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COMMENTARY

Responses to *FTO* genetic test feedback for obesity in a sample of overweight adults: a qualitative analysis

S. F. Meisel · J. Wardle

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Abstract Current evidence indicates that genetic testing for obesity risk has limited affective or behavioral impact, but few studies have explored the effects among individuals who self-identify as having weight problems. Here, we report findings from in-depth telephone interviews with seven overweight or obese volunteers who were genotyped for one weight-related gene (FTO), which may offer interesting insights into motivations to seek out genetic testing and immediate reactions to it. All participants had a BMI > 25. The gene test identified one participant as homozygous for the 'higher-risk' variant (AA), three heterozygous (AT), and three homozygous for the 'lower-risk' variant (TT) of FTO. All participants said they took part to find an explanation for their personal struggle with weight control. Those with one or two higher-risk variants experienced relief and saw the result as confirming their private assumption that they were susceptible to weight gain for reasons perceived as 'external' to them. However, at the same time, they described themselves as more motivated to overcome their genetic predisposition. Those with lower-risk variants reported brief disappointment, but then focused on alternative explanations, reinforcing the multifactorial nature of obesity. Despite objectively low 'information value,' all individuals derived some 'personal' benefit from FTO genetic test feedback. However, improving education about the multifactorial nature of complex conditions is important to decrease polarized thinking and associated genetic determinism and stigma to derive the greatest benefits of novel genetic technologies for individuals and their health.

Keywords Genetic susceptibility · Stigma · FTO gene · Obesity · Psychology

Obesity is a highly heritable condition with a complex etiology, probably comprising interactions between many genes of small effect and the 'obesogenic' environment (O'Rahilly and Farooqi 2008; Speakman and O'Rahilly 2012). *FTO* was the first 'common obesity' gene to be identified (Frayling et al. 2007; Scuteri et al. 2007). In population samples, the higher-risk variant (A) is associated with modestly higher body weight (1.2 kg per allele), and AA homozygotes have a 20 % higher lifetime risk of overweight or obesity compared with TT (lower-risk) homozygotes, although all genotypes are observed at all body weights. The function of *FTO* is beginning to be characterized, possibly influencing traits such as appetite avidity and satiety responsiveness (Llewellyn et al. 2012; O'Rahilly and Farooqi 2008; Wardle et al. 2008; Karra et al. 2013).

Despite uncertain clinical utility due to small effect sizes, the obesity genes identified to date are included in consumer-based genetic testing panels (e.g., www.23andme.com; www.pathway.com). However, debate continues in the wider genetics community about the benefits and harms of feedback for conditions with complex, multifactorial etiology (Grosse et al. 2009; Evans et al. 2011; Frueh et al. 2011). Supporters of testing anticipate that a higher-risk result might serve as a 'wake-up call,' motivating beneficial lifestyle changes (Collins 2006). Those cautioning against testing argue that genetic determinism means that a higher risk result could lead to

S. F. Meisel (✉) · J. Wardle
Department of Epidemiology and Public Health,
Health Behavior Research Centre, University College London,
Gower Street, London WC1E 6BT, UK
e-mail: susanne.meisel.09@ucl.ac.uk

fatalism and discourage efforts at behavior change (Marteau and Weinman 2006). This latter response would be particularly problematic for obesity where prevention and treatment depend primarily on behavior change.

The potential for harm from fatalistic responses makes it important to investigate the psychological impact of genetic test feedback for common, complex conditions. Vignette studies, where participants 'imagine' receiving genetic test feedback, were a first step. They typically find that people imagine that a higher risk results would make them more motivated to change their behavior, and there is little evidence of negative emotional or motivational outcomes (Sanderson and Wardle 2005; Frosch et al. 2005; Meisel et al. 2012; Meisel and Wardle 2013). However, although these results are encouraging, they cannot be assumed to generalize to *real* feedback conditions.

One small study incorporated feedback for the b3AR gene into a weight-loss program for obese women (Harvey-Berino et al. 2001). Similar to the results of hypothetical studies, women receiving a higher-risk result remained motivated to change their behavior without any indication of fatalism, although there was no comparison group receiving a negative genetic test result. A randomized controlled trial giving feedback for familial hypercholesterolemia (FH) also found no evidence that higher-risk genetic test feedback resulted in fatalism or reductions in dietary adherence (Marteau et al. 2004). However, consistent with a recent Cochrane review of genetic test feedback for a range of health behaviors (Marteau et al. 2010), neither study found any impact on behavior.

Studies investigating impact of lower-risk genetic test results are scarce. In the FH trial, those who had no genetic predisposition to FH perceived the disease as less controllable, and thought they would have less control over heart disease, although the differences were no longer evident at the 6-month follow-up (Marteau et al. 2004). To our knowledge, this is the only study explicitly commenting on the effect of lower-risk genetic test results.

The first large study to investigate effects of genetic testing for multiple conditions included over 2,000 individuals who received a reduced rate purchase of the 'Navigenics Health Compass,' which gives results for 23 conditions, in exchange for responding to surveys 6 and 12 months after receiving the results. Regardless of risk status, there was no change in anxiety nor any evidence of positive or negative behavior change either at short- or long-term follow-up. However, a 'healthy participant bias' among these early adopters of genetic testing may have contributed to the null finding (Bloss et al. 2011, 2013).

Although research has begun to explore the emotional and behavioral outcomes of genetic test feedback, few studies have addressed the question of why it has less impact (positive or negative) than anticipated. Here, we describe findings from in-depth telephone interviews with seven overweight or obese white British women (BMI range 25–39 kg/m^2), aged 34–54 years (mean age = 45, median age = 44), who volunteered to be genotyped for FTO.

Ethical approval for the study was granted by the UCL Research Ethics Committee for non-NHS research (ID Number 2471/001). Communication about the study was conducted largely by email (including result disclosure) to resemble the format used by companies offering consumer-based genetic test feedback. Before enrollment, and when receiving their FTO genetic test result, participants received written information materials, which clearly outlined the multifactorial nature of obesity and the modest contribution of FTO. Furthermore, population frequencies of FTO were described to ensure that participants understood that obesity can occur despite having the lower-risk genotype. This information was verbally reiterated during the interviews. One participant was homozygous for the higher-risk A variant (AA), three were heterozygous (AT), and three were homozygous for the lower-risk variant (TT). All participants correctly recalled their test result and could explain its meaning in their own words.

In the interviews, it soon transpired that despite being aware about obesity as a multifactorial disease, people's motivation to participate in this study was unanimously driven by the desire to find an 'explanation' for their weight status. For example, one participant took part to find out 'whether there are genetic reasons why I find it extremely difficult to lose weight or why I am larger than other people, is there a reason why, other than the fact that I do love food?' (P7, TT). Consistent with this, receiving a lower-risk genetic test result led to brief disappointment, perhaps because despite knowing 'rationally' about the many causes of obesity and FTO's modest contribution, people anticipated and hoped for the higher-risk FTO genotype. However, the disappointment did not last because all TT participants spontaneously drew on their knowledge about the alternative causes of obesity; for example: 'It's not all down to genetics because it's down to the environment, the way you have been brought up and all that that has an influence, I think, on you, the choices that you make and stuff like that, you know' (P6, TT). Another pointed out that the contribution of FTO is only small and that there may be other genes that are the cause of their weight gain: 'And it doesn't make a lot of difference having it. Because if you have got it you are 3 kilos, 7.3 pound, yeah, no, it's a very small amount […]. I still think that there's something in the genes, but not in these particular ones, which are simply related to body build […]' (P7, TT). One participant also considered potential advantages from not having the 'higher risk' variant, demonstrating evidence for positive active coping: '[…] in

a way I should be pleased because then, you know, there's less things that stop you from losing weight because if I did have the gene, maybe it's harder to lose weight.' (P6, TT).

Although those receiving AA and AT results also held multifaceted beliefs about the causes of obesity, these were only shared once prompted. They felt 'pleased with the result,' although it came as 'no surprise, because it just confirmed what I felt anyway' (P4, AA). One participant described her AT result as 'normal' genotype and explained that she was 'living that result' (P1, AT), perhaps reflecting the understanding that overweight is caused by a combination of genes and environment.

Regardless of their test result, many participants were quick to note that they never intended to use it an as *'excuse'* for their weight status, perhaps reflecting acceptance of broader societal attitudes toward obesity as a personal shortcoming for which the individual is to blame. Instead, having a genetic *'explanation'* helped confirm the perception that forces beyond personal responsibility contributed to their difficulties with healthy body weight maintenance: 'I understand that genetics and the things that we are likely to choose as a result of our genes or how we are likely to feel means that we can't always help the fact that we eat what we eat, if that makes sense' (P4, AA). Knowledge of the underlying genetics appeared to alleviate some of the guilt and stigma associated with overweight. In this context, some participants also mentioned that there might be value in popularizing the message that genetics is a contributor to overweight, because 'it could make some people more understanding, it would perhaps make the medical profession more understanding' (P7, *TT*).

Although the findings presented here are from a small volunteer sample, they nonetheless offer interesting insights into people's motivation to seek out genetic test feedback and their immediate reactions to it. Currently, consumer-based genetic tests emphasize the *predictive* value of genetic testing in their marketing strategies. However, these results suggest that the desire for an 'etiological explanation' of a condition may be an alternative driver for seeking out genetic testing, a hypothesis that could be explored in further research.

In line with findings from previous hypothetical and clinical studies (Meisel et al. 2012; Conradt et al. 2009), the results suggest that genetic test feedback for obesity risk may have beneficial psychological effects for overweight and obese individuals beyond 'objective' clinical utility. Despite the objectively low 'information value' of genetic risk information for an existing condition, people appear to derive 'personal' psychological benefits from the information.

There is often concern that a focus on genetics in disease etiology fosters deterministic views, and this did not appear to be the case. Far from resulting in fatalism, an 'explanation' for weight status in the form of a higher-risk result appeared to motivate a shift of focus toward taking action (beating my biology), while a lower-risk result helped reinforce understanding about the multiple causes of obesity. However, we were careful to emphasize the complex origin of obesity, and FTO's modest effects, throughout the study, which may have protected participants from engaging in genetic determinism. Furthermore, the participants were volunteers and may have selected themselves into the study based on their anticipated positive reaction to the genetic test result, an issue that is common to studies in this area (Sanderson and Wardle 2008).

In clinical practice, genetic feedback for a single gene conferring very moderate risk is unlikely to be used, not least because feedback for gene panels is now feasible and cost-effective and whole-genome sequencing is eagerly anticipated. Reactions to genetic test results from panel or whole-genome sequencing may differ because participants may assign a different meaning to these results. However, as findings presented here match those obtained from earlier studies, and from other areas of genetic testing and health, behavior change irrespective of whether genetic feedback was given for one or multiple conditions (e.g., Leventhal et al. 1997; Harvey-Berino et al. 2001; McBride et al. 2002; Marteau et al. 2004; Sanderson and Wardle 2005; Bloss et al. 2011; Hollands et al. 2012; Grant et al. 2013). On this basis, they provide some reassurance that people are generally unlikely to misinterpret and overstate the impact of genetic test results, although the limitations of self-selection have to be kept in mind.

With increasing understanding about the mechanisms through which genes affect behavior, it will be interesting to investigate whether behavioral advice tailored to the individual's genotype will be superior to giving individuals generic advice for behavior change. For example, FTO is thought to affect weight gain partly through low satiety sensitivity and high food responsiveness (Wardle et al. 2008; Karra et al. 2013), but no study to date has explored the benefits of information focusing on these specific characteristics. Furthermore, it will be important to carry on improving education about the genetic and non-genetic causes of multifactorial conditions not only to avoid genetic determinism, but also to diminish stigma in order to derive the greatest benefits of novel genetic technologies for individuals and their health.

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