implications of the diagnostic label.

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