

BRIDGING THE GAP

The role of epistemic virtues in navigating the complexities and uncertainties of translational animal research



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SUMMARY

Animal experiments have traditionally been employed to understand human diseases and find new treatments. However, a growing number of studies shows that the translation of results from animals to humans is often unsuccessful. Since animal experiments are justified on the basis of their expected benefits, translational failures represent an epistemic but also a normative problem. The purpose of this thesis is to address both problems by exploring the role of epistemic virtues in avoiding failures that can be reconducted to an individual's cognitive attitudes. I argue that epistemic virtues (1) further the moral imperative to do better at achieving successful translation while avoiding unnecessary experiments and (2) guide moral reasoning and decision making in harm-benefit analyses that precede the choice of an animal model in experiments.

After a literature review of contemporary virtue epistemology, Chapter 1 builds on a theoretical framework where epistemic virtues are intended in a responsibilist sense, as best intellectual *character* traits that should characterize any responsible knower.

Chapter 2 presents three arguments which focus on the normative significance of epistemic virtues. Here it is shown that a) better knowledge facilitates moral reasoning by reducing the margin of uncertainty and bias in the assessment of animal experiments and that b) epistemic virtues represent standards of behavior for members of an epistemic community who are supposed to be responsible for the way they acquire knowledge.

Finally, Chapter 3 considers a selection of epistemic virtues that can, more than others, mitigate the epistemic dimension of translational failures. Contextually, each virtue is examined and tested in practical cases.

LIST OF ABBREVIATIONS

Abbreviation

Definition

NE

Nicomachean Ethics

TAR

Translational animal research

TFs

Translational failures

VE

Virtue epistemology

INTRODUCTION

Every year a high number of animals is used across Europe for scientific purposes. According to the European Commission report on the use of animals in research in 2018, a total of 12.093.096 animals have been employed in research, while 10.572.305 of them were actively involved in experimental procedures. While the majority of test subjects is used for basic research (46%) - that is, for exploratory research, aiming at a better understanding of certain phenomena such as the behavior and the physiology of animals - an equally considerable part of them (27%) is destined to translational and applied studies.¹

With Translational Animal Research (TAR) I will refer here to the process of collecting and applying knowledge obtained from animal laboratory research to the clinical field with the goal of finding new treatments, preventive and diagnostic procedures that could benefit human populations (Pippin et al., 2019, p. 480; Seyhan, 2019, p.1). Preclinical animal models have been traditionally employed as surrogates in the study of patho-physiological mechanisms of human diseases as well as in drug testing. Indeed, it is widely acknowledged that animal experiments have contributed to many revolutionary discoveries in the history of biomedical science.²

¹ European Commission. (2021). *Summary Report on the statistics on the use of animals for scientific purposes in the Member States of the European Union and Norway in 2018*. https://ec.europa.eu/environment/chemicals/lab_animals/pdf/SWD_20part_A_and_B.pdf

² Animal experimentation was historically used to understand human anatomical and physiological mechanisms. In more recent times, many life-saving treatments such as vaccines and antibiotics have been found thanks to animal experiments. Nowadays, animals are still important sources of information for the understanding of complex diseases (Nuffield Council of Bioethics, pp. 5,6) but also in behavioral studies, where they cannot be replaced.

The translation of findings is only *prima facie* justified by the *continuum* argument, which relies on interspecies homologies at an anatomical, physiological and genetic level between humans and other animals - not only mammals - in the evolutionary chain (Berridge, 2022, p.1). However, the argument of the *continuum* is not sufficient to prove the validity of an animal model, which must recapitulate a human condition in three aspects: a) in symptoms (face validity); b) in cause or origin (construct validity); c) in response to treatment (predictive validity) (McGonigle and Ruggieri, 2014, p.163; Veening-Griffioen et al., 2019, p.2; Tadenev and Burgess, 2019, p.111).

The second, important constraint that applies to all animal experiments is of ethical nature and could be addressed as the *benefit requirement*. That means, the moral assessment of animal experiments cannot be detached by a calculus of their expected social utility (for animals and/or, like in the case of TAR, humans) to be balanced out with the inflicted harms, in terms of animal suffering, discomfort or irreversible damage.³

The recognition of animals' capability to suffer and the increasing attention to animal welfare issues in the last decades resulted in (a) an overlapping consensus on the moral consideration owed to animals and (b) the development of ethical guidelines that regulate animal testing. In this sense, the 3Rs principles (reduction, replacement, refinement)⁴ presented by Russel and Burch in 1959 were pioneering in addressing the exigency of

³ Harm-benefit analyses are commonly used in the justification of animal experiments, as they reflect the EU Directive on animal experimentation (Directive 2010/63/EU) (Cf. Meijboom et al., 2020, pp.2,3). However, the debate on the morality of animal experiments is characterized by a plurality of arguments that surpass the benefit requirement (Cf. Nuffield Council of Bioethics, 2015, pp.35-38)

⁴ "Replacement means the substitution for conscious living higher animals of insentient material. Reduction means reduction in the numbers of animals used to obtain information of a given amount and precision. Refinement means any decrease in the incidence or severity of inhumane procedures applied to those animals which still have to be used" (Russel and Burch, 1959).

posing limits to animals' commodification in research. The 3Rs principles are nowadays embedded in the EU Directive on animal testing (Directive 2010/63/EU, art.11-13) and guide ethical committees in the complicated task of assessing the quality of animal experiments and deliberating about their moral permissibility (Meijboom et al., 2020, p.2).

The debate on animal testing has been in the last decades at the center of animated public discussions and has become the subject of profound disagreements among defenders of more or less entrenched positions, which question animal experimentation on different grounds - epistemic and ethical - or, conversely, justify it (Nuffield Council of Bioethics, 2005, pp.8,9). However, as it often occurs, when debates polarize the risk of losing complexity and overlooking the various shades that characterize a certain phenomenon is high. In this context, the complexities (and uncertainties, as it will become more clear in the following chapters) that characterize translational studies are several and challenge the two conditions - epistemic and ethical - that should, on the contrary, satisfy their own permissibility.

First, animal experiments are still necessary to scientific and medical progress and are, as a fact, a mandatory regulatory step of most drug-approval processes; but, at the same time, the so-called "epistemic critique"⁵ of animal experimentation is supported by a conspicuous body of scientific studies which show that translation of basic results from preclinical animal experiments to clinical trials is often unsuccessful. Seyhan (2019) has described this translational gap between bench-to-bedside as "the valley of death", for the incredible loss of promising discoveries in the translation process.

⁵"At the core of the epistemic critique of animal experiments is the idea that such experiments are bad science. Bad is used as a synonym for inefficient, scientifically wrong, or misleading" (Ferrari, 2019, p.199)

Second, translational failures (TFs) become ethical issues since they do not allow the costs of animal research to be outweighed by its benefits. Furthermore, (although beyond the scope of this research) it could be argued that TFs represent a cost also for patients, who, in certain cases, invest time, money and hopes in ineffective treatments (Akhtar, 2015, pp. 207, 414).

Addressing TFs is therefore an epistemic as well as an ethical matter - insofar epistemic failures disattend the ethical premises on which translational animal studies are justified. Understanding why TFs occur means, first of all, inquiring about their causes, which have been already identified and addressed in the existing literature on the topic.⁶ On the basis of the literature review, here I suggest to conceptualize TFs in two sub-groups, which reflect their respective causes:

(1) The first group includes TFs which are due to epistemic failures, such as methodological flaws and biases. In particular, the lack of accurate description of animal experiments can be at the source of important (methodological) differences in the replication of the experiments, thus leading to irreproducibility of results and, *a fortiori*, untranslatability. (Seyhan, 2019, p.7). Statistical errors and failures in applying principles of good experimental practice such as randomization and blinding can also contribute to what in literature is frequently mentioned as “reproducibility crisis” (Ritskes-Hotinga et al., 2020; Frommlet, 2020). Further methodological issues are related to the design of animal models, some of which resulting from uncertainties about the causes of particular human

⁶ For the present introduction, the following studies on the limitations of animal experiments and translational failures have been considered: Akhtar (2015), Matthews (2008), Meijboom et al. (2020), Seyhan (2019), Pound and Ritskes Hotinga (2018), Ritskes-Hotinga et al. (2020), van Norman (2019), Varga et al. (2010), Veening-Griffioen et al. (2019)

diseases and disorders - such as in the modeling *in vivo* of neuropsychiatric disorders (Meijboom et al., 2020).⁷ Poor methodology is considered a problem of *internal validity* or the “scientific robustness of a study’s design, conduct, analysis and reporting” (Pound and Ritskes-Hoitinga, 2018, p.2). These and other types of failures⁸, including the lack of understanding of the entire translational process (Seyhan, 2019, p.7), lead to flaws and biases that can be eventually reconducted to individual subjects as consequences of their intellectual attitudes.

(2) In the second group, TFs are caused by structural constraints, that means they depend on external (social, political, economic) circumstances, which are beyond the control of particular individuals. They might include the lack of fundings and incentives from organizations and institutions to continue preclinical studies or provide the necessary support for such a challenging research field, which requires the cooperation of different subjects and fields of expertise (Seyhan, 2019, p. 5). Structural failures might occur also due to obsolete regulatory requirements, when, for instance, preclinical studies which are successfully conducted *ex vivo* on human biological material, fail the *in vivo* regulatory test on animals due to interspecies variability.

(3) There is, however, a third dimension of TFs, which is constituted by the intersection of the two main subgroups, that is, failures which can be reconducted both to epistemic and the structural causes. Lack of data

⁷ See Chapter 3, pp.47,48

⁸ The critical literature on the predictive value of animal models is indeed quite vast, with some further recurrent topics regarding a) interspecies variability and b) genetic standardization of laboratory animals, which are not representative of the great diversity of human populations. Such problems of extrapolation of results from one species to another regard the *external validity* of the model, namely the degree of generalizability of its findings. Pound and Ritskes-Hoitinga (2018) notice that while lack of internal validity and genetic standardization are surmountable issues, interspecies differences deriving from different evolutionary histories cannot be overcome and the biomedical community heavily relies on “an *assumption* of similarity (rather than its empirical demonstration)” (p.4)

sharing, academic pressure, research culture and transparency are some examples of issues that might contribute to translational failures. For instance, Ioannidis (2012) addresses the problem of transparency by noticing that research protocols and data should be of easy accessibility in order to be truly informative and be of help to those who want to replicate the study (p.3). Similarly, it has been suggested that the publication of negative results might contribute to translational success by avoiding the replication of unsuccessful experiments (Ritskes-Hotinga et al., 2020, p.8). The intersection of domains (epistemic and structural) in these cases is given by the fact that while the accessibility of results does not depend on the individual who starts a research, individuals can do their part in reporting all research outcomes, including the negative ones. Research and academic culture belong to this domain insofar the publication pressure might lead to the choice of a particular model for practical more than epistemic reasons or the performance of studies that are not well-designed in methodological terms (Pound and Ritskes-Hotinga, 2018, p.4). In all these circumstances individuals might tend to adjust to a consolidated system, although they can still opt for better epistemic practices.

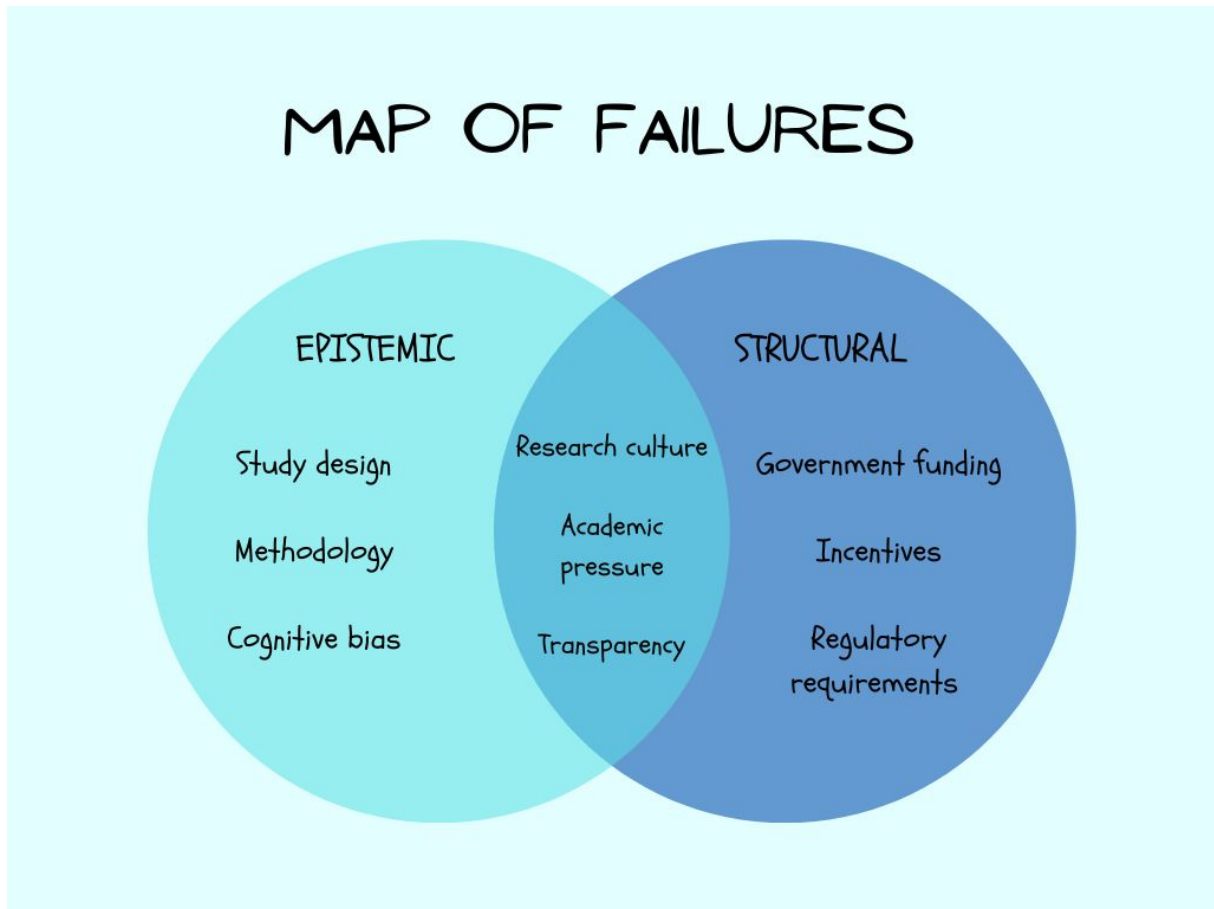


Fig.1

Now, considering that (P1) animal experiments do not always translate successfully to the clinical stage because of TFs which have been described above and that (P2) animal experiments should deliver (human or animal at least) benefits to be morally justified, it can be concluded that (C) there is a moral imperative to ensure that experiments' benefits exceed the harms done to animals by addressing TFs.

RESEARCH QUESTIONS AND HYPOTHESIS

As shown in fig.1, the problem of translation of findings in animal research to the clinical stage involves different dimensions - one epistemic and the other structural - which can be interrelated. While in literature suggestions have been advanced to mitigate the pervasiveness of TFs on an empirical level⁹, the scope of the present research is to restrict the focus on epistemic failures and the role that intellectual attitudes might play in their etiology, to answer the following questions:

- ❖ What, if any, is the role of **epistemic virtues** in the practice of TAR?
- ❖ How, if properly cultivated, can they help in furthering the moral imperative to do better at achieving the aims of TAR?

The hypothesis suggested here is that conceptualizing researchers' intellectual attitudes in terms of **epistemic virtues** (*excellencies of the mind*) and nurturing them appropriately could play a positive role in: a) addressing the epistemic causes at the basis of TFs and in b) guiding moral reasoning and decision making in harm-benefit analyses that precede the choice of animal models in experiments

METHODOLOGY AND OVERVIEW OF THE CHAPTERS

The thesis is based on a review of the literature on translational failures in preclinical animal research and on virtue epistemology (VE). This contributes to Chapter 1 that presents a succinct review of contemporary VE theories in a historical perspective; the literature review aimed primarily at

⁹ Frommlet (2020), Hirst et al. (2014), Hooijmans and Ritskes-Hotinga (2013), Ioannidis (2012), Ritskes-Hotinga et al. (2020), Seyhan (2019) propose important strategies to contain the risks of incurring in TFs; some of these strategies will be discussed in the next chapters, to exemplify how good experimental practices require the exercise of virtuous intellectual dispositions.

individuating the salient features of different VE theoretical frameworks, in order to finally outline one that could be convincingly applied to the specific case of epistemic failures in TAR.

Chapter 2 focuses on the three main arguments - and relative counter arguments - that support the application of a VE framework in such a context. This chapter focuses on the normative implications of TFs and our duty to do our best to prevent them. In particular, it is argued that: 1) the practice of epistemic virtues can contribute to better moral practices in TAR; 2) epistemic virtues can be significant beyond the individual dimension, providing a space for epistemic actions also in the domain of failures which results from the intersection of epistemic and structural causes; 3) epistemic virtues address the epistemic and moral dimension of responsibility, which is particularly relevant in research-related activities.

Finally, in Chapter 3 I discuss a selection of epistemic virtues that would be worth cultivating in order to prevent and mitigate the phenomenon of epistemic failures in TAR. In this chapter, each virtue is scrutinized in its salient features and tested “at work” in practical situations.

CHAPTER I

VIRTUE EPISTEMOLOGY

In this chapter, I will recall the salient steps that led to the birth of virtue epistemology as a branch of philosophy of knowledge with a focus on the theoretical stances which distinguish the two main contemporary ramifications of VE, namely virtue reliabilism and virtue responsibilism. Finally, following a responsibilist autonomous account of VE, I sketch the theoretical framework on which my analysis of the role of intellectual virtues in translational animal research is grounded.

Historical background

It goes without saying that the concept of virtue has played a role in the epistemological inquiry since the early philosophical speculation. It is in Plato's *Meno* that, while trying to answer the question "can virtue be taught?" - Socrates defines virtue as a sort of knowledge. While in the platonic dialogue it is still unclear what is the kind of knowledge Socrates refers to, Aristotle will later answer the question by systematizing virtues according to the type of excellencies they express: moral (*aretas ethikes*), intellectual (*aretas dianoetikes*) and technical (*aretas poetikes*), thus granting knowledge about the different types of objects which characterize the two fields (Cf. NE 6.1-6.10).

Although Aristotle's virtue theory has given birth to a successful and long-lasting branch of philosophy especially in ethics, VE has emerged as a particular school of philosophy of knowledge in much recent times. Nowadays, VE embraces a variety of positions more than a unitary

approach to epistemology; however, a common denominator can be found in the role granted to the notion of epistemic virtue in the knowledge acquisition process. According to virtue epistemologists, traditional -but also new - epistemological challenges can and should be tackled by appealing to the notion of intellectual or epistemic virtue (here used interchangeably). Even though such a notion can be differently defined in the various accounts, one of the merits of VE is to have brought the attention back to the individual, cognitive subject in the epistemological inquiry.

Until the early 1980s, in fact, the epistemological debate had revolved around the three conditions for knowledge - namely truth, belief and justification - and the solutions to the challenges posed by Gettier's problems (1963).¹⁰ Traditional epistemologists hold what could be called a 'neutral' model of knowledge, according to which a standard subject, who performs cognitive acts but lacks psychological characterization, adheres to a set of epistemic rules in the analyses of the three epistemic concepts (Zagzebski, 1998).

Such a view was first questioned by Ernest Sosa in 1980 with the article *The Raft and the Pyramid: Coherence versus Foundation in the theory of knowledge*, where he introduced the concept of intellectual virtues as "stable dispositions for belief acquisition", which contribute to "getting us to the truth" (Sosa, 1980, p.23). Sosa defined his proposal of virtue reliabilism, since the purpose of intellectual virtues - intended as innate cognitive

¹⁰ In 1963 Edmund Gettier published the paper "Is Justified True Belief Knowledge?", where he presented a series of cases that challenged the widely accepted definition of knowledge as true justified belief (Roberts and Wood, 2007, p.5). Gettier's problems showed how in certain circumstances holding a true justified belief is just a matter of pure luck and thus cannot be considered knowledge (Zagzebski, 1994, p.65)

faculties - is to increase the reliability of beliefs acquired through the exercise of such virtues, thus providing a new solution to disputes on epistemic justification.

Sosa's idea was developed shortly after by Lorraine Code and James Montmarquet, who gave birth to a different version of Sosa's original theory, known as virtue responsibilism. While acknowledging that the great intuition of Sosa was to consider the acquisition of epistemic goods (such as knowledge, truth and justification) as the result of an activity of the subject, however, according to responsibilists such as Code, the concept of reliability has limited explicatory value if we are to provide an account of knowledge and related concepts that really focuses on the epistemic subject (Code, 1987, p.39). Reliability, in fact, can be regarded as a passive feature: a knower is reliable if she records an experience with accuracy, but this is something that even a computer can do (Code, 1987, p.40). Therefore, the first responsibilists underlie how intending the epistemic subject as a cognitive agent, introduces a series of new concepts and topics in the epistemological inquiry, which bring epistemology closer to the normative field: among them, the problem of epistemic responsibility, the analogy between epistemic and moral virtues and the collective, social basis of human knowledge (Turri et al.,2021.).

The interest in VE has grown considerably in the last decades and led to the flourishing of a field, which is nowadays characterized by well-defined theoretical positions. In the following sections, I briefly recall those features that will allow a distinction between the two main approaches to VE as presented in primary and critical literature, namely virtue reliabilists and responsibilists. This distinction will be mostly introductory although particularly functional as to the understanding of the theoretical framework I will introduce immediately thereafter and use, in the following chapters, to read the problem of epistemic failures in TAR.

Virtue reliabilism and virtue responsibilism

In the previous section, it has been mentioned that Sosa conceived intellectual virtues as natural faculties, which enable the knower to achieve the truth in a reliable manner. This stream of thought is rooted in Aristotle's characterization of intellectual virtues as dispositions of that part of the human soul, the intellective one, which - through the contemplation of eternal objects e.g.: laws of mathematics - bring human beings closer to truth (NE 6.1 1139a).

Moreover, this notion of epistemic virtue reflects the classical idea according to which for everything that has a function or activity - including the human being - , the good for that thing corresponds to the performance of its function (NE 1.7 1097b26–27). Starting from Sosa, then, virtue reliabilists intend epistemic virtues as cognitive abilities such as memory, introspection, hearing, capability of making inferences that are “reliably successful” (Greco and Reibsamén, 2017, p.1). In particular, such innate faculties are part of our cognitive equipment since the moment of birth as much as other non-cognitive abilities (e.g.: breathing, walking etc.) and, as such, they do not have any impact on the moral development and flourishing of the agent that possesses and exercises them. That is to say, having a good memory does not make a subject morally good, as the moral worth of a subject is not judged on the basis of natural endowments of which she is not responsible; finally, these faculties do not require any intentional activity on the knowing subject, meaning that they are not the product of a conscious choice (Greco and Reibsamén, 2017, p.3,4).

Contrary to reliabilists, virtue responsibilists define epistemic virtues as excellent intellectual *character* traits. Responsibilists also maintain that

their concept of epistemic virtue is indeed the legitimate heir of Aristotle's tradition. In particular, Zagzebski (1996) notices that the classical thought, including Aristotle, does not identify virtues with natural faculties as a whole, but with the excellent side of these faculties (p.102). According to Aristotle, intellectual virtues are dispositions in accordance with reason, but they do not perfectly overlap with natural endowments (p.103); this is particularly evident in the case of wisdom (*sophia*) and practical knowledge (*phronesis*), which do not develop naturally in every subject but require training.

Although virtue responsibilism is concerned with epistemic activities, the theory is substantially grounded in Aristotle's theory of moral virtues, of which epistemic virtues become the intellectual counterpart.¹¹ That means, there are some features of the responsibilist's account of epistemic virtue that can be reconducted to Aristotle's virtue ethics and these features are essential to understand the peculiarity of the responsibilist's account. Among them, and in contrast with virtue reliabilism, the fact that epistemic virtues are intellectual character traits that need to be cultivated through repetition of virtuous (epistemic) actions and education to be properly acquired; furthermore, the exercise of these traits always implies an intentional activity of the subject. In fact, while the use of natural faculties is mostly automatic, a virtue like intellectual courage requires that the subject deliberately defends her beliefs in front of someone who, for instance, claims to be right because of her social power. Analogously, open-mindedness requires that the subject questions her own beliefs if evidence proves against them; finally, on the basis of Aristotle's notion of

¹¹ It is one of the main contributions of Montmarquet to have conceptualized epistemic virtues on the basis of Aristotle's concept of moral virtues, namely excellent character traits, which need proper cultivation to be solidly acquired and function as 'habits' that guide our epistemic actions (Montmarquet, 1987, p.486).

eudaimonia, in some accounts epistemic virtues contribute to the achievement of a flourishing, therefore happy intellectual life.¹²

Despite sharing an almost unified account of the notion of epistemic virtue, virtue responsibilists have disagreed with regard to the relationship between the notion of epistemic virtue and traditional epistemological problems. Conservatives argue that epistemic virtues do play a role in the solution of typical epistemological quarrels regarding, for instance, the nature of knowledge, Gettier's problems or the confutation of epistemological skepticism (Baehr, 2008, pp.471,472). In this sense, conservatives and virtue reliabilists offer competing accounts on the same types of problems.¹³

Autonomous accounts, instead, insists on the concept of epistemic virtue as it discloses the possibility of new approaches to epistemology. According to these authors, epistemic virtues can give an account of problems which are mostly related to the flourishing of the human being as epistemic subject, such as: (a) the interaction between epistemic and moral virtues and the nature of this relationship; (b) the link between epistemic goods and epistemic virtues; (c) the relation that connects epistemic virtues to the epistemic practice through the analysis of particular virtues (Roberts and Wood, 2007, p.26).

In conclusion, while all virtue responsibilists accepted the definition of epistemic virtue as excellent character trait proposed by Montmarquet, only the autonomous account dared to change the direction of a debate that for

¹² The characterization of virtue responsibilism is based here on those general features that distinguish the approach from virtue reliabilism. For a detailed review of virtue responsibilism, see Wright, S. (2017). *Virtue Responsibilism*. *Oxford Handbooks Online*.

¹³ Among the principal exponents of the conservative view, we can mention Montmarquet, Baehr and Zagzebski. However, Baehr proposed to 'weaken' Zagzebski's responsibilist approach by suggesting that intellectual virtues might have a secondary or complementary role in the definition of what counts as knowledge and, consequently, in the solution of epistemological problems (Baehr, 2008, p.483)

years had been cemented on very theoretical epistemological issues regarding the conditions of knowledge and of epistemic justification. In the next section I will show why the proposal of addressing epistemic failures in TAR by means of epistemic virtues should be read in this last, autonomous and responsibilist sense of VE.

AN ACCOUNT OF VIRTUE EPISTEMOLOGY

The goal of epistemology

In this section, I will establish the key points of a VE theoretical framework that supports the analysis of particular epistemic virtues in the context of epistemic failures in TAR, as it will be evident in the next chapters. However, before exploring the main features of this framework, a few preliminary considerations on the same scope of reflecting on epistemic virtues in scientific contexts are needed.

In the previous section, different theoretical positions in contemporary VE theories have been briefly presented. As mentioned, conservative virtue responsibilism - as well as virtue reliabilism - tend to deal with traditional epistemological topics in the inquiry about knowledge, such as truth, beliefs and justification. The type of knowledge that virtue and traditional epistemology have searched for is mainly propositional, being directed at investigating the conditions under which a certain proposition could be accounted as knowledge.

However, autonomous accounts of virtue responsibilism, maintain that VE can and should be able to design its own research program, independently from the analytic goals of traditional epistemology. Within this stream of thought, Robins and Wood (2007) have situated their analysis of independent virtues outside of the scopes of analytic epistemology to

propose that epistemic virtues should provide guidance for best intellectual practices; according to the authors, therefore, (virtue) epistemology can have a regulative function, in the spirit of a much older tradition that traces back to Descartes and Locke (p.21).

Robins and Wood (2007) depart from the consideration that knowledge characterizes human life and its experience in a very singular way; it is a pervasive phenomenon that not only allows humans to interpret the world, but also to exercise their control over it. In this sense, epistemology is never, as the authors notice, “merely descriptive” (p.4), but crosses other dimensions of the human life, such as the moral, social and political one. The fact that people’s epistemic conduct is still deficient in many ways becomes, therefore, one of the main concerns at the basis of Robins and Wood’s work (2007), which aims at bringing epistemology back to the practical world while showing that the acquisition of epistemic goods is never a matter of pure science, but also of character.

Analogously, the scope of my research is not to provide a theory of epistemic justification in the context of TAR. It rather aims to help filling the gap between epistemic failures on one hand and their normative implications on the other hand, as well as to shed light on the potential that the cultivation of better intellectual practices discloses to this regard. It is in this sense that the proposed VE theoretical framework for TAR should be read.

A responsibilist account

Intellectual character traits and the challenges of TAR

Following the literature, in the account of VE I propose in this section, I will intend epistemic virtues in a responsibilist sense, as ‘best intellectual character traits’; this choice does not correspond to a rejection of the notion

of reliable virtue in ontological terms, but to the fact the responsibilist account of epistemic virtues can better meet the epistemic and moral challenges of TAR for the reasons I will explain hereafter.

First of all, responsible epistemic virtues - as argued by Baehr (2011) - are better suited to explain complex forms of knowledge, that require more than 'mechanistic' capabilities such as those embodied by reliable virtues (p.52); as mentioned in the introduction to this chapter, while reliability is a passive feature (a computer can have an excellent reliable memory, higher forms of knowledge require more than a well-functioning innate faculty in order for the knower to formulate justified beliefs (p.51); there are indeed some fields of knowledge in which the achievement of truth is less straightforward - and this is exactly the case of TAR.

Here, the achievement of translational success depends - to different extents - on intellectual attitudes, which cannot be entirely identified with the possession of cognitive capabilities, but require "the possession of certain intentions, beliefs, and desires" (Baehr, 2011, p. 53); for instance, the design of a research model might require attentiveness and inquisitiveness, while, on the other hand, the acknowledgment of fallacies in the same design might require an act of open mindedness and intellectual humility.

Moreover, the interdisciplinary character of TAR suggests that such a field is not exempt from the challenges of every interdisciplinary research, among which the lack of a common 'language' between disciplines or, more exactly, of a shared epistemology (in a traditional sense). As noticed also by Seyhan (2019), the ability to successfully innovate in translational science is strictly dependent on the interactions and the feedback coming from a multiplicity of sectors, public - such as academia and government - and private, like industries (p.3). This consideration points at the role that intellectual attitudes - such as intellectual flexibility - might play in the

attempt of finding common grounds for proficuous collaboration among fields.

Although the responsibilist definition of epistemic virtue seems to respond better to the kind of intellectual traits that would be relevant in TAR, reliable virtues can still play a secondary or complementary role. For instance, let us consider a person with an excellent memory who is called to conduct a fair discussion on attrition rates of Alzheimer's treatments; she will probably easily recall those important figures and facts read in scientific papers that must be considered in order to provide a clear understanding of the topic. Similarly, excellent reasoning capabilities (such as the one of inference) will help the same person to draw acceptable conclusions on the basis of her analysis.¹⁴

Agency and responsibility

If responsibilist epistemic virtues are conceived as intellectual character traits or, in other words, attitudes which imply the holding of "intentions, beliefs and desires" (Baehr, 2011, p.53), then: (1) epistemic virtues can be acquired and perfectionated as much as character traits, through habit and education; (2) epistemic virtues are relevant for ethical discussion (de Bruin, 2013, p.585), because of (1) and because their exercise is always the result of an active choice of the subject.

The sorts of virtues which would be relevant to TAR seem to respond to these characteristics. The reason is that the discussion on TFs in TAR, as seen in the introduction, touches an epistemic but also a normative dimension, which could not be addressed by means of epistemic virtues if

¹⁴ Baehr (2011) argues that responsibilist and reliabilist virtues are interrelated and somehow inseparable, since "an exercise of character virtues is sometimes (perhaps always) manifested in and partly constituted by an operation of faculty virtues" (p.58), as in the examples provided above.

the margin of agency of the knowing subject, in terms of acquisition, improvement and practice, was minimal. Probably the best example to show how epistemic virtues require an act of choice is intellectual courage. In the context of TAR, intellectual courage could play a positive role when the selection of a particular animal model for a certain experiment is mostly due to contingent circumstances such as its familiarity within a certain research group/field. Not only, in fact, is ‘thinking outside the box’ the result of intellectual creativity and flexibility; in such cases, the researcher who ‘thinks outside the box’ needs to show a certain amount of determination to challenge established practices. Moreover, in critically confronting the epistemic heritage of a research community, one might be epistemically cautious and wonder to what extent one’s own contribution would be an advancement towards the acquisition of epistemic goods.

This notion of intellectual virtue cannot be detached from a conception of the epistemic subject as active cognitive agent, which virtue responsibilists such as Code have placed at the center of their account. While reliability, in fact, can be regarded as a passive feature (a knower is reliable if she records an experience with accuracy without interfering with it), on the contrary, according to Code, a subject has a great margin of freedom in deciding how to structure her knowledge; and, if we assume that a knower or believer is a cognitive agent, then we must also assume that she has responsibility over her cognitive choices or epistemic actions¹⁵ (Code, 1987, p.39,40). In other words, the cognitive agent view as formulated by Code implies that being able to decide when and if to exercise an epistemic virtue makes individuals responsible for their epistemic choices and their consequences; but also, as will be argued by Montmarquet (1987), it implies that being epistemically responsible means to do one’s own best to achieve

¹⁵ “Epistemic actions are actions which result in our gaining knowledge with respect to a particular proposition” (de Bruin, 2013, p.587)

the epistemic goods (p.483.). Attaching the notion of responsibility to the one of epistemic virtue is particularly important to the present discussion, since epistemic failures in TAR - as result of epistemic choices - bring about consequences that are normatively relevant.¹⁶

Motivation

As in almost every account of virtue responsibilism¹⁷, in the present framework motivation occupies a primary role. Motivation is what - in the phenomenology of intellectual virtues - enables the performance of virtuous intellectual character traits and is usually identified with the love or desire to acquire epistemic goods.

Indeed, it seems *prima facie* obvious that the epistemically virtuous subject will act virtuously out of intrinsic motivation instead of coercion. Let us suppose that Jack has written a very influential and successful article with the mere scope of increasing his own prestige within the academic community. In this case, no one would intuitively say that Jack is epistemically virtuous, since he lacks that proper 'motive' that would lead him to the performance of all a series of virtuous behaviors which are now prevented by his personal interests. It could be argued that the motivation requirement of epistemic virtues sounds very strict or even unrealistic, since in real life people have mixed motivations for undertaking certain actions. Jack, for example, might be interested in growing in his career and, at the same time, interested in acquiring knowledge through his studies. Indeed, if Jack had mixed motivations for writing his article he would still

¹⁶ This point will be further discussed in argument 3 of chapter 2.

¹⁷ In her *Virtues of the Mind* (1996), Zagzebski establishes two features that characterize the notion of epistemic virtue with respect to truth achievement. The first is motivation (*motive*), or the emotional side of a virtue, which she regards as fundamental in the performance of an epistemically virtuous action. In the intellectual realm, the motive corresponds to the love for truth or, as she puts it, the desire for a "cognitive contact with reality" (p.270.). According to Zagzebski, then, without the presence of a motive, the *prima facie* epistemically virtuous subject would not be able to properly achieve knowledge (167).

be virtuous without contradicting the motivation requirement, for his love for knowledge would motivate him to be inquisitive, to acknowledge the weaknesses of his arguments and be open-minded about competing views. However, if Jack's motivation was *only* instrumental, it would be hard to see how he could be virtuous consistently. In fact, epistemic virtues are not put in practice occasionally or only under certain convenient circumstances. They are rather traits that become fundamental parts of the identity of an epistemic agent, and sometimes they might even require the sacrifice of some putative personalistic goals.¹⁸

Therefore, only the genuine appreciation of knowledge and the desire for its acquisition, - in general, for the acquisition of epistemic goods - can be considered as proper triggers of other epistemic virtues. .

Epistemic success

Jack's case showed how motivation is important to the definition of the notion of epistemic virtue; however it is still not clear how the reverse scenario - where Jack is properly motivated to the acquisition of epistemic goods but does not succeed in it - should be read. This point - the one of epistemic success - is quite relevant to virtue (epistemology) theories, especially with regard to the influence of external circumstances such as environmental and structural factors on several aspects of human life.

According to Zagzebski (1996), success is one essential feature of epistemic virtues; that is to say, Zagzebski maintains that from an act of intellectual virtue it always follows the acquisition of some epistemic goods - such as knowledge, understanding and truth - and without such a successful result, the subject in question could not be considered, properly

¹⁸ The problem of how an epistemic agent can be intrinsically motivated to acquire some epistemic goods in such a way is discussed in the Argument 2 of Chapter 2.

speaking, epistemically virtuous.¹⁹ While the statement is somehow intuitive, as we would expect a virtuous agent to be more successful at inquiring than one who is not, making epistemic success a necessary condition for the existence of epistemic virtues is here quite problematic. In particular, it would mean the exclusion from the virtue domain of a plurality of cases where circumstances that are beyond the subject's control obstruct the successful achievement of epistemic goods, although the subject has given proof of virtuous (intellectual) behavior. This objection, however, does not correspond to the refusal of the notion of epistemic success in relation to epistemic virtues, but it breaks the necessary bond between the two by admitting the possibility of unsuccessful results while limiting them to circumstances which cannot be ascribed to a deficiency of the intellectual dispositions of an epistemic subject. Following Baehr (2007), the motivation or desire to achieve certain epistemic goods is what guarantees the nexus between epistemic success and intellectual virtues. In other words, the strong desire of reaching the truth, which must accompany a virtuous person, provides sufficient ground to believe that virtues will lead to success (p.468).²⁰

This conception of epistemic success is particularly relevant in the case of TAR, where, as argued in the introduction, structural constraints

¹⁹After motivation, the second requirement of Zagzebski's notion of epistemic virtue is *success*. In her view, the possession of a certain epistemic virtue must result in the achievement of its respective epistemic goal(s). In practice, for Zagzebski the motivation of an epistemic agent to achieve the truth through an act of intellectual inquisitiveness in the context of an investigation is a necessary, but not sufficient condition to define an epistemic agent virtuous if his investigation leads to unfruitful results. Starting from these premises, Zagzebski concludes that "Knowledge is a state of true belief arising out of acts of intellectual virtue" (Zagzebski, 1996, p.271).

²⁰ Baehr (2007) extensively discusses the notion of epistemic reliability of moral and intellectual virtues to conclude that while reliability does not essentially belong to the notion of virtue per se, it is concomitant to it. Here Baehr distinguishes between two types of reliability: a) categorical, which stays for universal reliability; b) indexical, or reliability only in certain sets of environments or circumstances, and concludes that only the second can be regarded as a necessary feature of virtue (pp. 468, 469).

could play an important role - as facilitators or obstacles - to translational success, regardless of the intellectual dispositions of individual researchers. Let us consider the following example: animal experiments are *de facto* still a mandatory step of many drug approval processes, while pre-clinical research for drug development might - depending on the cases - be entirely conducted *in vitro* on human biological material. In such situations, TFs might occur paradoxically as the result of untranslatability of human results to animals for the same interspecies differences that affect translatability from animals to humans. It is clear that in the present circumstance, even the most virtuous researcher, who, as a result of her inquisitiveness and open-mindedness chose to use the best research model for her research, has no margin of agency in the etiology or avoidance of the translational failure. This is the reason why the proposal to read TFs through the lenses of VE can be applied only to epistemic failures, excluding all those cases where structural constraints play a primary, decisive role (Cf. Fig.1).

Epistemic imperative

One of the main topics that has kept philosophers busy for thousands of years is the problem of how to recognize a certain character trait (moral or epistemic) as a virtue. Indeed, both reliabilists and responsibilists rely on lists of virtues which should grant the achievement of certain epistemic goods thanks to their reliability or due to the fact that they allow us to become responsible knowers. However, no universal criterion has been identified for the identification of a virtue as such if not throughout its analysis and application to particular cases which would 'test' the trait in question. This problem has been treated by Elzin (2013), who suggests that Kant's categorical imperative, when transferred to the epistemic domain, could function as such a criterion. Although the identification problem is not *per se* particularly relevant to our discussion of epistemic virtues in

TAR, the solution offered by Elzin (2013) is. By arguing that “an epistemic agent should believe only considerations that she could advocate and accept as a legislating member of a realm of epistemic ends” (Elzin, 2013, p.144), she provides a) a criterion for agreement among the members of a certain epistemic community on what epistemic actions could count as virtuous and b) a way to promote the collective achievement of epistemic ends. Elzin’s ‘epistemic imperative’, implies that one’s own epistemic commitments work in the epistemic arena only if they can be shared by agents who are equally committed to the achievement of the same epistemic goods (Elzin, 2013, p.144). In this perspective, epistemic virtues in the responsibilist sense are rather mandatory attitudes in this process of ‘universalising commitments’, as “legislators of the realm of epistemic ends” cannot merely suppose that their stances are forever valid or acceptable by their fellow members, thus requiring a permanent, stable disposition towards those intellectual character traits (such as love for knowledge, open-mindedness, intellectual humility) that satisfy the epistemic imperative (p.145).

Moreover, the epistemic imperative reflects the responsibilist idea according to which knowledge is not something that happens in isolation in the mind of a certain subject, but that our structural cognitive interdependence makes knowing and acting epistemically social and collective enterprises (Code, 1987, p.48). The universal requirement of epistemic virtues guarantees that people that have different expertise - such as in the case of the variegated research community involved in TAR (including the ethical boards that assess the acceptability of animal experiments) - can nonetheless “share background beliefs, methods, standards, and goals” (Elzin, 2013, p.146).

Conclusion

In this chapter I presented the salient features that characterize the notion of epistemic virtue when applied to the context of TAR. On the basis of the literature, I have proposed to read epistemic virtues in a responsibilist sense, as best intellectual character traits. The main advantage of virtue responsibilism is to have conceived the epistemic subject as a responsible cognitive agent, whose epistemic choices have an impact on the outcomes of her epistemic activities. This notion of epistemic virtue is particularly relevant since: a) it explains how epistemic failures can be the product of non-optimal intellectual choices ascribable to epistemic agents and b) it suggests a way in which the epistemic agents can work on their cognitive habits to mitigate such failures. Within this framework, the characterization of epistemic success as an unnecessary requirement of virtue explains how translational failures are not always attributable to individual attitudes. Furthermore, the epistemic imperative provides ground for a universalization of the virtues as standards of behavior within a certain epistemic community (the one of TAR) that shares the same epistemic ends (successful translation).

CHAPTER 2

WHY VIRTUE EPISTEMOLOGY?

In this chapter, I will discuss the three main arguments that support the application of a VE framework, as introduced in the previous chapter, to the problem of epistemic failures in the context of TAR. The three arguments, and relative objections which I present, aim at showing how the VE framework designed in the previous chapter has the potential of addressing one of the most relevant but problematic dimensions of epistemic failures: the one where the cognitive choices of epistemic agents are epistemically and normatively relevant at the same time.

In argument 1 I will discuss two ways²¹ in which epistemic virtues are linked to morality and how they can: a) facilitate the practice of ethical decision making in the assessment of animal experiments and b) contribute to the pursuit of the moral ends of TAR. In argument 2 I will show that the practice of epistemic virtues - intended as standards of behavior of an epistemic community - is relevant and required when structural constraints play a *partial* role in the etiology of TFs. Finally, following Montmarquet (1987) and Cusimano (2012) I will argue that addressing the epistemic causes at the basis of TFs by means of epistemic virtues is a matter of epistemic responsibility. Since the notion of epistemic responsibility is applicable to every epistemic agent, here I will argue that, *a fortiori*, it should be binding for individuals who conduct research related activities

²¹ While the first part of the argument is mine, the second one has been formulated by Baehr (2011).

Argument 1

The practice of epistemic virtues can contribute to better moral practices

The first and maybe more obvious reason why we should start considering the role of epistemic virtues in the achievement of translational success is that the exercise of excellent intellectual character traits can lead to better intellectual and moral practices. Firstly, it has been established that epistemic virtues are intellectual character dispositions which are directed to the pursuit of certain epistemic goods, among which truth, understanding and knowledge. In this sense, epistemic virtues have the function of guiding the subject towards excellencies of the mind, which should translate, in turn, in best epistemic practices. As an example, the formulation of a good hypothesis in a study (the outcome) is the result of a literature review, which has been conducted with attentive inquisitiveness (the epistemic virtue).

In the previous chapter, the notion of epistemic success has been discussed with regard to whether it can be considered an essential feature of epistemic virtues or not. I have argued that while epistemic success is not a necessary feature of epistemic virtues, it is linked to them through the notion of motivation. Epistemic success, in fact, is not just an accidental byproduct of virtuous behaviors, but the natural consequence of a desire for knowledge, which, nonetheless, might be undermined by external circumstances beyond the subject's control. Following this line of reasoning, it is possible to see a stable connection between epistemic virtues and epistemic success, which grounds the claim that epistemic virtues lead to better intellectual practices. Similarly, by leading to epistemic success, epistemic virtues also facilitate our moral reasoning by reducing the margin

of uncertainties - which might be the result of poor knowledge -in moral deliberations. For instance, when deliberating about the moral permissibility of an animal experiment in the context of a translational study, we are often confronted with limited knowledge on methods and information about previous studies, while this knowledge would contribute to the capability of predicting results and, therefore, making a more accurate assessment of harms and benefits.

The second important consideration on the link between epistemic virtues and moral practice is offered by Baehr (2011). While his argument is deliberately designed to provide an account of the distinction, if any, between epistemic and moral virtues, it also clarifies the nature of their relationship, thus - although indirectly - suggesting a way in which epistemic virtues might lead to better moral practices.

The key idea of Baehr (2011) is that epistemic virtues have a self-oriented dimension, since they benefit, at least in the epistemic sense, the one who possesses them (p.214). The typical case would be the one of a brilliant scientist who is epistemically virtuous - he is intellectually careful, patient and open-minded - but, at the same time, he is interested only in his career and intrinsically careless towards other people's wellbeing. In this sense, the practice of epistemic virtues is primarily directed at benefitting the epistemic subject towards, for instance, the social recognition that might derive from a successful career or the satisfaction of one's own curiosity. However, Baehr argues that epistemic virtues can have, similarly to moral virtues, an "other-regarding' dimension" (p.216). In fact, if the supposed scientist was to be epistemically virtuous with the goal of creating a life-saving vaccine or sharing his knowledge with other people to improve their lives, then we could see how the practice of epistemic virtues intersected the moral domain; it is in this sense, that Baehr maintains that

“the traits in question are moral as well as intellectual virtues” (Baehr, 2011, p.217). That said, it should be clear that the possess of epistemic virtues does not necessarily implicate the possession of their moral counterpart, as the “other-regarding’ dimension” of epistemic virtues is only a particular subset of them, which does not perfectly coincide with the full category (p.219).

In the case of epistemic failures in TAR, it seems clear that the practice of epistemic virtues in this second, particular sense - namely their being directed at others - might contribute to better moral practices and, therefore, to the achievement of TAR-related moral goals. For instance, designing a good animal experiment requires the performance of certain epistemic virtues. Such virtues can be certainly directed at the acquisition of epistemic goods such as an improved understanding of the mechanism of a pathology, the possible discovery of a new drug etc. However, in the same scenario, the practice of epistemic virtues contributes to non-epistemic ends, when carefulness, attentive inquiry and other virtues are directed to the design of the best research model, both for animals and for humans who will have to participate in clinical trials or future patients.

Since the pivotal role given to motivation in the definition of epistemic virtue and its link to epistemic practice and success, it might be counter argued that VE does not concretely explain how it is possible that someone is motivated to act virtuously (in the epistemic sense). This objection seems to be particularly valid in the light of empirical research on human behavior and heuristics, which shows that people tend to stick with their consolidated beliefs regardless of evidence, a phenomenon also known as confirmation bias (Kaanders et al., 2022).²² De Bruin (2012) addressed this

²² Kaanders et al. (2022) lean on previous studies on confirmation bias to show that bias exists even in the way people gather information. Specifically, it is proved that: a) people collect information on the basis of their prior beliefs, determining their future choices and causing “a continuous cycle of belief reinforcement that can be hard to

problem - also known as the situationist critique of virtue (epistemology) theories - in his application of epistemic virtues to business ethics, noticing that a “behavioral economics approach” (in his case) is needed to link motivation to epistemic actions (de Bruin, 2012, p. 586). Analogously, research has shown that cognitive biases are widespread where we would not expect them to be, namely in scientific research, commonly thought as the cornerstone of objectivity (Gao, Z., 2020).²³ This problem of cognitive bias is also the reason to apply the VE framework to epistemic failures in TAR. Therefore, the situationist objection could be rephrased here as follows: given that epistemic virtues might function as a therapy for epistemic failures by leading to better epistemic and moral practices, how can we ensure that motivation actually plays the role claimed by VE without disregarding empirical evidence? How do we actually come to be more responsible knowers?

An interesting proposal to this question has been advanced by Iizuka (2018), who argues against the situationist critique of VE by showing that motivation is a powerful driver of human desirable behaviors. According to Iizuka, social psychological studies which claim to have refuted the empirical plausibility of VE have merely shown that most people are not virtuous, while falling silent on the empirical (in)adequacy of virtue theories (Iizuka, 2018, p.2317).

In particular, he argues that we come to the achievement of certain valuable ends when our character dispositions are formed out of *intrinsic*

break”(Kaaanders et al., 2022, p.15); b) this mechanism is widespread and applies also to beliefs that do not have an immediate impact on people’s lives (p.13).

²³ Gao (2020) analyzes a series of common researchers’ biases and highlights the pervasiveness of such a phenomenon. While some researchers’ biases are unconscious - such as confirmation and sampling bias (pp.31,32) - others depend on the socio-cultural context in which researchers operate (p.33). In this framework, it is evident how, for certain aspects, the analysis of translational failures in TAR is a particular subset of the broader problem of objectivity in science.

motivation - namely the motivation to do something because it is regarded as inherently desirable or interesting (similarly to a passion). In other words, intrinsic motivation can lead to higher performances compared to its extrinsic counterpart, emphasizing the role of our consideration of a certain activity to our behaviors and the achievement of desirable goals (Iizuka, 2018, p.2321). To substantiate his claim Iizuka (2018) reports many examples of studies conducted in the field of sports and education; in the last case, subjects that were self-determined to study or to participate in school activities have shown to be more consistent in their study paths (pp.2324,2325).

Related to the main issue of my thesis this entails that the fact that motivation is an essential component of epistemic virtues and that it identifies with the intrinsic desire of acquiring certain epistemic goods, such as knowledge (Cf. Chapter 1), means that subjects who are intrinsically motivated to, for example, understand the cause of a certain disease, will perform better at the activity while showing better intellectual character traits. Furthermore, Iizuka (2018) notices that the cultivation of these character traits that emerge out of intrinsic motivation corresponds to the process of virtue acquisition, where the value of a certain activity becomes a stable part of the subject (p.2326).

A further legitimate objection to the idea that motivation is *de facto* a trigger of epistemic virtues regards is the following: given that intrinsic motivation manages to have the essential role that VE claims in epistemic practice, how do we ensure that a subject is intrinsically motivated? Social psychological studies show that it is not self-evident for people to be virtuous. Knowing that their intrinsic motivation can make them so does not mean that they are automatically motivated to become virtuous.

A way to tackle this problem of how to encourage motivation in epistemic settings would be to appeal to a consolidated concept of virtue theories, namely the role of mentorship in leading people to perfectionate their cognitive habits. As argued by Resnik (2012, cited Wocial, 1995; Institute of Medicine, 2002; Anderson et al., 2007; Wright et al., 2008), research has shown that mentorship is a particularly successful educational resource to vehiculate rules of ethical conduct in scientific research. In fact, while formal education is usually focused on showing in theory what principles to apply in research practice, the mentor shows what it is to be a good scientist through her professional behavior, stimulating the acquisition of the same traits by imitation (Resnik, 2012, p.7), while limiting the cognitive effort. Although the discussion on mentorship in research practice has been focused mostly on moral character traits to promote research integrity, the analogy between responsible epistemic virtues and moral virtues allows the comparison. Roberts and Wood (2007) dedicate an entire section to the role of models in the development of intellectual autonomy, arguing that while modeling is definitely a crucial part of the development of every individual, autonomy in epistemic practice consists in recognizing good models and incorporating those excellencies that they represent (pp. 267, 268). Defining what a good model is goes beyond the scope of this study; however, providing good models in TAR could be considered a strategy to encourage the development of epistemic virtues in research environments, with the scope of supporting better epistemic and moral research practices.

Argument 2

Epistemic virtues address the epistemic causes at the basis of TFs, even when these are intertwined with structural ones

The second reason why VE is significant to the issue of epistemic failures in TAR, is that epistemic virtues can address the multiplicity of epistemic causes, even when they are only partially contributing to the onset of TFs.

As discussed in the introduction, the phenomenon of translational failures in translational animal research is related to a multiplicity of factors, partially ascribable to individual's intellectual attitudes such as cognitive biases, which have been conceptualized as epistemic failures. However, some TFs cannot be fully reduced to this category nor to the one of structural constraints, since they are the product of the intersection between epistemic and structural causes at the same time (cf. Fig.1). This implies that in such cases individuals: a) are still given a margin of agency, granted by the practice of epistemic virtues; b) they are contemporarily limited by external factors. Here I claim that epistemic virtues, when applied to the intersection domain, can lead to excellent epistemic practices while causing little shifts in the structural pattern on the basis of the epistemic imperative (Cf. Chapter 1).

To show how this principle might work in practice, let's consider the following example: Tom is a PhD student who has long worked on an animal cancer model with his research team and they are now ready to publish the results of their study; this publication is very important for Tom, as it is the last of the three papers he is supposed to publish in top journals to obtain his PhD degree. However, before the final submission Tom realizes

that the data they used to compare the anticancer drug toxicity for their animal model²⁴ contain an important statistical error, which, when corrected, shows that their animal model has no predictive value. Now, Tom could bring up the problem to the research team, and, depending on the research culture of his department, expect the following scenarios: (1) first, that the study is submitted for publication anyways and without any correction; (2) second, that the study is not published, with consequences for Tom's PhD degree; (3) third, that the study is corrected and submitted with negative results, although it is known that the journal they are submitting to is probably not willing to publish negative results. Alternatively, Tom could decide not to act, which would certainly lead to scenario (1).

In this example, publishing bias, academic pressure and the research culture of Tom's department are certainly important element which might play as constraints to Tom agency, since he might be led to comply with the system in order not to face unwanted consequences for his studies. Even in these circumstances, however, Tom does have the option to act alternatively; the choice of an alternative option - in this case -would be a necessary result of an act of epistemic virtue.²⁵ It might be good to remind here that epistemic virtues intended as intellectual character traits, in fact, require an intentional activity of the subject (cf. Chapter 1).²⁶ In other words, the practice of epistemic virtues in situations akin to the one affecting Tom implies that Tom has had the option of doing otherwise. This, nonetheless, does not imply that every time that Tom finds himself in a similar situation

²⁴ The scenario is based on Matthews (2008) study-case review of the poor published evidence of predictive value of certain animal models (p.97)

²⁵ This does not mean that Tom can choose to report the mistake out of unawareness of the consequences or because forced to by his best friend. But, if Tom was a virtuous agent he would certainly report the mistake.

²⁶ Epistemic virtues increase the margin of (epistemic) agency of the Tom in the attempt to avoid epistemic failures, since Tom has control on the belief that data is incorrect, takes responsibility for it and acts consequently.

he has to make an active choice between option A or B; on the contrary, the epistemically virtuous agent will tend to act virtuously out of habit and choose the option that leads to the acquisition of real epistemic goods and the avoidance of epistemic vices.

In Tom's example, choosing to report the mistake could follow from an act of intellectual autonomy or intellectual courage. When the practice of such epistemic virtues leads to epistemic success, one could argue that the structural pattern that would contribute to the perpetuation of TFs is somehow tackled: in the contingent, practical situation in which Tom finds himself, he manages to consolidate a character trait that makes him an active supporter of a different academic culture.

In this case, however, the influence of intellectual character traits on structural causes can be minimal or still too weak, although not void. One could legitimately counter argue that again VE fails the 'empirical challenge' as it is not clear how in practice the epistemic community would come to the acquisition and the practice of epistemic virtues in a way that they could have significance beyond the individual dimension (Tom is virtuous despite the hostile environment) and undermine consolidated structural patterns that are still within Tom's reach (the virtuous epistemic community of which Tom is part changes the hostile environment).

To answer this objection, I will refer to the notion of epistemic imperative as explained in Chapter 1. According to the epistemic imperative, the fact that the practice of epistemic virtues must respond to a criterion of universality, implies that if epistemic virtues were seriously adopted as standards of behavior within a certain epistemic community, they could potentially determine large-scale changes in that part of the structural panorama - in this case, the academic culture - where their

practice is still particularly relevant. To come back to Tom's example, finding a statistical mistake and reporting it as a result of virtuous behavior, is - in our VE framework - what every responsible epistemic agent would and should do in a similar situation, thus reflecting an academic and research culture where the quality of the results is privileged over the quantity while contributing to its maintenance.

Therefore, in the prospected optimal situation an epistemic community comes to agree on the adoption of some virtuous intellectual character traits, as the result of a serious commitment of all its members to the attainment to certain epistemic standards and the achievement of epistemic goals. In so doing, they shape an environment which is favorable to the practice of epistemic virtues and where individuals like Tom will make their epistemic choices accordingly.

Argument 3

Virtue epistemology addresses the implicit normativity of epistemic failures through the notion of epistemic responsibility of researchers

The third and last argument addresses a key normative issue at the heart of every scientific research practice, namely the problem of epistemic responsibility, or the idea that people can be held accountable for their beliefs and the implications of such an idea for the concept of moral responsibility.

In the introduction as well as in other passages of the text, it has been claimed that a consistent part of translational failures in TAR could be reconducted to intellectual attitudes and that bringing intellectual attitudes to their excellences would contribute to mitigate the pervasiveness of

epistemic failures in TAR. At the same time, the choice of a responsibilist notion of epistemic virtue (Chapter 1), implies not only that (1) epistemic agents should, through the acquisition and practice of epistemic virtues, become responsible epistemic agents, but also that (2) they *can* - in principle and in practice - be held responsible for their epistemic activities.

As far as points (1) and (2) concerns, it is inherent to the formulation of responsibilist VE- as discussed in Chapter 1 - that epistemic responsibility occupies a primary role in the account of knowledge. Being epistemically responsible means - as suggested by Code (1984) - to be active in the quest for knowledge and to make cognitive choices (pp.39,40); but also, as suggested by Montmarquet (1987), to be motivated and do one's own best at reaching the truth and avoiding the falsity, just as a morally responsible subject would do her best to avoid bad actions and pursue good ones (p.483). In this sense, for Montmarquet epistemic responsibility coincides with what he claims to be the highest epistemic virtue, namely epistemic conscientiousness. However, it follows naturally from Montmarquet's definition that being responsible in an epistemic sense requires more than this general although necessary commitment to the achievement of epistemic goods. Eventually, epistemic responsibility must be actualized through the exercise of other auxiliary (and sometimes joint) epistemic virtues (e.g.: open-mindedness, intellectual courage etc.). which - as shown throughout various examples in the text - are specific and apply differently according to the situation.

In this light, there is a sense in which epistemic failures in TAR are all due to lack of epistemic responsibility, intended broadly as shortage of 'activity' and 'conscientiousness'. Let us consider the following examples: first, a failure in formulating a good hypothesis for an animal experiment could be read as poor intellectual perseverance. Second, the tendency to

illegitimately exaggerate the potential future applications of findings of animal experiments, on the other hand, could be due to a lack of intellectual humility. In both cases, epistemic failures derive from a shortage of motivation in doing one's own best to the achievement of the epistemic *desiderata*.

A second point that has been characterizing the account of VE presented in chapter 1, is that while not every kind of knowledge is the product of epistemic virtues in the responsibilist sense, high-grade, interdisciplinary knowledge such as the one required in TAR, is linked to the practice of such epistemic virtues, which make us responsible knowers. Now, considering that epistemic virtues have been proposed as a mitigator of epistemic failures in TAR, and that such failures are problematic also in a normative sense, is there a way in which a broad concept of epistemic responsibility as described here can be related to the one of moral responsibility? Or, in other words, in what way how we should know something (epistemic responsibility) has an impact on the way we should act (moral responsibility)?

Montmarquet (1992) manages to elucidate the nature of this relationship in singular terms by arguing that an agent can be held accountable for a certain action when she can be accountable for the beliefs that produced that action (p.332). This type of responsibility is called doxastic, a sort of intermediary concept between epistemic and moral responsibility (pp. 332,333) . To clarify how it is possible that a certain agent is responsible in the (doxastic) sense, Montmarquet (1992) explains that the agent in question must be in the position to revise her own beliefs, to scrutinize them before reaching conclusions about their validity and such scrutiny consists exactly in the performance of intellectual virtues (pp. 335,336). As a consequence, being epistemically responsible - namely

exercising epistemic virtues with the goal of doing the best in order to reach the truth - is guarantee of moral stature, regardless (for the reasons explained in Chapter 1) of the result of one's own actions.²⁷ In this framework, moral responsibility for epistemic failures is not given only when everything has been done to avoid them, in terms of good methodology, experimental design, hypothesis formulation, implicit bias and so forth and, in the process, epistemic virtues - starting from conscientiousness to its auxiliaries - have been exercised.

Now, one could counter argue that if it is true that responsibility as a moral concept always implies an epistemic condition (I am responsible for x , only if I am aware of the consequences of x), this kind of epistemic control implied by the notions of epistemic and doxastic responsibility is way more than mere awareness. Montmarquet's idea of having one's own beliefs and character traits always under check to avoid accountability in akin situations is a very strict, almost unrealistic requirement; aren't we asking too much from cognitive agents? The objection is particularly relevant, as it is intuitive that normative requirements (ought to) must somehow reflect what people are able to actually accomplish (can). The objection, in its strongest version, touches on a core issue of epistemic responsibility, namely the extent to which people's beliefs are voluntary. Although an exhaustive discussion of the objection is beyond the scope and space of this study, Montmarquet's argument is important for us, since it reflects the idea that there is a range of epistemic activities that people can engage with in order to self-determine their beliefs. The same idea is defended by Cusimano (2012), who argues that our beliefs are affected by voluntary actions such as "search for evidence, talk to our friends, consult

²⁷ I have discuss the problem of epistemic success as part of epistemic virtue in Chapter 1; here, analogously, moral success is not a necessary product of the practice of epistemic virtues although often linked to it.

experts, and so on” (p.47), and to the extent we have a voluntary control over these inquisitive actions, then we have also responsibility for the resulting beliefs (p.52).

The above arguments provide a clear link between epistemic and moral responsibility while limiting the inference of the second from the first to circumstances under the subject’s control. However, it is important to consider that epistemic obligations - such as the cultivation and performance of epistemic virtues - in our case do not apply to any cognitive agent, but to researchers who are professionally engaged in epistemic activities. Therefore, if the suggestion to hold people accountable for actions resulting from bad-formed beliefs seems reasonable, *a fortiori* it is sound to expect researchers to be responsible for the way they acquire their knowledge as well as actions that might follow more than any other epistemic agent (Cf. Mertens, 2021, p. 148).

Conclusion

The aim of this chapter was to show how epistemic virtues can bring together the epistemic and the normative dimensions of TAR. In argument 1 and part of argument 2 it has been discussed how epistemic virtues can contribute to the achievement of non-epistemic ends, such as the normative desirability of successful translation. However, the appeal to the notions of epistemic imperative and epistemic responsibility in argument 2 and 3, showed that if epistemic virtues play a role in TAR as shown so far, then their practice is not only a suggested means to the achievement of some desirable (translational) ends but it is expected and required from members of a certain epistemic community, whose epistemic activities should reflect the normative premises that justify them.

CHAPTER 3

WHAT EPISTEMIC VIRTUES ARE NEEDED FOR TAR?

After having shown that epistemic virtues can and should play a role in translational animal research, in this last chapter I will consider a limited selection of renowned epistemic virtues in the literature on VE that could be applied to our case. Here I will focus on (1) when it is appropriate for a certain intellectual character trait to be considered an epistemic virtue and (2) how the epistemic virtues so described might function as mitigators of epistemic failures in TAR through the analysis of practical examples. As far as point (1) concerns, it might be good to stress that intellectual character traits (like moral ones) are not *per se* inherently positive or negative, but that intellectual virtues represent the excellent counterpart of these same traits. As amply discussed in the VE literature (Baehr 2011; Robins and Wood, 2007), epistemic virtues must on one hand respond to certain general conditions to be considered as such, while, on the other hand, their application requires an accurate analysis of the circumstances in which they come into play, and thus point (2).

In this chapter I will introduce only a limited set of epistemic virtues if compared to the abundance of lists of epistemic virtues that can be found in VE literature and that could be applied to the problem of epistemic failures in TAR. The reasons for this choice are two: first, the scope of the thesis is to show that (and not what) epistemic virtues have a role in TAR; second, the set of epistemic virtues I introduce (love for knowledge and conscientiousness, intellectual humility and open-mindedness) are the most relevant to the discussion of TAR-related problems and represent well how their proper application can make a difference in the prevention and genesis of epistemic failures.

1. Love of knowledge and conscientiousness

Love for knowledge occupies a special position in the pantheon of epistemic virtues; since, in general, it identifies with a *desire*, it is a fundamental (although not the only) motivator of epistemic actions and the basis for the acquisition of other virtues. Roberts and Wood (2007) consider love of knowledge as a “disposition of the will”, or its mature orientation towards evidence-based beliefs and relevant epistemic goods (pp. 154,155). The idea behind their definition, which traces back to Thomas Aquinas, is that not every type of knowledge is equally worthy to be desired and pursued. Indeed, there are certain epistemic goods, which we have reasons to love more and consider as more significant than others. The reason is twofold: firstly, some epistemic goods come with a whole epistemic baggage that increases our knowledge of a certain object x and supports or refutes previous established beliefs; analogously, significant knowledge can expand our understanding of other x related subjects (pp.156,157). Secondly, the authors argue that some epistemic goods are qualitatively superior than others, because they are related to objects which are intrinsically important for human beings (pp.158,159). While I agree with the authors, in our case the set of ‘intrinsically important objects’ includes also those which are not immediately related to our wellbeing but, nonetheless, are normatively important.

Let us consider TAR: here, like in other scientific practices, knowledge is interdisciplinary and interrelated, meaning that preclinical studies, when well-designed, clarify mechanisms of diseases and drugs efficacy in the human body, thus carrying an entire epistemic baggage that contributes to the refinement of previous beliefs and the acquisition of new ones. Furthermore, such knowledge is qualitatively superior to the knowledge that my neighbor goes for a walk every day at noon, because it is oriented to the

improvement of human health, which is worthy to be pursued; but also, the refinement of translational strategies fosters the moral imperative to make sure that the benefits of animal experiments exceed the harms done to animals.

As noticed by de Bruin (2013), love of knowledge is what motivates investigation, while its contrary, namely the lack of love of knowledge, translates into “a failure to perform investigative activities” (p.589). One of the “investigative activities” that has been highly recommended to face the challenges of TAR related to problems of internal validity²⁸ is the use of systematic reviews. As suggested by Hooijmans and Ritskes-Hoitinga (2013), there are several benefits in reviewing and synthesizing existing literature on animal studies: from the unnecessary replication of animal experiments to the evaluation of best animal models and the collection of information about drug safety and efficacy; moreover, systematic reviews highlight biases and methodological inadequacies in study design (pp. 1,2). Therefore, systematic reviews should be encouraged as part of good epistemic practices.

Considering that systematic reviews are complex and long processes, which take up time (up to several years) and require substantial resources (Tsertsvadze et al., 2015, p.2), love of knowledge intended as the desire for evidence-based beliefs (less biased studies) and the mature appreciation of certain relevant epistemic goods (the knowledge required to achieve translational success) is what best motivates and supports the epistemic action of conducting the investigation (systematic reviews). In addition, love of knowledge stimulates the cultivation and practice of other epistemic virtues, which are necessary to epistemic success, such as - in this case - intellectual perseverance.

²⁸ Cf. Introduction.

However, both Roberts and Wood (2007) and Baehr (2013) acknowledge the possibility that, depending on the cases, love of knowledge might not be sufficient to the performance of some epistemic actions. This does not mean that one can be virtuous without loving the epistemic goods, but sometimes, as realistically noticed by the authors, the motivation to persevere in particular tasks of inquiry might fall short regardless of our desire to acquire knowledge. For instance, in our case one might be tempted to conclude a database search of animal experiments too early or to skip chapters of that handbook that provides guidelines for standardized procedures in systematic reviews. In these situations, when love of knowledge fails to function as motivator, the motivation to endure should arise out of duty or obligation towards our epistemic actions; such a disposition is known as intellectual conscientiousness or “the susceptibility to be motivated by the consideration that behaving well epistemically is *required* of us, is what we *ought* to do, is our *duty*” (Roberts and Wood, 2007, p.79). Interestingly, Montmarquet (1987) tends to address epistemic responsibility as a synonym of conscientiousness, that “trying [the] best to arrive at the truth” (p. 483), implying that truth-achievement is - as amply argued in chapter 2- a matter of responsibility, which might require a certain amount of self-discipline when obstructed by internal constraints.

In conclusion, while love of knowledge is a necessary and sufficient element of every virtuous inquiry, intellectual conscientiousness is a necessary additional component in certain circumstances. In particular, in the context of TAR intellectual conscientiousness is required when the original desire that motivates the search of more evidence (e.g.: the clinical relevance of animal models) is blurred by less exciting or ambitious tasks, which are nonetheless fundamental to the achievement of translational goals.

2. Intellectual humility

As has been discussed in the introduction, several epistemic failures in TAR can be attributed to methodological issues. Lack of internal validity has for long been considered one of the main hurdles to the performance of good animal experiments, and the literature is unanimous in concluding that randomization and blinding - as well as better study design and adequate use of statistical methods - should be reinforced (Hirst et al., 2014; Pound and Ritskes-Hotinga, 2018; Seyhan, 2019; Ritskes-Hotinga et al., 2020). Although such research principles are frequently recommended as standards of good epistemic practice, Ritskes-Hoitinga et al. (2020) raise the important question on why there are no major improvements to this respect (p.2). The consequences of weak methodology in animal studies amount to more coherent but less accurate results, whose interpretation and predictability power is misleading and therefore contributes to TFs.

In what sense epistemic virtues can address such problems? Hoekstra and Vazire (2021) have recently argued that intellectual humility, intended as a commitment to putting flaws and uncertainties at the center, should be a core research value in order to increase the credibility of scientific studies and address the so-called “replication crisis” (p. 1602).

Intellectual humility has been defined in several ways in VE literature. Nonetheless, a common feature of different accounts is that intellectual humility is a key element of research integrity. Roberts and Wood (2007) focus primarily on the social aspects of such a trait and its vicious counterparts to argue that the epistemically humble person shows “low dispositional concern for [...] self-importance [...], especially where such concern is muted or sidelined by intrinsic intellectual concerns—in particular, the concern for knowledge with its various attributes of truth, justification, warrant, coherence, precision [...]“ (p.250). The type of

self-importance to which the authors refer here such as social power, arrogance or vanity, might not always explain the type of intellectual disposition underlying epistemic failures in TAR, although the general unwillingness of recognizing one's own fallibility is key in the understanding of intellectual humility.

Therefore, the definition applies to the case if we intend self-importance as the concern in presenting clear, homogenous results and the prioritizing of this interest over transparency and evidence to avoid the acknowledgment of the limitations of one's own work (Hoekstra and Vazire, 2021, p.1602). On the contrary, an act of intellectual humility requires that capability, as Baehr (2011) would say, to contain self deception, namely our tendency "to distort or even block out considerations or evidence within our ken or to fail to recognize logical tensions or inconsistencies among our beliefs" (p.20).

Conscious of the negative consequences of overconfidence and lack of transparency in scientific studies, Hoekstra and Vazire (2021) give suggestions on how to concretely increase intellectual humility when presenting the outcomes of a research in a scientific paper. Regarding the methods, they advise to report all the information that is necessary for the readers to evaluate the choice of a particular method and to provide an accurate description of the study design for a critical assessment of its validity (p.1605). Humility in reporting results is best achieved by distinguishing initial hypotheses and expectations from actual findings as well as by interpreting and underlying uncertainties behind design and statistical results instead of insisting only on their significance and potential future applications (pp.1605,1606).

Their observations are particularly relevant to the case of methodological issues in TAR as sources of epistemic failures. Let us suppose the following scenarios: in scenario A, an intellectually humble

researcher reports positive results in study x but admits that randomization and blinding have not been performed. In scenario B, another virtuous researcher performs randomization and blinding in study y but reports negative results. In both cases, transparent reporting that derives from intellectual humility ensures that the results of studies - even when positive - are not overestimated, thus contributing to avoidance of epistemic failures. Humble epistemic conduct, furthermore, is desirable during the entire research process, from the methodological choices done in the design of a protocol to the presentation of the research outcomes.

As noticed by Ritskes-Hoitinga et al. (2020), the publication of biased results might lead to the performance of unnecessary animal experiments - which should be reduced and replaced instead - and unnecessary human trials (p.8) with the waste of great amount of resources, time and hopes for new treatments.²⁹

Similarly, intellectual humility plays a role in the mitigation of epistemic failures that derive from the same design of animal models. As mentioned in the introduction, it is essential that an animal model resembles a human condition in terms of cause, symptoms and response to treatment to be considered its valid approximation (Tadenev and Burgess, 2019, p.111). Difficulties in the construction of valid models are somehow characteristic of any animal study, since interspecies differences cannot be overcome even by the most well-designed experiment (Pound and

²⁹ Hoekstra and Vazire (2021) also address the problem of external validity, namely the degree of generalizability of the results of scientific studies (Cf. footnote 8)(p.1606). Here the authors recommend that when for contingent reasons it is not possible to apply a strict methodology (internal validity), limitations of external validity are reported in order to avoid the overestimation of the findings. In the context of TAR, we have seen that one of the “insurmountable” hurdles of translational studies - as defined by Pound and Ritskes-Hoitinga (2018) - is the problem of external validity of animal models, which is undermined by profound interspecies differences (cf. footnote 8) and, according to reasoning, should be similarly acknowledged in the discussion of results.

Ritskes-Hotinga et al., 2018). However, Meijboom et al. (2020) argue that such difficulties are more evident in animal studies of neuropsychiatric disorders, where our knowledge of the triggering causes in humans is often limited, and the symptoms may be subjective, varying from individual to individual (p.4). Moreover, as noticed by the authors, while these limitations are acknowledged, “they are rarely discussed within the scientific community” (Meijboom et al.,2020, p.4).³⁰

On the contrary, intellectual humility intended as a high concern for knowledge demands that the limitations of a model are seriously considered in the discussion of its predictive value, especially when uncertainty is high. In this and other similar cases in TAR, the practice of intellectual humility represents an important cognitive starting point not only for the improvement - where possible - of the epistemic reliability of animal experiments, but also for a more informed and evidence-based assessment of their ethical permissibility.

3. Open-mindedness

In the section on intellectual humility it has been shown that the landscape in which TAR operates is complicated by uncertainties regarding the predictive value of animal experiments. Besides methodological bias, however, it is argued that animal experiments are not and probably will never be ideal models of human conditions because of interspecies differences (Pound and Ritskes-Hotinga, 2018), which seriously jeopardize successful translation.³¹ Considering that animal experiments have

³⁰ Given the complexity of assessing the epistemic validity and the ethical permissibility of animal models, Meijboom et al. (2020) recommend to avoid dichotomies and generalizations, but to consider each animal model in relation to the study it serves (p.5).

³¹ As discussed in the introduction (footnote 8) TFs can also be the result of important interspecies differences, which complicate or impede the application of findings of animal studies to humans. In his discussion of the scientific limitations of animal

contributed and still do to the progress of scientific research, especially in those fields where animals cannot be replaced, how should we deal with disagreements and uncertainties on the reliability and predictive power of animal experiments?

Here I shall consider the role of the virtue of open-mindedness in ensuring that assessments of animal experiments are conducted impartially, so that best research (animal or non-animal) models are chosen in the attempt to meet translational goals.

Baehr (2011) gives an account of open-mindedness that applies finely to akin situations, where conflicts between rival positions require that assessments of the two parties are conducted as impartially as possible in order to achieve some epistemic goods (p.149). He identifies the conceptual core of open-mindedness in that capability “to transcend a default cognitive standpoint in order to take up or take seriously the merits of a distinct cognitive standpoint” (p.152), in the context of an intellectual challenge (p.154).

It could be argued that in this sense open-mindedness does not really differentiate itself from intellectual humility, as they both require the temporary suspension of one’s own partisan beliefs or attitudes for the achievement of some kind of epistemic good. However, as discussed by Baehr (2011), open-mindedness requires the capability of actually putting oneself in someone else’s shoes to *seriously* take up their “cognitive standpoint” (p.156) in a context of disagreements. The key core of intellectual humility, on the other hand, consisted in the deviation of

experiments, Akhtar (2015) recalls several cases of unsuccessful clinical trials, whose failures can be reconducted to the poor external validity of preclinical animal models. In all these cases, - such as the research of HIV/AIDS vaccine or the testing of the immunomodulatory drug TGN 1412 - preclinical studies that had been conducted successfully on non-human primates resulted ineffective (in the HIV case) or extremely dangerous for the patients health (in the TGN 1412 case) (p.413). In such and other cases, the use of non-human primates in the preclinical phase led to an overestimation of their predictive value for human health.

concern and attention from the self to knowledge and other relevant epistemic goods. Therefore, although the two virtues are related - as open-mindedness can contribute to and support intellectual humility and vice-versa - they imply two different types of activities (p.157).

In this sense, the virtue of open-mindedness suggests that discussions on the epistemic validity of animal experiments are conducted following some intellectual attitudes that are characteristic of the virtue in question. The first, important implication of the attitude of keeping an open-mind towards a competing position is to give it equal consideration, that is, trying to acknowledge its merits or strong points besides its pitfalls, as one would do with her own position. What are the reasons behind the belief that animal experiments cannot meet the translational challenge? What is the evidence supporting such a belief and how or to what extent such evidence informs the competing position, namely that animal experiments are critical in translational medicine? When one starts inquiring with an open-mind will probably find discouraging, if not alarming, translational and drug attrition rates figures with a variation according to sub-fields. At the same time, one will find that animal experiments are still the only resources in some fields, whether for ethical reasons (such as in behavioral research) or for the impossibility of reproducing *ex vivo* the complexity of a living organism.

As shown above, keeping an open mind in a virtuous sense suggests that coming to generalizations is not an easy task, especially in contexts where complexity is high and inadequate reduction of complexity leads to conceptual loss. One of the main takeaways of virtuous open-mindedness is that assessments of animal experiments need to be conducted on the basis of that retrospective knowledge acquired through a history of failures and successes, while evaluating the explanatory power of animal models and

possible replacements that allow the achievement of translational goals minimizing harms.

The core idea behind the virtue of open-mindedness is that we are attached to our positions exactly because they are ours; we formulate them out of personal or professional experience, education, home environment or, in other cases, out of lack of experience and education. In every case, such cognitive stances receive justification in our minds and set a standard of truth. The virtue of open-mindedness requires that we make the effort of undergoing this same justificatory process with competing positions; while doing that, the position of the other becomes clearer and more familiar, more ‘ours’. In this sense, open-mindedness is a key virtue in mitigating disagreements and preventing debate-polarization.³²

A final relevant feature for the practice of open-mindedness as defined here, is that “keeping the mind open” to competing positions does not correspond to: (1) an undetermined openness or (2) openness to every sort of position. Indeed, there are ways in which being too open-minded (as its contrary, namely being close-minded) can result in bad epistemic practices. In the first case, the openness to other cognitive stances should be contextualized within a particular intellectual challenge (Baehr, 2011, p.154), meaning that the goal of open-mindedness is to come to an informed understanding of a particular topic. Having said that, being open-minded does not correspond to refraining from taking a particular position, but it regards the way in which we come to embrace it.

³² Kaanders et al. (2022) have also shown that overconfidence about one’s own beliefs increases the risk of confirmation bias in information sampling (p.13). Their research adds on previous studies which have proved the role of overconfidence in the formation of extreme political views (Ortoleva and Snowberg, 2015; Rollwage et al., 2018 in Kaanders et al., 2022, p. 13). Indeed, open-mindedness has often been investigated as a civic virtue capable of promoting good citizenship and orienting political thinking (Landemore, 2018; Baron, 2019).

Secondly, not every position counts as equal. Engaging with competing stances is a sign of intellectual virtue only if there are good reasons to believe that such stances are somehow relevant to the achievement of the epistemic goods in question.³³ In our case, TAR is an interdisciplinary practice which requires the cooperation of several researchers, from basic scientists and biomedical researchers to behavioral neuroscientists and clinicians. There are strong reasons to suppose that their cognitive standpoints matter, as one could argue that in assessing the limits to the amount of stress³⁴ for ensuring good translation or the amount of permissible harm in animal experiments the perspective of a veterinarian matters most. Analogously, Ritskes-Hoitinga et al. (2020) suggest that to really improve translational strategies and outcomes the perspective of the patient should be incorporated in the design of experiments from their very beginning, starting with the formulation of relevant research questions. In the same context, they also mention a successful case in the context of the Priority Setting Partnerships project³⁵, where asthma patients were engaged in the preliminary phases of the study. It was found that patients preferred to treat their condition by learning breathing exercises rather than a new drug and the clinical trial that was started on such preferences had positive results (p.7). This is probably one of the clearest examples of how the virtue of open-mindedness - intended as taking another relevant cognitive standpoint into account - can contribute to successful translation in the most desirable way, that is, without unnecessary harm.

³³ “A person S’s engaging in the activity characteristic of open-mindedness under circumstances C is intellectually virtuous only if it is reasonable for S to believe that engaging in this activity in C may be helpful for reaching the truth.” (Baehr, 2013, p.160).

³⁴ Stress that derives from laboratory environmental conditions has been found to be cause of altered physiological parameters (e.g.: hypertension, inflammations) that negatively affect the results of experiments (Akhtar, 2015, p. 408).

³⁵ *About Priority Setting Partnerships | James Lind Alliance*, n.d.

Conclusion

In this final chapter I discussed a selection of epistemic virtues in order to illustrate how virtuous intellectual character traits can, in everyday research practice, facilitate the achievement of TAR-related epistemic and moral ends. Indeed, while in chapter 1 and chapter 2 I have shown that epistemic virtues do and should play a role in TAR on a theoretical level, the discussion of particular virtues aims at implementing the theoretical work to concrete situations as discussed in the literature on translational failures.

Love of knowledge and conscientiousness, intellectual humility and open-mindedness were chosen here because of their relevance in TAR. In fact, each of them addresses some particular causes of epistemic failures and can be applied to a different stage of the translational chain: from the starting of the inquisitive activity with the right motive to the assessment of the adequacy of an animal model in a landscape of complexity and uncertainty.

CONCLUSION

In this research I have investigated the problem of translational failures in the context of translational animal research and proposed that epistemic virtues could play a role in furthering the moral imperative to avoid them and achieve successful translation.

After having defined the scope of my research to that particular subset of TFs which can be reconducted to an individual's cognitive attitudes - namely *epistemic failures* -, in Chapter 1 I proceeded to review the literature on virtue epistemology. The scope of this first Chapter was to design, on the basis of the literature, a theoretical framework that could explain how and in what sense epistemic virtues would function as mitigators of epistemic failures by promoting excellent intellectual and moral practices. The main outcome of this part is the conceptualization of epistemic virtues in a responsibilist sense, as best intellectual *character* traits that should characterize any responsible knower. By conceiving epistemic agents as capable of making choices about their epistemic conduct, virtue responsibilism shows how epistemic failures are often the result of poor intellectual behaviors. Furthermore, although virtue responsibilism focuses on individual's epistemic virtues, it is compatible with the idea that individuals that act in epistemic communities are: a) not always directly accountable for epistemic failures, as epistemic success might be hindered by structural constraints; b) required to prevent epistemic failures by adhering to certain standards of behavior inherent to their epistemic community.

While Chapter 1 already shows that epistemic virtues can play a role in TAR, Chapter 2 constitutes the argumentative core, where it becomes more clear how epistemic virtues can address the problem of epistemic failures in normative terms, thus contributing to the pursuit of successful translation as a moral duty.

Here I relied on the theoretical framework designed in Chapter 1 and relevant literature to argue that: a) epistemic virtues have a positive impact on our moral choices and conduct in two ways: first, they provide solid knowledge on which we base our moral deliberations and second, they are exercised to benefit others, like in the case of TAR; b) epistemic virtues have a normative power when they represent the standard of behavior at which the members of an epistemic community should attain; the respect of this standards is a matter of both epistemic and moral responsibility in their reciprocal relationship, as amply shown in argument 3.

Chapter 3 consisted in the more detailed exploration of some epistemic virtues and their application to practical cases. This shows how epistemic virtues function in the mitigation of methodological problems, biases and overestimation of the predictive value of some models at the basis of epistemic failures. In particular, love of knowledge and conscientiousness should be the source of any investigative activity, as together they provide the right motive to continue such activities, even when they are highly demanding and not immediately rewarding, as illustrated in the case of systematic reviews. Intellectual humility has proven to be a key epistemic virtue in our discussion, since a fundamental part of good methodological practices which would contribute to successful translation is the disposition to acknowledge the limitations of one's own work. Finally, open-mindedness applies to the complex task of assessing

animal experiments, where entrenched positions do not contribute to the improvement of translational strategies. On the contrary, being open to considering alternative positions - such as the one of patients in the design of studies - constitutes a promising approach for the achievement of translational goals through more human-relevant research.

The discussion of particular epistemic virtues presented here is rather limited, as the main goal of the research was to show the general claim that epistemic virtues could be successfully applied to the problem of epistemic failures in TAR, which required the construction of a suitable framework and arguments that supported such application as the main focus. On the other hand, the choice of intellectual humility and open-mindedness resides in the fact that they, more than other virtues, exemplify how to navigate the *complexities* and *uncertainties* inherent to TAR while leaving space for the arduous task of moral deliberation.

However, it could be worth exploring the role of other virtues such as intellectual courage and intellectual autonomy and how they would apply to the third subdomain of TFs, where epistemic and structural causes intersect (Cf. Chapter 2, Argument 2 and Fig.1). Analogously, one could analyze the role of intellectual creativity - an underestimated virtue in VE literature - in conceiving alternative research models in the replacement of animal experiments.

Another direction in which the discussion could develop is less applied and more theoretical and regards the exploration of collective epistemic responsibility in contexts where the prevention of harms can be done only by means of collective actions (Fleisher and Seselja, 2020). Such a perspective could shed light on how mistakes at a certain level of the translational chain regard the entire epistemic community, extending the

discourse on responsibility beyond the individual domain in unprecedented terms.

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