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Shooting a moving target. Researching autism genes: An interview study with professionals

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ABSTRACT

Background: Given the wide variety of the phenotype, the uncertain genetic origins and the discussions surrounding the status of autism itself, genetic research on autism genes generates specific ethical questions that are not completely analogous to the ethical issues of genetic research in general.
Method: In order to map ethical issues surrounding research on autism genes, as experienced by professionals in the field of autism, we interviewed 15 Belgian professionals.
Results: We found that respondents believed that the heterogeneity of the autism phenotype affects the ethics of research on several levels. It affects issues regarding who to include in research on autism genes, regarding what the aim is of such studies, and how the research is done.
Conclusions: Although genetic research on autism genes is proliferating, a systematic ethical reflection and protocol is missing. With this study we have shown that autism professionals in Belgium express both skepticism and hope with regard to genetic research and raise important points with regard to the effect that the complexity of autism has on research aims and methodology.

1. Introduction

Autism Spectrum Disorder (ASD) is a diagnosis that is given after behavioural observations, and that spans a spectrum ranging from individuals with severe mental retardation and malfunctioning to individuals who score normal or high on IQ tests. The DSM-V, which is the most recent version of the Diagnostics and Statistical Manual of Mental Disorders (DSM) describes the following traits: persistent deficits in social communication and social interaction across multiple contexts, restricted, repetitive patterns of behaviour, interests, or activities, and qualitative impairments in communication (American Psychiatric Association, 2013). The DSM also states that "symptoms cause clinically significant impairment in social, occupational or other important areas of current functioning", hence explicitly adding the fact that the person should be dysfunctioning in order to warrant a DSM diagnosis. Whereas in previous versions of the DSM, Pervasive Developmental Disorder – Not Otherwise Specified (PDD-NOS) and Asperger syndrome were considered separate conditions, they are now all collected under the umbrella term of Autism Spectrum Disorders.

Although the identification of an individual as autistic is done through behavioural observation and checklists, much research has been done to find a biological explanation for the phenotype. Although originally, autism was thought to be a psychogenic disorder and caused by certain parental behaviour (the 'refrigerator mother' theory), there is now consensus that it has a biological cause, a finding that has been welcomed by many parents. Research into the nature and aetiology of autism includes research into the brain function and the structure of the brain of autistic individuals through neuroimaging (Dichter, 2012; Pelphrey et al., 2011). But also the genetic basis of these neurological differences have been widely studied. That autism has at least partly a genetic basis was already known through concordance studies in monozygotic twins, through the fact that it seems heritable and through the fact that it is a symptom of some known genetic and chromosomal disorders such as Fragile-X, tuberous sclerosis and neurofibromatosis type-I. But only in 5–10% of the individuals presenting themselves their autism will have a clear monogenic cause (Jeste and Geschwind, 2014). In 20–30% of these individuals, known genetic risk variants can be found, which include copy number variants (CNVs) and sequence variants (Chung et al., 2014; Ronemus et al., 2014; Sebat

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et al., 2007), representing a spectrum of *de novo* and inherited variants with different levels of penetrance. Hence, in many cases, autism is considered to be multifactorial, and other factors besides the mere genetic variation must play a role. Factors currently being studied include epigenetic modifications, perinatal problems (Kolevzon et al., 2007), intra-uterine testosterone levels (Auyeung et al., 2009; Baron-Cohen et al., 2015), immune dysfunction (Goines and Van de Water, 2010), pesticides (Roberts et al., 2007), in utero exposure to medication (Bromley et al., 2013; Rai et al., 2013), alterations to the gut microbiome (Mayer et al., 2014), and many others as reviewed by Herbert (Herbert, 2010).

Next to the etiological complexity of autism, there is uncertainty regarding the status of autism itself. Especially with regard to so-called high functioning autism, or Asperger's syndrome, which as of the DSM-V is gathered under the umbrella term of Autism Spectrum Disorder, authors of academic papers and people with the diagnosis themselves have argued that it may be a natural and potentially healthy human variation or difference (Jaarsma and Welin, 2011; Kapp et al., 2013). Therefore difficulties may be caused by socially constructed barriers, and Asperger's or high functioning autism may be considered as a difference rather than a disability and is associated with certain strengths, such as musical ability and technical insight (Perry, 2012; Walsh, 2010).

Given the wide variety of the phenotype, the uncertain genetic origins and the discussions surrounding the status of autism itself, we and others have argued that genetic research on autism genes generates specific ethical questions that are not completely analogous to the ethical issues of genetic research in general (Walsh et al., 2011). In order to map these ethical issues as experienced by professionals in the field of autism, we interviewed 15 Belgian professionals working in the field of autism. In this paper we present the findings of this interview study.

2. Methods

In order to investigate the opinions of autism professionals on ethical issues related to genes and autism we interviewed 15 Belgian professionals. We designed a semi-structured topic list based on a literature review. Topics included genetic research, clinical genetic testing and counselling and reproductive choice. In this paper we present our findings with regard to the ethics of genetic research.

KH and HP made a list of 12 possible interviewees, from a mix of relevant professions. We made sure to include also professionals with experience with autistic children with severe mental retardation. Three extra respondents were added after the interviews were ongoing, because respondents suggested their names, after assessing their relevance in the field. An overview of the different professions of respondents can be found in Table 1. Interviews took between 30 min and 70 min, and were transcribed verbatim by KH. They were then coded using NVIVO 10 software. Before analysis, and based on our literature review, we hypothesized that the complexity of autism research and the variability of the phenotype complicated ethical questions surrounding autism genetics. For our analysis we took a grounded theory approach and created codes based on our data. We did not use an initial list of codes. In a first round of open coding we extracted and coded into several subthemes all pieces of text that were relevant for the question for genetic research and concepts of autism. In the next two rounds of coding, the axial coding and the selective coding, we connected the different subthemes into broader concepts. KH, did the initial rounds of coding, the subsequent results and story were agreed upon by KH, HP and KD.

A limitation of our study may be that we used a relatively fixed set of respondents, rather than adding respondents and interviews based on suggestions of interviewees. Coding was done after all interviews were done and transcribed, which may be considered a shortcoming. However, we still believe we obtained saturation as during coding no new themes seem to emerge after a while. Interviews were done in Dutch, the native language of all interviewees, and selected quotes were transcribed for this paper. Hence, some of the nuances may be lost in translation. We used *she* to denote all respondents in this paper, to ensure anonymity of the respondents. Quotes are accompanied by numbers, to demarcate different respondents with the same profession.

The study was reviewed and approved by the KU Leuven Social and Societal Ethics Committee.

Table 1
Information about the interviewees.

		#
Profession	Psychologist	3
	Clinical Geneticist	2
	Educational specialist	5
	Pediatrician	1
	Child neurologist	2
	Child psychiatrist	2
Setting	Academic	12
	Non-academic	3
Gender	Female	7
	Male	8

3. Results

We found that our respondents believed that the heterogeneity of the autism phenotype affects the ethics of research on several levels. It affects issues regarding who to include in research on autism genes, regarding what the aim is of such studies, and how the research is done. An overview of the results is given in Table 2.

3.1. The genetics of dysfunctioning: who is a research subject?

Autism is a diagnosis based on behavioural checklists. Researchers investigating autism genes hence have to rely first and foremost on such diagnosis to decide who is a research subject to be included in their study. Participants mentioned the behavioural categories as it is described in the DSM-V to define what they thought was the core of autism, but several also mentioned each autistic individual is different. Respondents stressed that a diagnosis of autism should not be done solely on the basis of the behaviour as such, but that the individual should be sufficiently dysfunctioning to warrant a diagnosis. In this respect, one respondent was worried that the aspect of dysfunctioning was not always taken into account: “Diagnostics should always depart from dysfunctioning, if there is no dysfunctioning, it should not happen. But it *does* happen” (psychologist, #3). So this respondent was worried that in some cases individuals were diagnosed as autistic on the basis of certain behavioural traits without experiencing problems with functioning in everyday life. For her, good clinical care implies assisting people with their problems, not labelling certain character traits. Another respondent, however, was worried that by stressing too much the dysfunctioning component, a child with certain developmental problems would be too easily diagnosed with autism, as she states:

> *If a child is dysfunctioning, it is often in the areas of social abilities, communication, imagination … there are not many other aspects in which a child can malfunction. So I think we too often or too quick … each child that malfunctions almost has autism. And that certainly is an evolution. (educational specialist, #4)*