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Shooting a moving target : researching autism genes : an interview study with professionals

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1 Shooting a moving target. Researching
2 autism genes: an interview study with
3 professionals.

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25

1 **Abstract**

2 **Background**

3 Given the wide variety of the phenotype, the uncertain genetic origins and the discussions
4 surrounding the status of autism itself, genetic research on autism genes generates specific ethical
5 questions that are not completely analogous to the ethical issues of genetic research in general.

6 **Method**

7 In order to map ethical issues surrounding research on autism genes, as experienced by professionals
8 in the field of autism, we interviewed 15 Belgian professionals.

9 **Results**

10 We found that respondents believed that the heterogeneity of the autism phenotype affects the
11 ethics of research on several levels. It affects issues regarding who to include in research on autism
12 genes, regarding what the aim is of such studies, and how the research is done.

13 **Conclusions**

14 Although genetic research on autism genes is proliferating, a systematic ethical reflection and
15 protocol is missing. With this study we have shown that autism professionals in Belgium express both
16 skepticism and hope with regard to genetic research and raise important points with regard to the
17 effect that the complexity of autism has on research aims and methodology.

18 **Keywords**

19 Autism research, genetics of autism, research ethics, interviews

20

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1

2 Introduction

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

15 Although the identification of an individual as autistic is done through behavioural observation and
16 checklists, much research has been done to find a biological explanation for the phenotype. Although
17 originally, autism was thought to be a psychogenic disorder and caused by certain parental behaviour
18 (the ‘refrigerator mother’ theory), there is now consensus that it has a biological cause, a finding that
19 has been welcomed by many parents. Research into the nature and aetiology of autism includes
20 research into the brain function and the structure of the brain of autistic individuals through
21 neuroimaging (Dichter, 2012; Pelphrey et al., 2011). But also the genetic basis of these neurological
22 differences have been widely studied. That autism has at least partly a genetic basis was already
23 known through concordance studies in monozygotic twins, through the fact that it seems heritable
24 and through the fact that it is a symptom of some known genetic and chromosomal disorders such as
25 Fragile-X, tuberous sclerosis and neurofibromatosis type-I. But only in 5-10% of the individuals
26 presenting themselves their autism will have a clear monogenic cause (Jeste and Geschwind, 2014).
27 In 20-30% of these individuals, known genetic risk variants can be found, which include copy number
28 variants (CNVs) and sequence variants (Chung et al., 2014; Ronemus et al., 2014; Sebat et al., 2007),
29 representing a spectrum of *de novo* and inherited variants with different levels of penetrance. Hence,
30 in many cases, autism is considered to be multifactorial, and other factors besides the mere genetic
31 variation must play a role. Factors currently being studied include epigenetic modifications, perinatal
32 problems (Kolevzon A et al., 2007), intra-uterine testosterone levels (Auyeung et al., 2009; Baron-
33 Cohen et al., 2015), immune dysfunction (Goines and Van de Water, 2010), pesticides (Roberts et al.,
34 2007), in utero exposure to medication (Bromley et al., 2013; Rai et al., 2013), alterations to the gut
35 microbiome (Mayer et al., 2014), and many others as reviewed by Herbert (Herbert, 2010).

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

44 Given the wide variety of the phenotype, the uncertain genetic origins and the discussions
45 surrounding the status of autism itself, we and others have argued that genetic research on autism

1 genes generates specific ethical questions that are not completely analogous to the ethical issues of
2 genetic research in general (Walsh et al., 2011). In order to map these ethical issues as experienced
3 by professionals in the field of autism, we interviewed 15 Belgian professionals working in the field of
4 autism. In this paper we present the findings of this interview study.

5 **Methods**

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

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

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

33 The study was reviewed and approved by the KU Leuven Social and Societal Ethics Committee (file
34 number G-2014 12 112)

35 **Results**

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

40 **The genetics of dysfunctioning: who is a research subject?**

41 Autism is a diagnosis based on behavioural checklists. Researchers investigating autism genes hence
42 have to rely first and foremost on such diagnosis to decide who is a research subject to be included in
43 their study. Participants mentioned the behavioural categories as it is described in the DSM-V to

1 define what they thought was the core of autism, but several also mentioned each autistic individual
2 is different. Respondents stressed that a diagnosis of autism should not be done solely on the basis
3 of the behaviour as such, but that the individual should be sufficiently dysfunctioning to warrant a
4 diagnosis. In this respect, one respondent was worried that the aspect of dysfunctioning was not
5 always taken into account: “Diagnostics should always depart from dysfunctioning, if there is no
6 dysfunctioning, it should not happen. But it *does* happen” (psychologist, #3). So this respondent was
7 worried that in some cases individuals were labeled autistic on the basis of certain behavioral traits
8 without experiencing problems functioning in everyday life. For her, good clinical care implies
9 assisting people with their problems, not labelling certain character traits. Another respondent,
10 however, was worried that by stressing too much the dysfunctioning component, a child with certain
11 developmental problems would be too easily diagnosed with autism, as she states:

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

16 So in this quote the respondent worries that the diagnosis of autism is nowadays given too quickly
17 based solely on the basis of dysfunctioning, and she states that this is a recent evolution. Other
18 respondents also worried about the evolution or even inflation of the term autism, and several linked
19 this to the access the diagnosis would give the child and her parents to support services.

20 The causes of dysfunctioning are in itself complex, and whether an individual with autistic traits will
21 dysfunction and warrant a diagnosis will depend on internal as well as external causes. All
22 respondents mentioned intelligence as a protecting factor and saw a clear difference between the
23 person with autism and mental retardation and the person with average or high intelligence. In the
24 following quote, one respondent expresses the view that these phenotypes may be so different as to
25 warrant a different name:

26 *In fact we should have different names for it. Because a child flapping her hands in*
27 *a corner or a very autistic adults have the same spectrum of disorders as the civil*
28 *engineer with some social issues.(...) Of course it is a bit an expression of the same*
29 *thing, the person with mental retardation will retire under the table if she hears*
30 *loud noises and the highly able person will be extremely annoyed if someone is*
31 *nibbling in the sofa besides her. But this person will become angry or just step*
32 *away, not start flapping. But it is in both cases the hyperacousis that provokes it.*
33 *(child neurologist, #1)*

34 So in this quote the respondent acknowledges that two completely different levels of reacting to
35 what may be the same underlying condition (being hypersensitive to noises) may be in one case
36 more severely dysfunctioning than in the other one. The trope of the engineer, computer
37 programmer or university professor was used by her and by several others to illustrate how
38 intelligence may protect against some of the disabling features of autism, and may even yield
39 advantages for certain types of careers.

40 The fact that dysfunctioning is an integral part of the diagnostic process for autism, and hence
41 research subjects will be selected not only on behavioral characteristics assessed by checklists is not
42 necessarily problematic for genetic research: the level of dysfunctioning may depend on internal
43 coping strategies related to intelligence or severity that may in itself have a genetic basis. However,
44 dysfunctioning is not only a matter of having personal coping strategies (which may very well be

1 defined by personal or genetics), but also of societal factors, as several of the respondents argue. The
2 following respondent stressed that fact as well:

3 *I believe you should only call it autism if it leads to problems in functioning in*
4 *everyday life in our current society, but then you automatically bump into societal*
5 *aspects. Our society of today is a different one than that one of twenty years ago.*
6 *We expect more flexibility and openness for new experiences, which means that*
7 *people with a certain constitution will malfunction quicker and get the label of*
8 *autism quicker. (educational specialist, #2)*

9 If concepts of what is autism are fluid, and if the fact whether people would get a diagnosis or not is
10 dependent on their societal context, this may create a bias in which research subjects are chosen to
11 contribute to genetic research and may hamper the extent to which meaningful results can be
12 obtained. One of the respondents, a genetic counsellor, was very adamant and believed that the
13 proliferation of autism diagnoses would interfere with fundamental research:

14 *It is now in fashion to have autism without mental retardation. I have serious*
15 *ethical concerns, how a diagnosis is used to get certain services. While at the*
16 *same time it disturbs fundamental research. (clinical geneticist, #1)*

17 In this quote, the discrepancy between the field of clinical care and fundamental research is
18 apparent. A diagnosis of autism may be warranted in the context of clinical care, if such diagnosis
19 opens up the way to support for families and children with certain challenges, and the fact that
20 assessing dysfunctioning is an integral part of the diagnosis accommodates for exactly that. However,
21 since this may lead to the fact that a diverse set of individuals carry the same diagnosis without
22 potentially the same underlying biology, this impedes the generation of valid results. This respondent
23 continued by stating that “we have to describe the phenotype with more specifics and details: for
24 example this is someone who scores low on theory of mind. OK, then we investigate what is the
25 genetics of having a deficient theory of mind.” The need for a good phenotypical description of
26 research subjects, beyond a mere diagnostic label, was also mentioned by other respondents,
27 otherwise genetic research in the field of autism would, as one respondent stated, remain “shooting
28 a moving target” (child psychiatrist, #1).

29 **Complex aims**

30 The fact that autism is a complex phenomenon is reflected in the uncertainties our respondents
31 expressed when queried what the aim is of fundamental genetic research on autism genes. One of
32 the aims that respondents named was the possibility that a genetic marker or biomarker may aid
33 diagnosis and remove some of the ambiguities that are inherently linked with a diagnosis based on
34 behavioural observations:

35 *I believe autism is a difficult case, they say you have it or you don't have it. But at*
36 *the moment it is still a diagnosis based on behaviour. I will be very happy when*
37 *the doctors have a blood test, and we can say, OK this is someone with autism.*
38 *(educational specialist, #1)*

39 This person, an educational specialist, states that she struggles with the lack of objectivity associated
40 with a behavioral diagnosis and hopes that finding a biological substrate will resolve some of the
41 ambiguity and complexity of how to decide who is autistic and who is not. Along the same line,
42 respondents expressed hope that genetic findings will contribute to understanding the development
43 of autism and how certain genetic variations cause specific developments of the central nervous

1 system. Hence, this would contribute to more accurate predictions of how children with a specific
2 genetic 'subtype' of autism would develop and what the prognosis is, as this is one of the questions
3 parents have when their child is first diagnosed. One respondent mentioned the fact that good
4 genetic knowledge may enable earlier detection of autism than possible with current diagnostic
5 tools:

6 *One clinical application is early intervention, we can now only reliably diagnose*
7 *autism around the age of three, before that age you can find some clues but it*
8 *remains difficult, whereas there are more and more indications that intervening*
9 *early helps. (educational specialist, #2)*

10 This respondent believes that it would be beneficial if a genetic test could offer a reliable way of
11 diagnosing autism earlier on, in order to provide adequate early intervention. Another respondent, a
12 child psychiatrist (#1), first agreed with this stance but then changed her mind, stating that "now that
13 I am telling you this I am starting to have doubts, maybe we want to know too much and we should
14 just have to accept some things", expressing her opinion that early intervention and presymptomatic
15 knowledge of a propensity to develop autism may not be straightforwardly positive.

16 A substantial subset of respondents mentioned the possibility to create, based on autism genetics,
17 better pharmaceuticals, as for the moment there is no pharmaceutical treatment of autism, and a
18 better understanding of biological pathways may enable exactly that. But one respondent had
19 doubts regarding the desirability of medication for autism:

20 *I am very ambiguous about this one, I am thinking, are we then going to develop*
21 *drugs to make them all normal? I found that very difficult, because I do not believe*
22 *in medication for that, especially not in the developmental disorders. (educational*
23 *specialist, #4)*

24 This respondent, who in other parts of the interview also stated that she believed that autism also
25 has positive sides, struggles with the concept of 'normal' as a baseline. She considers autism not
26 necessarily a disease to be cured and is hence sceptical whether developing cures for autism is a
27 desirable aim. Hence, this quote is another example of how the complexity of autism, in this case its
28 status as a disease or a mere difference, pervades discussions on the aim of research.

29 The prevention of autism through prenatal screening and the possibility to inform parents about
30 further reproductive options was named as a real, albeit not a very articulated aim of genetic
31 research. One responded explicitly called this underlying aim as "very ethically sensitive". Another
32 respondent mentioned deep dilemmas, especially for the group without mental retardation, which,
33 according to her, was the group they had been teaching to accept the diagnosis as a difference:

34 *We are giving an ambiguous message. On the one hand we say that it is not bad*
35 *to have it, on the other hand we say it is better to prevent it. Especially for the*
36 *people with ASD I believe that it is a kind of ethical dilemma, is it bad to have it or*
37 *not. I doubt that geneticists ever wonder about this, but they should.*
38 *(psychologist, #3)*

39 This respondent believes that genetics should reflect more on the message they convey to the group
40 of people without intellectual disability and states that one cannot at the same time perform
41 research with as an aim to prevent something and insist that this condition is a valuable difference
42 with positive aspects.

1 Some respondents were sceptical that genetics could really contribute something substantial to
2 understanding autism or for the benefit of people with autism. One respondent, a child psychiatrist
3 (#2), thought research money on autism genetics “well spent, not to discover new genes but as
4 tuition to understand its complexity”. Another respondent, a psychologist (#2), stated that “proteins
5 do not think in DSM terms”, and that autism is a “construct to understand a compound of
6 behaviours”. Whether genetic research would ever contribute something substantial to the quality of
7 existence of those with autism was considered highly doubtful.

8 **A different type of mind: the ethics of doing genetic autism research**

9 When queried what they would describe as the essence of being autistic, respondents often
10 mentioned the fact that autistic individuals have another way of thinking, another way of
11 information processing, interpreting reality and different processing of sensory input. One
12 respondent states that:

13 *Thinking in context, the lack thereof, and related language pragmatics and literal*
14 *interpretations, that you do not see with those children who are extremely*
15 *demanding and unruly but who do not have autism. (child neurologist, #1)*

16 Hence, she explicitly names how autistic individuals process information as an important
17 characteristic that sets them apart from other developmental disorders. This has important
18 ramifications for how research is done with these subjects. Respondents named informed consent
19 forms and information brochures as specific items which may need to be modified in order to
20 accommodate for that difference. For example, the following respondent mentions that researchers,
21 when giving information or writing informed consent forms should need to take into account the fact
22 that many autistic individuals, even when they have average or above average intelligence, may not
23 be able to foresee the implications of research beyond what is written literally in the text:

24 *There is the imaginative power of the child, let's say he is sufficiently intelligent or*
25 *literate to read the text, he will never be able to break loose from the text because*
26 *of his autism, whereas a 17 year old without autism may have this imaginative*
27 *power to ask himself the question, what will they do with this and what will it*
28 *mean for my brother who is ill and such things. (child psychiatrist, #2).*

29 In the same line, another respondent, an educational professional (#5), mentioned the fact that
30 people with autism often use difficult words and complex terminology, but that this does not
31 automatically imply that they thoroughly understand what is meant, and researchers should be
32 aware of that. Also, respondents mentioned the fact that parents of autistic research participants,
33 although they may not have an official diagnosis, may share characteristics of their diagnosed
34 offspring, and may have the same different type of information processing. Hence, informed consent
35 and information that is tailored for autistic research participants who can give informed consent for
36 themselves, may also be adequate for parents giving consent for their incompetent children. Hence,
37 for example the use of visualization to explain certain aspects for research may be a more
38 appropriate means to inform parents as well.

39 One of the ethical principles of non-therapeutic research on children or incompetent individuals,
40 such as those with mental retardation, is that this research should be minimal risk and should not
41 harm research subjects. Although not all respondents agreed with the statement that the
42 invasiveness of procedures such as blood draws was more harmful when research participants were
43 autistic children, especially those respondents who were actively involved in the care of children with
44 severe mental retardations were worried about this. One respondent called venipunctures to draw

1 blood of an autistic child often “a bloody fight” (educational professional, #3) and another stated
2 that:

3 *I heard stories that they had to pin down the child with three people to draw*
4 *blood, that cannot be but traumatic. It is also very difficult to explain to them*
5 *what is going to happen, strange environment, doctors in white coats who come*
6 *with all kinds of strange materials, they do not know what is happening to them, it*
7 *is very difficult to explain (educational professional, #5)*

8 Hence, the lack of understanding of the severely disabled autistic individual and the lack of a
9 language or means of communication to explain to them what was going to happen was seen by this
10 respondent as factors that increase the harm done to autistic individuals during procedures that may
11 be acceptable with research subjects without autism. Respondents considered the hypersensitivity to
12 sensory input as the cause of problems during research. For example, one respondent mentioned
13 noisy brain scans as being very difficult for these children, because probes make much noise. Another
14 stressed that mouth swabs, which are often used when research subjects object to blood draws, may
15 not be a solution for autistic children, because many of these children have a special sensitivity
16 around the area of the mouth. Therefore, a subset of respondents mentioned the need for research
17 protocols and forms specifically for autism research, and thought that novice autism researchers
18 should be trained on the specifics of working with these subjects.

19 Discussion

20 Bioethicists have discussed the ethics of genetic research to great length. They have discussed the
21 need to protect data from third party access, such third parties including insurance companies, the
22 need for informed consent and issues related to the return of research results or incidental findings.
23 If research is done on DNA from minors, extra ethical caution is needed: principles of nontherapeutic
24 research on children include the subsidiarity principle (it can only be done with children if it cannot
25 be done on adults), the requirement that such research does not pose more than minimal harm or
26 burden to the child and that children are allowed to information on their level and should be given
27 the opportunity to assent or dissent to research participation (Hens et al., 2011).

28 Research on autism genes is already done on a large scale. As the majority of persons diagnosed with
29 autism are children, DNA used for fundamental research will most of the time come from children
30 with such diagnosis. Our respondents agreed that although all diagnosis are or should be based on
31 DSM criteria, the phenotype varies widely in expression and in severity, to the extent that some of
32 them questioned whether there is really *one* autism. In this respect, Walsh et al have also questioned
33 whether there may be many autisms, possibly with different biological origins (Walsh et al., 2011).
34 Respondents stressed that in order to warrant an autism diagnosis, the autistic traits must lead to
35 dysfunctioning. And although dysfunctioning may be dependent on factors that are intrinsic to the
36 individual, such as the level of hyperacusis or the IQ, it is also dependent on social environment and
37 acceptance. For example, respondents often referred to the ‘civil engineer’ or ‘academic professor’
38 as a person who may have autistic traits, but may also have, because of these traits, advantages
39 which allow them to function on a professional level. Along the same lines, Norbury and Spark have
40 argued that the point at which individual differences in behavior constitute abnormality, and warrant
41 a diagnosis of autism, are largely arbitrary decisions and can be strongly influenced by cultural values
42 and expectations (Norbury and Sparks, 2013). Hence, whether a person with autism traits would
43 benefit from an autism diagnosis, and where to draw the line between autism as a character trait and
44 autism as a disorder is often uncertain. In a historical analysis on the concept of autism, Verhoeff has
45 demonstrated that what is considered essential in autism has undergone major changes that are not

1 adequately described as mere broadening of the concept or inclusion of milder forms (Verhoeff,
2 2013). As the rationale behind clinical decisions to diagnose someone with autism is to help the
3 specific individual in specific circumstances, and to offer prospects and a course of action, the fact
4 that a diagnosis is partly based on factors that are not intrinsic to the individual may be acceptable.
5 However, if research participants' DNA is included in studies based on an autism diagnosis alone this
6 may be problematic, as it may skew research results. Respondents have argued that research in
7 autism genes without proper phenotypical description that includes other variables such as IQ etc
8 cannot yield satisfactory results. It also has ethical consequences. Some authors and autistic
9 individuals have argued that at least in certain cases, ASD is not pathological, and there are some
10 advantages to having autism (Jaarsma and Welin, 2011), a thought that was confirmed by some of
11 our respondents. If in certain cases autism is to be considered a character trait that is only
12 dysfunctioning because of lack of support or societal acceptance, this has ethical repercussions.
13 Should children, who in principle cannot consent to research due to their age, diagnosed with
14 'milder' forms of autism or Asperger's syndrome, be enrolled in research investigating what is in their
15 case essentially a character trait? Is research in this area warranted at all?

16 This question is exacerbated by the uncertainties regarding the aim of genetic research for autism
17 genes. Respondents expressed uncertainty as to whether this research will ever yield benefit to the
18 vast majority of autistic children themselves, a principle that is often considered a prerequisite for
19 non-therapeutic paediatric research. Possible benefits of such research named by the respondents
20 included the possibility that genes would predict the development of 'true' autism and allow for a
21 more solid diagnosis than one merely based on observational analysis. In this respect, Walsh et al
22 have stated that genetic research findings may also help delineate disease versus non disease status
23 of autism traits (Walsh et al., 2011). However, as dysfunctioning is an essential prerequisite of
24 receiving an autism diagnosis, it is uncertain whether genetics can ever predict dysfunctioning. Other
25 aims that were named were a better understanding of the development of the phenotype, the
26 possibility of early and even presymptomatic treatment and the development of more targeted
27 pharmacogenics, aims that have been discussed in the ethics literature on autism genetics (Pellicano
28 and Stears, 2011; Marchant and Robert, 2008; Gershon and Alliey-Rodriguez, 2013). However, in
29 both the context of early intervention and pharmaceutical intervention, some respondents
30 questioned the extent of this endeavor, as they doubted whether the elimination of autism in an
31 individual was realistic or even desirable. In this respect, Walsh et al have stated that research should
32 focus on those forms of prevention, cure and amelioration that protect the positive aspects of autism
33 while working against the negative, and not make people fit in more with specific cultural norms
34 (Walsh et al., 2011). In an empirical study of opinions of parents of children with autism and people
35 with a diagnosis of autism in the UK on research goals, Pellicano et al have found that people
36 expressed a preference for research that focusses on helping people live with autism (Pellicano et al.,
37 2014). Verhoeff has questioned the current focus of autism research to discover neurobiological
38 causes altogether and instead has argued that research should focus more on notions and
39 experiences of impairment, disability, suffering and distress, and on how these experiences relate to
40 particular (autistic) behaviors in particular circumstances (Verhoeff, 2015). Whether and how the
41 search for autism genes can contribute to this aim remains to be seen.

42
43 Although respondents differed in what they thought was the 'essence' of autism, and many referred
44 to the DSM criteria to define that essence, all stated that autistic individuals process information
45 differently. This has repercussions for how genetic research on autism genes should be done,
46 ethically, but also applies to other types of autism research. The fact that autistic individuals may
47 have a more literal way of interpreting information, and in some cases respond better to visual
48 representations should be taken into account when information sheets and informed consent forms
49 are designed, and 'anti-friendly' leaflets should be available for teenagers and possibly also their

1 parents, who may share the same information processing characteristics. With regard to small
2 children, who will often also suffer from mental retardation, blood draws and even mouth swabs
3 may be extremely intrusive and traumatizing, and in these children, the threshold for minimal risk or
4 minimal burden may be different than for the general population of children. Hence, respondents
5 have argued that researchers should be trained specifically to deal with autistic children, a point
6 stressed by Tabor et al as well (Tabor et al., 2011). None of the respondents explicitly named the
7 possibility of enrolling autistic individuals as part of research groups, but as the ‘academic colleague
8 with autistic traits’ was used as an example by several of the respondents, this possibility seems real.

9 Our study has several limitations. We only interviewed 15 professionals from Belgium, which may
10 hamper the generalizability of the results. In order to offer a more complete picture, also the views
11 of other stakeholders, such as parents of autistic children and especially people with a diagnosis of
12 autism should be investigated. Still we hope to have demonstrated that although genetic research on
13 autism genes is proliferating, a systematic ethical reflection and protocol is missing. Our respondents
14 have expressed both skepticism and hope with regard to genetic research and have raised valuable
15 points with regard to the effect that the complexity of ASD has on research aims and methodology.
16 Relying on general ethical principles for fundamental genetic research or fundamental genetic
17 research on minors is insufficient, and research groups and consortia should consider the points
18 specific to autism raised in this study, besides more general ethical issues such as privacy and
19 confidentiality. Moreover, consideration of these points should preferably be done in communication
20 with stakeholders such as representatives from the autism community itself.

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1 **Table 1: Information about the interviewees**

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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

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2 **Table 2: Overview of themes**

<i>Who is a research subject?</i>	Clinical diagnosis and research participation -dysfunctioning + DSM criteria Behavioral diagnosis -uncertainty of what is real autism Severity of dysfunctioning -linked to characteristics of individual and environment Trope of academics, IT professionals, engineers
<i>Complex aims of genetic research</i>	Removing ambiguity of behavioural diagnosis Understanding the development of autism Pros and cons of early intervention and detection Pros and cons of medication
<i>Ethics of doing genetic research</i>	Autism as a different way of processing information -Perhaps also the parents -Affects how informed consent is written -Concepts of harm/risk may be different -Need for training for researchers

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