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Lay and scientific categorization of New Breeding Techniques: Implications for food policy and GMO legislation

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Abstract:

The rapid development of new genetic breeding techniques (NBTs) is accompanied by a polarized debate around their risks. Research on the public perception of these techniques lags behind scientific developments. This study tests a method for surfacing lay people's perceptions and attitudes about different genetic techniques. The objectives are to enable laypeople to understand the key principles of NBTs and to permit a comparison of their modes of classification with those of scientific experts. The combined method of a free sorting task and focus groups showed that the participants distinguished the techniques that did not induce any change in DNA sequence, and applied two different logics to classify the other breeding techniques: a *Cartesian logic* and a *naturalistic logic* with a distinct set of values. The lay categorization differed substantially from current scientific categorizations of genetic breeding techniques. These findings have implications for food innovation policy and GMO legislation.

Keywords: GMO, New Breeding Techniques, lay categorization, public understanding, GMO regulation, food policy

1. Introduction

New Breeding Techniques (NBTs) promise endless applications in medicine, agriculture, aquaculture and food. The recent development of genome editing techniques, like the CRISPR-Cas⁹¹ (Jinek et al., 2012) that enables a precise cut on a selected locus of the DNA of plants or animals, illustrates the significant progress in BTs. The key advantages of these NBTs over the earlier random BTs are higher speed and very precise plant breeding, which make it possible to target a predefined region of DNA and to minimize hazards associated with the disruption of genes and/or regulatory elements in the recipient genome (EFSA, 2012, p. 1). Most of these NBTs are under development for further commercial breeding programs although two critical points have not yet been solved (Lusser et al., 2012): firstly, technical difficulties in DNA tracking impede the detection of products derived from most of those techniques; secondly, international differences in regulations create asynchrony in approvals of new crops, thereby increasing the risk of trading unauthorized genetically engineered plants and foods.

A recent decision of the European Court of Justice (ECJ) (July 25, 2018), whereby the products resulting from genome editing techniques will be treated just as strictly as genetically modified organisms, is currently blocking their roll-out across the European Union. Numerous challenges to this decision claim that European crops will be at a competitive disadvantage vis à vis imported crops issued from undetectable NBTs. Different stakeholder groups - e.g., companies in the seed industry, representatives of farmers' interests or of organic producers, and non-governmental associations - tend to bring their own classification criteria to challenge the inclusion or exclusion of certain products from the scope of legislation. Thus, understanding how different actors classify the various kinds of NBTs is an urgent matter. Currently experts treat the classification of the most recent BTs as Genetically Modified Organisms (GMOs) or non-GMOs as a differentiation that can be based on objective comparison criteria with conventional plants. This question has not yet surfaced for the public. However, past experience

with genetically engineered food - around which initial attitudes were highly polarized and difficult to change (Malyska et al., 2016) - suggests that the way consumers first perceive NBTs and express concern for environmental and health risk is extremely significant.

It is for this reason that scholars in the field of the public understanding of risk (Renn, 1998; Stilgoe et al., 2014) have recommended that ethical issues and applications should be discussed upstream to the research, before dissemination in the public arena². Success depends on the possibility for consumers to engage in an informed dialogue and for scientists to be aware of the symbolical dimensions underlying the lay conceptions of genetic science. The gap between experts and non-experts regarding NBTs could be reduced by moving towards more effective science communication efforts (Simis et al., 2016). The purpose of this paper is to present the results of testing a method to reveal the perceptions of laypeople and to highlight convergences/divergences between lay and expert categorization of a wide range of NBTs. Policy makers could use the outcome of this research to anticipate crises or to avoid the rejection of the very principle of NBTs by involving citizens early in the process of deliberation.

After the literature review on the issues raised by the most recent BTs, we address the methodological challenges for analyzing public categorization of NBTs. The experimental procedure that was tested in this study is then described. Results and the discussion section consider the differences between lay and scientific categorizations. The concluding section addresses the implications for achieving a better alignment of food innovation policy and GMO legislation with consumers' perceptions.

2. Societal and legislative challenges around NBTs

Plant genome editing methods are probably the most promising techniques making precise changes possible in DNA without addition in the genome of genetic material from a foreign organism. Their application scope covers the improvement of agronomic traits, the rewilding or "reverse breeding" (see Palmgren et al., 2015; Andersen et al., 2015), the production of greater diversity by accelerating natural processes and the development of healthier food (For a complete review of NBTs' applications see Schaart et al., 2016). A development that has triggered controversy is a fungus whose browning process was reduced with NBTs. It was exempted from the US regulation in 2016³, and allowed for cultivation and sales without further oversight but it did not find any market. Public mistrust was also expressed in 2011 by French citizens who destroyed an experimental field of sunflowers that were created with NBTs to be resistant to one herbicide. Other products are under development whose commercial development could face similar societal and legislative challenges.

Terminological issues of GMOs and NBTs

In many countries, the generic term of "GMO" is still widely used by consumers protesting against the technology, even though they do not know what it means exactly and do not distinguish between all development stages (Popek and Halagarda, 2017). The first generation of GMOs was based on random BTs like conventional trans/cisgenesis and mutagenesis. The NBTs also called 'genome editing techniques' use new tools (Site Directed Nucleases (SDN)) allowing a tracking and precise cut of targeted DNA sequences.

Knowledge about new BTs has rarely been shared with the public. The underlying factors shaping the science agenda tend to be closed to public scrutiny, partly because of lack of basic knowledge required for public engagement (Mayer, 2003). As a result, the public remain rather unaware of the increasing research in DNA modification (Lucht, 2015; Malyska et al., 2016). As Hagemann and Scholderer (2009: 1052) explained a decade ago, the risk is an 'overgeneralization of the negative as well as the positive specificities of GM foods' to all novel foods in development.

Food policies and NBTs: the European Court of Justice decision (July 25, 2018)

Integrating the NBTs and questioning their actual governance have become a challenge for European legislators responsible for re-assessment of the GMOs regulation and the Novel Food regulation. Since 2003, GM foods have been excluded from the scope of the European legislation on Novel Food (Initial regulation 258/97/CE of January 25, 1997 modified by regulation 2015/2283/UE of November 25, 2015) and are under a special regulation (Regulations 1829/2003/CE and 1830/2003/CE). According to these regulations, the methods/process used, rather than the end results, define whether or not an organism must be considered as genetically modified. The recent ECJ decision of July 25, 2018, specifies that organisms obtained by NBTs are subject to the obligations laid down by the GMO Directive 2001/18/CE, in so far as the techniques alter the genetic material in 'a way that does not occur naturally'. This decision is challenged by the biotech industry, which is demanding a fresh review of the status of genome editing techniques in order to reduce confusion in commercial exchange, and pointing out that imported products can have undetectable DNA changes. Several NGOs and representatives of the organic food and farming sector have expressed concern about the risk to environment and public health of deregulating NBTs.

Regulators, advisory bodies and scholars who address the issue of the legal classification of these NBTs and of the resulting products face the significant challenge of having to take into account the diversity and increasing complexity of DNA-related research (Lusser et al., 2012). In France, a report by the Higher Council for Biotechnology (HCB) provides a synthesis of the debate between key actors (seed companies, non-governmental organizations, public and professional associations) and their expectations regarding the classification of a wide range of genetic engineering techniques (HCB, 2016). The HCB report (2016) proposed a general categorization of a broad range of plant BTs, old and recent (Figure 1). Three main scientific criteria were suggested: (1) the site targeting--or not, (2) the insertion of DNA sequences--or not, (3) the random change (mutation) of DNA sequences--or not.

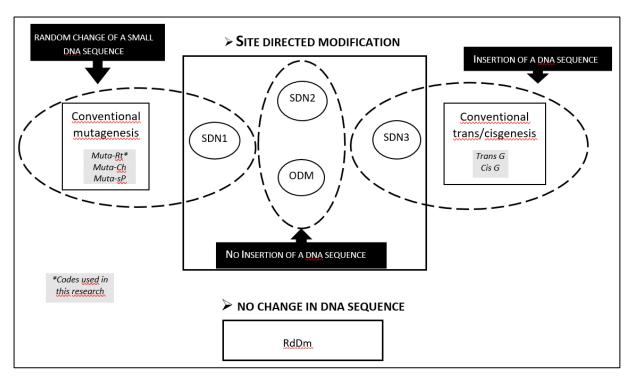


Figure 1. Scientific categorization of plant breeding techniques (adapted from HCB (2016), p.13)

Note: SDN1, SDN2, SDN3 techniques are recent genome editing techniques using a tracking and precise cut of targeted DNA sequence where the modification is expected. ODM technique is directed-mutagenesis technique. RdDm technique is impacting the 'reading' of DNA without any oligonucleotide change.

The current debate outlined in the French HCB report focuses on the scientific criteria that permit a subtle comparison of the effects of BTs on plant or animal genetics with DNA changes that could occur spontaneously in the natural environment (spontaneous mutagenesis). The status of several new, targeted mutagenesis techniques - allowing a mutation of some nucleotides on a targeted site or through temporary change of DNA reading - is one of the critical points of the debate while random mutagenesis, widely used since the 1930s to produce thousands of plant genotypes, is not under the scope of the European GMO regulation (Annex I B of Directive 2001/18/EC). According to the ECJ decision of July 25, 2018, organisms obtained by those new, targeted mutagenesis techniques are now subject to the obligations laid down by the GMO directive, while the oldest ones are still not classified as GMOs. The great heterogeneity of mutagenesis techniques illustrates the difficulty legislators face in dealing with the growing diversity of NBTs.

The scientific categorization of NBTs by experts and stakeholders from public funding agencies is an essential resource for European and French legislators trying to understand the complexity of the techniques (Menozzi et al., 2017). However, Renn (1998) pointed out, the social perception of new techniques is also a crucial factor in their acceptance and use.

The determinant role of public acceptance of genetically engineered food

Consumers may not perceive mutations resulting from human selection for commercial applications in the same way as "successful" mutations maintained in the natural environment, so public opinion also needs to be taken into consideration (Pollock, 2016). Studies have shown that consumers are more likely to accept food produced by cisgenesis than transgenesis because the former does not use foreign genes (Colson et al., 2011; Lusk and Rozan, 2006; Gaskell et al., 2010; Lusk et al., 2018). However, some authors argue that cisgenesis is still perceived as unnatural (Mielby et al., 2013) and that the full equivalence of plants produced by cisgenesis with natural plants is not exact because they carry a combination of sequences not available in nature (Pacifico and Paris, 2016). There is no consensus on the definition of "natural" in this area. However most lay people will probably go on using this term as a reference for building their opinion about NBTs.

A second angle to consider for public acceptance of GM food relates to the range of possible applications. GM foods were initially widely perceived as being unhealthy and not trustworthy (Miles and Frewer, 2001), but a meta-analysis showed an increase of both risk and benefit perceptions over time, and greater acceptance for plant-related applications than for animal-related ones. Moreover, there are intercultural differences: risk perceptions are greater in Europe than in North America and Asia and the reverse is observed for benefit perceptions (Frewer et al., 2013).

However, so far, there is no research examining the lay classification of the main BTs, covering the oldest/recent ones. This paper addresses this gap by testing a method to make the key principles of these complicated NBTs understandable to lay people, and then to reveal consumer perceptions of these techniques.

The need for new approaches to understand public perceptions of NBTs

Researchers who have addressed the issue of public perceptions have emphasized the importance of several factors: the perception of risks associated with BTs that cannot be fully compensated with any benefits (Grunert et al., 2001), the 'symbolical risk' (the break with natural process) that remains irreducible (Debucquet, 2011), and lastly, beyond the 'deficit model' opposing lay and expert knowledge (Simis et al., 2016), the huge role of values, moral judgments, and cultural influences (Irwin and Wynne, 2003). However, different paradigms and methods in order to generate new knowledge in this area can be explored.

There are several methods for eliciting the opinion of lay people on a topic. Questionnaires, interviews and focus groups are commonly used and rely on pre-determined questions to elicit the respondents' views of the issues at hand. However, the formulation can produce a somewhat biased effect, i.e. induce non spontaneous ideas/responses from the interviewee. Unlike questionnaires with closed questions, interviews and focus groups make it possible to explore a subject more broadly. However all these methods do not allow a clear distinction between implicit and explicit attitudes. This objection is, however, mitigated by Greenwald (2020), whose review indicates that in many cases positive correlations exist between implicit and explicit measures. Some authors have proposed methods such as the Implicit Association Test (IAT), based on categorization tasks, to measure the implicit relations between concepts and consumer attitudes (Greenwald et al. 1998). However, this method leads participants to use pre-defined categories and does not allow them to define their own category structure. Thus, a key methodological concern of our study is to find a method that does not guide the participants according to a pre-established thought pattern and enables them to define their own choices and ranking criteria. The free sorting test removes the pitfalls inherent in other methods by giving a panel of citizens or consumers complete freedom in the choice of categorization criteria. Over the last fifteen years, this method has been undergoing a revival in sensory evaluations (Faye et al., 2004; Varela and Ares, 2012). The free sorting technique is a rapid process for bringing to light the features that the consumer considers important. The ease of comprehension and use has made this technique suitable for different kinds of populations, such as elderly people (Cliceri et al., 2017) or young children (Varela & Savador, 2014).

This kind of approach, developed early in cognitive and social psychology (Rosenberg and Olshan, 1970), has been applied to elicit consumer perceptions in a variety of ways, such as classifying food (by odor and taste), cloth (by touch), food images and concepts (Nguyen and Murphy, 2003). It therefore seems pertinent to experiment with this method to enable people to use their own criteria for spontaneous categorization of a set of objects relating to non-traditional BTs in order to reveal their perceptions while reducing external influences as far as possible.

3. Experimental procedure

For this study an experimental procedure was developed, using a combination of two methods: a free sorting exercise and a series of focus groups, in which French consumers were invited to participate. By starting with the free sorting exercise the participants were triggered to classify features they perceived without the drawbacks identified above. The subsequent focus group situation stimulated them to explain the thoughts that had guided their spontaneous classifications. Each step of the process is explained below.

Subject sample

Forty-five French subjects were recruited by public announcement through internet advertising. The advertisement informed potential participants that the project was about recent techniques that make it possible to select plants/micro-organisms, and that no specific scientific background was required (without excluding subjects with scientific background). In order to establish the relevance of our method it was important to test it with a diverse sample, including participants with low/medium/high educational background/ scientific knowledge. A financial incentive was offered for participating in the study (a gift certificate of \notin 40). In order to reach a wide variety of subjects, no constraints were given in terms of age, gender or professional education. The only requirement for participants was not to be an expert in BTs. The sociodemographic profiles of the volunteers showed a higher number of women (73%) and of young people (44.4 % under the age of 35). Despite the wide dissemination of the announcement, most of the participants had medium (28.9%) and high levels (62.2%) of education, and medium (21.1%) and high (65.8%) socio-economic levels. The lower proportion of participants with lower education, in spite of financial incentive, can be explained by a mechanism of selfexclusion from a meeting they perceived as dedicated to educated people (Dawson, 2018; Marris et al., 2001).

Procedure

Six sessions of free sorting exercise and subsequent focus groups were organized, with 6 to 10 people in each session (45 participants in total). An introduction explaining the aim of involving the public in questions of new genetic techniques for selecting plants and micro-organisms opened each session.

• *Free sorting:* a set of objects consisting of eleven sheets about genetic techniques was successively presented in a random order. In order to reduce the risk of bias, particular attention was paid to the formulation of the text presenting each technique: the words

used were exactly the same as those on the sheets. The participants received the following instructions:

"Please sort all eleven sheets into groups according to the similarities or differences perceived according to your own criteria. You should form at least 2 groups of sheets but no more than 10 groups."

People took the time they needed to perform the task and were then invited individually to describe, in a few words or sentences, the characteristics of each group identified. Finally, once the sorting task and verbal description had been completed, the experimenter asked the participants to indicate whether they associated positive, neutral or negative perceptions to each of the groups of sheets. The overall introduction and the free sorting phase lasted about 40 min.

• *Focus groups:* After completing the free sorting task, the participants had an in-depth discussion of subject perception of these genetic techniques, at which each person explained his/her sorting strategy. This permitted the researchers to identify key words or concepts, which were then discussed together in greater detail.

Design of the sheets on genetic techniques

Eleven technical sheets on genetic techniques were elaborated on the basis of the main broad types of NBTs (Lusser et al., 2012; HCB, 2016)⁴. Each sheet was identified simply as "Technique 1", "Technique 2", etc. (For detailed presentation, see Supplemental material A). Each code provided below was for the researchers only and in accordance with Figure 1:

- **Conventional trans/cisgenesis:** random insertion of a gene from distantly-related species (*TransG*) or from closely-related species (*CisG*).
- Conventional mutagenesis: random mutagenesis induced respectively by radiation treatment, chemical agent or selective pressure (*Muta-Rt, Muta-Ch, Muta-sP*)

- New genome editing techniques: targeted techniques using a site-directed nuclease, involving on the selected site the random mutation of one or several nucleotides (*SDN1*), the controlled mutation of a single nucleotide (*SDN2*) and lastly involving the insertion of a gene from distantly-related species (*SDN3-Trans*) or closely-related species (*SDN3-Cis*).
- Directed-mutagenesis technique: allowing transient changes of oligonucleotides (*ODM*)
- Epigenetic technique: impacting the 'reading' of DNA without any oligonucleotide change (*RdDm*).

The preparation of these sheets entailed extensive discussions between five researchers both from genetic engineering and the social sciences in order to find a balance between simplification and precision. One of the authors has a double competence in both the social sciences and in genetics, with specific expertise in the area of communicating about OGMs with lay people. The sheets were pretested with two groups of six participants, then edited to ensure all the formulations were clear to every participant. A sample sheet is provided in Supplemental material B.

Each sheet presented information in clear schematic figures and with a short text in concise, accessible language for non-experts. The choice of terms used to describe genetic engineering techniques is critical. Care was taken not to oversimplify the technique, and to avoid misconceptions about the BTs. This approach helps lay people overcome an overly simplistic (e.g., binary) approach to NBTs or one that is based on mere heuristics (Malyska et al., 2016). Care was also taken to help consumers enter into more active deliberation while avoiding the common "boomerang effect" that can be generated when some terms trigger "dormant" thoughts on risks (Hagemann and Scholderer, 2009). In order to avoid polarized views of NBTs the terms "natural" and "GMO" were never present on the sheets.

The sheets provided information about the transmissibility of DNA-induced changes, the origin of DNA, the number of nucleotides involved (from a few number of nucleotides to a large stretch of DNA), the comparison with changes in the natural environment, and lastly whether there were targeted or random changes. A metaphoric and accessible language was used: DNA was called the "book"; a gene a "sentence"; a small amount of nucleotides a "word" and a nucleotide a "letter" (Supplemental material C). These familiar terms enabled the participants to undertake the categorization task.

Data analysis

A two-fold analysis was undertaken of the data from the sorting task: a subjectoriented analysis to identify possible segments of consumers with distinct perceptions of BTs; and an object-oriented analysis to identify areas of consensus from the sorting associated with a global description of the techniques using words from the subjects.

Subject-based analysis: The classification of subjects was based on the comparison between partitions of subjects. Subjects who sorted the same objects into the same groups were part of the same segment of consumers, whereas two subjects with a totally different partition were in different groups of consumers. The Adjusted Rand Index (ARI) (Rand 1971) is a classical measure of agreement between partitions and (1- ARI) has been used to obtain a distance matrix between subjects in order to apply a Ward's hierarchical clustering analysis (Courcoux et al., 2014).

Object-based analysis: In the analysis of the differences perceived between techniques, for each segment of subjects, the number of subjects who separated two techniques into different groups was considered as a measurement of dissimilarity between these techniques. This dissimilarity was used as a distance to establish a hierarchical clustering and to illustrate the difference between the genetic techniques, perceived by each segment of participants. To analyze the universes of perception of each genetic technique, the terms spontaneously used for

the description of one group were associated with each technique in the group. Thus a general matrix was constituted for each segment of subject, with the number of occurrences of each term used to describe each technique. Attributes were selected for analysis when mentioned by at least 3 subjects. When two words were considered to be synonyms, they were pooled in the same category.

All the focus groups were video recorded and the audio files were fully transcribed to allow textual data analysis and the identification of themes raised about NBTs. This approach follows the recommendations for systematic qualitative data analysis (Miles and Huberman, 1994), and permitted the identification of recurrent ideas in the arguments of lay people. We discussed the discrepancies between the terms, the meaning associated to each group of techniques by respondents according to their affiliation with the clusters revealed by the statistical analysis of the sorting task.

4. Results

This section first presents the outcomes of the clustering of the subjects, then provides the data analysis relating to the two clusters formed around the perception of techniques. For both clusters the sorting results are followed by a presentation of the meaning associated with the sorting.

Clustering the subjects

The hierarchical clustering applied to a distance matrix between subjects based on the Adjusted Rand Index showed two clear clusters of quite similar size (Supplemental material D), 24 people for cluster C1 and 21 for cluster C2. Each cluster was composed of subjects who produced close partitions of genetic techniques. In order to identify the main difference in sorting between the two clusters, a hierarchical clustering was applied to each dissimilarity matrix between techniques, calculated from each segment/cluster of subjects.

While these statistics must be approached with the usual caution due to the small sample size some socio-demographic differences between the two clusters are noteworthy (Table 1). Cluster 1 had more young people (under the age of 35), students and people with lower education and socioeconomic levels. Cluster 2 had more middle-aged people (aged 35-50) and people with higher education and socioeconomic levels.

Table 1.

Socio-demographic characteristics of the sample and for the two classes of individuals identified from hierarchical clustering on individual sorting partitions

	Total	Cluster 1	Cluster 2	
Gender (%)				
Male	26.7	25.0	28.6	
Female	73.3	75.0	71.4	
Education (%)				
Lower	8.9	16.7	0.0	
Medium	28.9	29.2	28.6	
Higher	62.2	54.2	71.4	
Age (%; mean)				
Under 35	44.4 (27.0)	54.2 (25.8)	31.8 (29.0)	
35-50	31.1 (44.1)	16.7 (41.5)	45.5 (45.2)	
Over 50	24.4 (54.5)	29.2 (54.6)	22.7 (54.2)	
Employment status				
(%)				
Retired	0.0	0.0	0.0	
Not working/Student	15.6	25.0	4.8	
Working	84.4	75.0	95.2	
Socio-economic level				
(%)				
Working				
Lower	13.2	27.8	0.0	
Medium	21.1	27.8	15.0	
Higher	65.8	44.4	85.0	

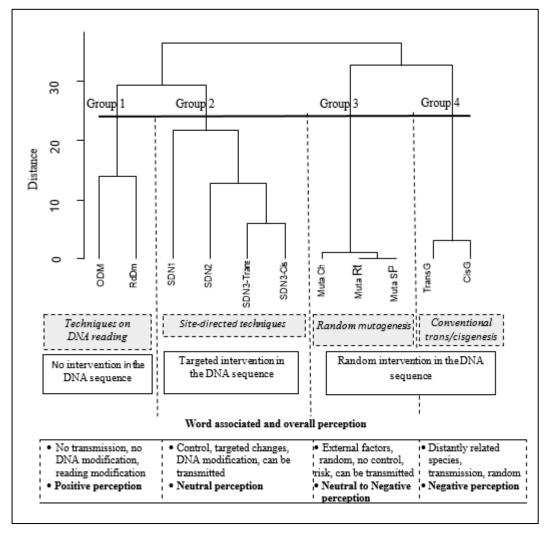
Categorization of techniques

In this section, the results of the way the participants categorized techniques and the criteria they applied are described for each cluster. Both quantitative and qualitative data are used to analyze how criteria make sense to participants. A clear difference emerged between two clusters, which we characterize as the Cartesian logic and the Naturalistic logic to reflect the key features of each cluster.

- Cluster 1: the Cartesian logic
 - a. <u>Sorting results</u>

The hierarchical classification applied on the dissimilarity matrix of genetic techniques is presented in Figure 2. To describe these groups, twenty-two criteria were used. The number of occurrences of each term used to describe a group of techniques was used to interpret the main characteristics attributed to each technique and the associated perception among the subjects (Supplemental material E).

Figure 2. Hierarchical classification of genetic techniques for Cluster 1 and word associated



In conclusion for cluster 1, people first distinguish "Random" (Gr.3 and G.4) from "Targeted" (Gr.1 and Gr.2) techniques and then they split "Reading techniques" (Gr.1) from "Targeted interventions on DNA sequence" (Gr.2).

b. Meaning of the sorting logic

The analysis of the meanings of the terms associated with the techniques by the subjects after the sorting task revealed the classification logics. Cluster 1 relies on a Cartesian logic, a classification based on rather "rational" interpretations of interventions on DNA and of their efficiency. Subjects have a positive perception of techniques from group 1 modifying DNA reading (ODM and RdDm) (Figure 2). As there is no intervention in DNA sequences, and potentially reversible changes, the participants do not associate this technique with a risk of transmission to the descendants (for additional quotes, see Supplemental material F):

"[...] So, it's an intervention, but one that is only for a short period of time because afterwards it's going to go back to its original state" (Woman, age 25)

Moreover, with those techniques they see no harm to the integrity of species:

"If the book doesn't get changed, the technique preserves the nature of the species" (Woman, age 21)

Furthermore, they have a neutral perception of targeted techniques (SDN1, SDN2 and SDN3) of group 2 because although some interventions on the DNA sequences, those can be balanced by the targeting, the control and the predictability of consequences:

"For me, it was very clear in my head. "Targeted", that's really positive for me. It means control, mastery." (Woman, age 40)

Following this 'Cartesian logic', they have a neutral to negative perception of all random mutagenesis and a negative perception of conventional trans/cisgenesis techniques, because they may lead to some unexpected results:

"So when we make random modifications, can the characteristics always be positive? And mightn't we have negative repercussions in certain cases? As a result, we really don't have any control and there's an unknown quantity" (Woman, age 21)

It is this "*unknown*", "*inherent risk*" of random techniques that is the source of the anxiety. Lastly, the issue of transgene/cisgene was also tackled in a rather rational way. The relevance of the inserted gene depends on its complementarity with the host organism:

"Some species are going to have characteristics that others don't have and so there could be complementarity that we couldn't find in species that are close." (Woman, age 23).

Ultimately, they consider genetic material from distantly-related species as having higher "added value" than that from closer species:

"If it's not the same species, I imagine it can feed itself in a positive manner all the same." (Woman, age 24)

Lastly, for this cluster 1 the perceptions of BTs, although not strongly positive, revealed a relative confidence in science and the purposes of some techniques.

Cluster 2: the Naturalistic logic
a. Sorting results

Participants from cluster 2 first distinguish techniques inserting "Exogenous DNA" (Gr.1 and Gr.2) from those with no insertion of exogenous DNA/no intervention in DNA sequence (Gr.3 and Gr.4); then they split "Reading techniques" (Gr.3) from the others (Gr.4) (Figure 3). Twenty-four criteria were used to describe these groups (Supplemental material E). Unlike cluster C1, the conventional/random and site-directed trans/cisgenesis were grouped all together as techniques using insertion of exogenous DNA, but with two subgroups based on the origin of the inserted gene, or otherwise species proximity or not. Techniques with no change in DNA sequences were grouped as in cluster C1. Lastly, all random and site-directed mutagenesis were grouped together as techniques without insertion of exogenous DNA.

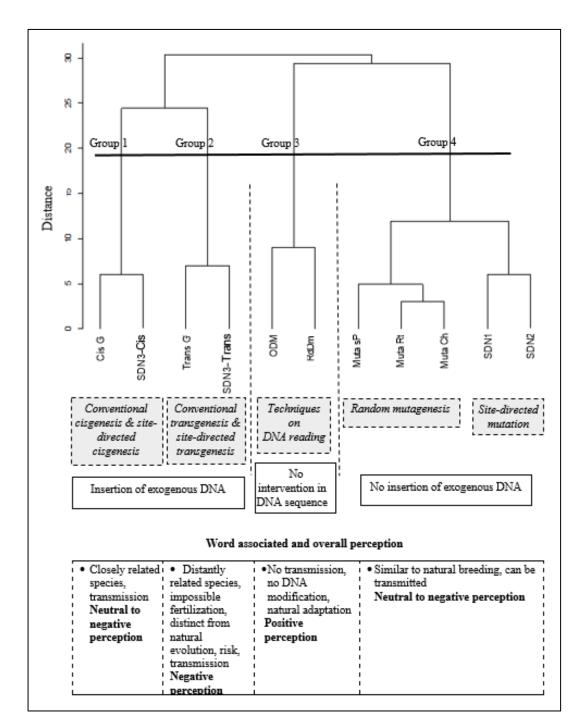


Figure 3. Hierarchical classification of genetic techniques for Cluster 2 and word associated

In conclusion, the sorting results suggest that for cluster 2, the primordial criterion is intervention on DNA/insertion of exogenous DNA or not. In case of insertion of exogenous DNA, a second criterion is applied relating to the origin of the exogenous DNA: the presence or absence of proximity between the donor and organisms.

b. Meaning of the sorting logic

Like Cluster 1, subjects from Cluster 2 have a positive perception of techniques without intervention on DNA sequences (ODM, RdDm) (Gr.3) but they gave more importance to the comparison with the "natural adaptation processes". However, they have a very different perception of certain criteria. They follow what we characterize as *naturalistic logic:* the mechanisms and laws of nature make up their frame of perception. They thus have a more neutral perception of random mutagenesis, SDN1 and SDN2 techniques (Gr.4) because of no use of exogenous genes. They are perceived as pretty close to natural mechanisms:

"I think that modifying the natural environment is simply natural evolution since time began. Well yes, it's speeding up pre-existing processes. We decide to change the environment precisely to test evolution in DNA, but at a greater speed, you know. And even if there is human intervention, it respects the randomness of nature." (Man, age 43)

Respecting natural randomness is of highest importance for people from Cluster 2.

Moreover, SDN1 and SDN2 techniques were likely seen to make just small changes, one or

several base pairs (SDN1) or a short repair template (SDN2). These modifications could be

considered as similar to mutations spontaneously observed in nature. This was not the case for

SDN3 techniques (Gr.1 and Gr.2), which appeared to have a high degree of human intervention:

"It's the "targeted" aspect specifically, and if there's a major intervention by man, on something really specific and extensive that means there's an aim somewhere or at least there's a desire to do something, to force nature to do something." (Woman, age 40)

Some subjects connected this idea of human intentionality with the fear of eugenics

and when going further into the concept of randomness, a very subtle and ontological difference

between the "natural random" and the "random induced by scientists" was set up. The first one

is the "real randomness" and the second one the "controlled randomness":

"Genetic mutations, before man intervenes, happen randomly in relation to the environment.[...]. Nature does randomness anyway, and that's how evolution happens. In that case, we don't know it, it happens or it doesn't and we observe it. While when it's human randomness, we're supposed to be able to control it, to observe it. That is, having a previous state, we do something random and then we have the "after" state and we observe the difference" (Man, age 50)

For these reasons, the subjects distinguish "natural mistakes", as the basis of natural

selection, from "human mistakes", perceived as a "technological avatar":

"When nature makes mistakes, it makes things that aren't viable. I mean, for man, the question doesn't come up, that is, effectively, Mother Nature, when she makes mistakes in man, she makes it that he isn't viable [...]. Plants and animals that aren't viable disappear all by themselves and that's part of evolution. [...] Should nature never make a mistake and what's so bad about that? And should it be repaired, are we, humans, omnipotent enough to repair the mistakes made by nature or not?" (Man, age 50)

Through this opposition, this subject raised the issue of the legitimacy of human intervention and the underlying idea of demiurgy. Conventional cis/transgenesis and SDN3 techniques were more negatively perceived than in Cluster 1 because of the insertion of exogenous genes, whether they come from distantly- or closely-related species. The idea of transgression of the natural order was clearly evoked for the transgenesis technique:

"So in fact naturally, it's not possible. And that makes me say, "if it's effectively not possible naturally, is it legitimate for us to modify nature?" with a big N, I mean, a capital N. Us, humans, just passing through earth." (Man, age 33)

With the cisgenesis technique, the risk was the greater proximity between the host and

the gene, leading to a loss of natural bearings and identity:

"Too far but also too close! With cousinhood, we're losing our genetic diversity, our real origins from the plants and all. It's important to keep the originals, really keeping the basis." (Woman, age 49)

In conclusion, while a consensus was found between the two clusters for the techniques without modification in the DNA sequence, they used different criteria for sorting certain techniques leading to some opposite perceptions. One of the most interesting results concerned the difference in interpretation of concepts such as "random" versus "control/targeted", and of the usefulness of "cisgene" versus "transgene" when insertion of exogenous DNA.

5. Discussion

In line with literature, our results showed that for non-experts, in both clusters, plants/food produced by NBTs will never be equivalent to plants/food from traditional BTs (Mielby et al., 2013; Siipi, 2008) and that there is no evidence that developing plants/food with higher 'benefits' for consumers would increase their acceptance (Siegrist and Sütterlin, 2016). Following Hagemann and Scholderer (2009), our research explored the discrepancy between the lay/holistic understanding of non-traditional BTs and the scientific/rational assessment. Our

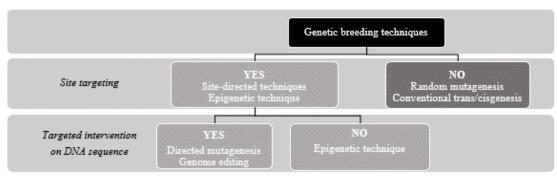
results brought to light two clusters of people with some distinct logics on categorization. Figure 4 compares, for the techniques considered here (see Part 3.), the two lay logics to the scientific logic, the latter as suggested in the HCB report (2016).

Figure 4. Scientific and lay classification logics of genetic breeding techniques

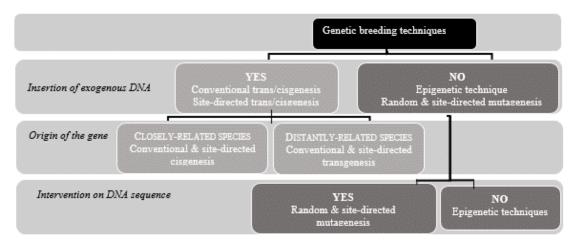
SCIENTIFIC CATEGORIZATION

	Genetic breeding techniques						
Overall mechanism	Trans/cis genesis	Genome editing		Mutage	nesis	Epigenetic techniques	
Genetic tool used	Viral/bacteria vector	Site Directed nucleases (SDN)	Inductive agent	Selective pressure	Directed by nucleotides	DNA methylation	

NON-EXPERT "CARTESIAN LOGIC"



NON-EXPERT "NATURALISTIC LOGIC"



Similarities and differences between classification logics of experts and lay people

While scientists classify genetic BTs according to the overall mechanism and the genetic tools used to intervene on DNA, non-expert people use more complex heuristics to assess the "degree" and the "nature" of human interventions on DNA. Both clusters have clearly isolated and gathered techniques leading to no intervention in the DNA sequence (epigenetic techniques and oligonucleotide directed-mutagenesis). As the DNA alphabet is not scorned, those techniques are perceived to be the least contentious, although this intervention can actually lead to silence in gene transcription.

For the techniques with intervention in DNA sequences, non-expert people addressed three main issues: the level of control of the change on DNA sequences, the insertion - or not of exogenous nucleotides and if so, the origin of the exogenous nucleotides (distance/proximity between specifies to which donors and recipients belong). The two clusters identified nevertheless had contrasting perceptions, which could be explained by a different relationship with science and technology.

Some previous research on GMOs acceptance showed that people with higher level of acceptance have a more functional approach to food, greater confidence in science, and a more distant relationship with nature (Debucquet, 2011). Conversely, people with lower level of acceptance show strong anchoring of the representations of BTs in the symbolism of nature. Our results correspond to these two kinds of attitude: people with *Cartesian logic* (Cluster 1) had more confidence in targeted techniques, which they perceived as more controlled, and people with *naturalistic logic* (Cluster 2) had a more positive perception of random techniques, which they perceived as more in line with natural mechanisms. The same interpretative forms of logic were involved regarding the issue of exogenous genes. Cluster 1 judged the relevance of the exogenous gene with the yardstick of gene complementarity. Cluster 2 focused on the

taboo of infringement of natural barriers. Moreover, Cluster 1 was composed of more students and younger people, of various education and socio-demographic levels, while Cluster 2 was composed of more middle-aged and older people, of higher education and socio-demographic levels. These results were in line with previous research on GMOs, showing that even if more educated people were more likely to accept them, the relationship was equivocal (Magnusson and Koivisto Hursti, 2002). Indeed, the very principle of human intervention on DNA can remain ethically disputed.

Methodological reflection about the generalization of the sorting experiment with NBTs

This study was designed to avoid some pitfalls of elicitation methods (Dannenberg (2009), in allowing individuals to give their free/own interpretation of the information. The sorting task seemed the best suited method with the least influence on people, provided that there was no particular bias. Like Grygorczyk et al. (2017), we were aware of biases in the choice of words (to use/avoid), so we never used the terms mutagenesis, GMO, or natural/unnatural; instead we used the neutral metaphors book and letter. This choice reduced misconceptions. The participants (including those with little education/scientific knowledge) requested almost no additional explanations about the sheets.

The sorting experiment was an effective tool for generating spontaneous classifications of BTs. The focus groups were an essential subsequent step to collect comments to permit the interpretation of similarities/individual discrepancies. We analyzed how lay people in our French sample make sense of terms/concepts used in non-traditional breeding. This study serves as a proof of concept of a method that can be deployed on a representative population sample. Further research in a cross-cultural perspective could be carried out in other countries to compare lay categorization, to bring out permanent/universal and contingent/cultural principles used by non-experts in formulating their opinion of NBTs. Moreover, a larger sample would make it possible to confirm the relevance of the two different clusters identified, and to provide their respective proportions in different countries.

6. Conclusion and implications for policy making and future research on improving public-experts dialogue

The aim of our research has been to provide inputs for an informed dialogue around NBTs between experts and non-experts, innovators and public, by building on a long tradition of work to improve the public understanding and trust of science (Dierkes and v. Grothe, 2000; Araki and Ishii, 2015; Stilgoe et al., 2014). We tested an elicitation technique avoiding the pitfalls of simplistic misrepresentations and excessively complicated explanations. The results, obtained with a convenience sample, obviously require validation with a larger population. However, these first results provide some food for thought on the issues of NBTs.

Lay classifications highlighted opposite perceptions based on two main heuristics, which challenge the status of random mutagenesis regarding the ECJ (July 25th, 2018) and of transgenesis vs cisgenesis. The latter is definitely not perceived as more 'natural' than transgenesis while finer criteria/heuristics were used in each cluster. These results demonstrate how some scientific criteria can be assessed with personal values.

Our study documents that with a moderate cognitive effort, consumers are able to deal with the diversity of BTs. Moreover, the sorting task and focus group provided additional input about the concept of "random" and showed, by highlighting two interpretative forms of logic, that uncontrolled experiments/unpredictable outcomes did not resonate for all participants in the same way. The ambivalence of the concept for lay people should be addressed carefully by innovators to anticipate the success or failure of further developments in BTs according to different audiences/targets and by legislators to a better alignment of GMO regulation with consumers' expectations.

The findings of our study and the approach we have developed are particularly pertinent in light of the ongoing race around CRISPR-Cas9 to develop new BTs quickly, and the recent ECJ decision (July 25th 2018) indicating that products from new, targeted BTs will be under the scope of the GMO regulation, and possibly not for those from random mutagenesis that was used for a long time without any safety problems. We highlight some fundamental differences between lay and scientific taxonomy, because values, the relationship with nature/science contribute to public attitudes. We concur with Lucht (2015, p. 4273) that those outcomes will not resolve the conflict but may help to make clear the 'core of the dispute' and clarify the possible criteria for decisions. The lay classification of NBTs suggests that innovators and legislators should carefully address the underlying questions raised by consumers:

- i) Does the technique intervene on the DNA sequence?
- ii) Does the technique rely on random changes or targeted changes?
- iii) Does the technique rely on the insertion of exogenous DNA?
- iv) Does the exogenous gene come from distantly or closely-related species?

Suggestions have been made to require public participation in the framing of research agenda around NBTs (Mayer, 2003). The public qualification would not rely on public expertise; instead it would rather consist in increasing citizen involvement in "challenging the normative social commitments projected and performed by science" (Wynne, 2007, p. 108), such as claimed advantages, technology efficiency or precision. Our procedure to elicit lay people's assessments could be a useful tool in this process.

Improving scientists-citizens dialogue in order to stimulate active public commitment in new technological choices could also help define the future common research needs and priorities. It would help anticipate which NBTs are desirable or not, conflicting or not within a society (Bonney et al., 2016), and which are worthy of particular in-depth detail for scientific knowledge enhancement. Moreover, the current weaknesses in the tracking of products derived from NBTs should not be neglected as the presence of inopportune genetic modification would inevitably provoke public outrage. Last but not least, public debate could be engaged at an early stage on the range of the applications for emergent BTs. The lowest acceptance of applications in the area of food, already observed in Europe with the first GM food, is worth taking into account to assess the probable success or failure of forthcoming products based on emergent BTs.

Notes

¹ This technique refers to CRISPRs (*Clustered Regularly Interspaced Short Palindromic Repeats*) (For further explanations, see Jinek et al., 2012).

² A few conferences have been held to engage a dialogue with lay people (e.g., CRISPRcon conference - Conversations on science, society and the future of gene editing, Wageningen, 20-21 June 2019).

³ <u>https://www.aphis.usda.gov/biotechnology/downloads/reg_loi/15-321-01_air_response_signed.pdf</u>

⁴ We decided to keep eleven main categories of techniques identified in the French HCB report (HCB 2016). The other techniques cited in the report were subcategories too complex to be presented to non-experts.

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