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Luca Chiapperino, 'Environmental Enrichment: An Experiment in Biosocial Intervention', *BioSocieties*, 23 December 2019, https://doi.org/10.1057/s41292-019-00181-5.

Environmental enrichment: an experiment in biosocial intervention

Abstract

This paper reports on ethnographic research conducted in a behavioural epigenetics laboratory working on the transgenerational inheritance of "early-life stress" in rodents. The article describes the experimental steps that lead to the production of an understanding of "stress" as a nexus of molecules and experiences, biological and biographical events. In particular, the paper focuses on the experimental protocol of Environmental Enrichment (EE). EE is a housing regime for experimental animals that the lab employs to correct the "aberrant" epigenetic effects of "stress". The use of EE gets narrated as a therapeutic intervention restoring, within the experimental system of the lab, the centrality of the body as entity endlessly modified by the interactions with its (material and social) environments.

Drawing from these observations, I detail the lab's mixed factual and value-laden work going into the production of a biosocial understanding of "stress". This process, I argue, oscillates between an emphasis on the material, organic and molecular traces of experiences and circumscribed attempts to deal with the biosocial complexities of this phenomenon in experimentation. As such, the practices reported here may be of interest to current STS engagements with post-genomics and the ways it forays into complex thinking of body-environment entanglements.

Keywords

Biosocial; epigenetics; environmental enrichment; early-life stress; laboratory studies.

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Introduction

Epigenetics is one of the most rapidly growing and polarised fields of contemporary biomedicine (Pinel, Prainsack, and McKevitt 2017). On the one hand, it is a major driver of the shift towards post-genomic models of explanations in biology. Epigenetics establishes – or rather revives – the fundamental centrality of biological plasticity and gene-environment interactions for the understanding of diseases and health (Papadopoulos 2011; Fox Keller 2015; Meloni 2018b). On the other hand, epigenetics is also a very polarised domain of biosciences (Meloni and Testa 2014). The field is fraught with radical disagreements around (i) the causal primacy of the genome vis à vis the environment in the determination of phenotypes, and (ii) the temporal frames over which epigenetic modifications extend (Morange 2002; Deichmann 2016). Some postulate that epigenetic effects strongly depend on genetic control and are confined to the temporalities of somatic cellular differentiation (Stricker, Köferle, and Beck 2016). Others hold instead that epigenetic modifications are caused by the embodiment of environmental stimuli (Kanherkar, Bhatia-Dey, and Csoka 2014) and can potentially be passed to future generations (Szyf 2015). Among the latter, some have focused on so-called 'intergenerational epigenetic inheritance', which happens when multiple generations are directly affected by a given environmental exposure (Heard and Martienssen 2014)[1]. Other scientists have instead further explored the transmission of epigenetic marks and postulated that these effects may constitute mechanisms of heredity. This controversial claim (Daxinger and Whitelaw 2010; Isbel and Whitelaw 2015) is also referred to as "transgenerational epigenetic inheritance", and requires that passing a given phenotype across generations is explained by an epigenetic mark being transmitted "even in the absence of the initial trigger" (Choi and Mango 2014, p.1)[2].

This paper reports on ethnographic research conducted in an epigenetics laboratory working on the transgenerational epigenetic inheritance of "early-life stress" in a mouse model. Going under the label of 'behavioural epigenetics', this type of research seeks to explain how gene expression is modulated by experiences and the social environment. These scientists postulate that gene-environment interactions result into patterns of behaviour, cognitive skills, personality traits and

[1] Typically, intergenerational epigenetic inheritance happens through the exposures of a pregnant individual (generation F0) to an environmental stimulus (e.g. a toxin, a pollutant, a nutrient, a stressful situation), which affects the foetus' epigenome (F1) and its developing germline cells, thus having long-term consequences also on the foetus' progeny (F2).
[2] This means that, differently from intergenerational transmission, transgenerational epigenetic inheritance takes place only if the epigenetic effect is passed through the gametes – hence, to a generation not directly affected by the environmental stimulus under study (i.e. generation F3 if we follow the example of footnote 1). Much of the controversy spurred by evidence of transgenerational effects relates precisely to the role of gametes as mediators of such transmission. This idea goes in fact against established views of gametogenesis and early embryonic development, which are taken to entail the complete resetting of parental epigenomes. Only recently transgenerational epigenetic inheritance has found support in a few "robust, paradigmatic examples, which are often specific to particular species or genomic loci" (Burgess 2019, p.3; see also Bošković and Rando 2018 and Perez and Lehner 2019).

mental health (Powledge 2011; Sandi and Haller 2015). Furthermore, the research I follow in this article is a prominent example of those above-mentioned approaches that have spurred much controversy by postulating the possibility of a transgenerational transmission of epigenetic changes (Champagne 2010; Horsthemke 2018). Epigenetics, in the context at issue here, is therefore the study of the molecular events that govern the ways in which nurture (i.e. experiences and the social environment) shapes nature (i.e. the genome of the organism) in ways that may affect health and behaviour across multiple generations.

Beyond the confined space of this and similar labs, knowledge of the traffic between nurture and nature has become a prolific terrain of inquiry and engagement for science studies scholarship. As Margaret Lock has argued, epigenetic researchers add "their considerable weight to [the] claim that biology must be understood as situated to the same extent as are sociohistorical forces" (Lock 2013, p.1897). In fact, epigenetics seems "to complement what has already been gleaned from some psychiatric, psychological, sociological and epidemiological studies"; namely, that biographical and biological "pathways are intensely individual, temporal, varied, contingent and multi-factorial" (Chung et al. 2016, p.180; see Ingold 2004; Ingold and Pálsson 2013). For this reason, several scholars have recognised the potential of epigenetics to enter into conversation with the social sciences for the sake of promoting a plastic and socially situated understanding of our biology (Rose 2013; Niewöhner 2015; Niewöhner and Lock 2018). Epigenetic studies provide a repertoire of knowledge converging with social scientists' attempts to capture how life is neither purely biological nor purely social. In doing so, epigenetics may provide the opportunity to create multiple interconnections across the social and life sciences that go by the qualifying adjective of *biosocial* (Meloni, Williams, and Martin 2016; Meloni et al. 2018a). Overcoming century-old disciplinary boundaries is however fraught with several difficulties. Although post-genomic studies of how bodies interweave with their contexts may contribute to a biosocial understanding of health, several limitations and resistances can be found in the life sciences' renderings of a socially entangled biology. For instance, many authors have recognised how epigenetics reinforces causal narratives that affirm the primacy of "the molecular" over "the social" while at the same time declaring to account for their biosocial entanglement (Landecker and Panofsky 2013; Lock 2013, 2015; Lappé 2016; Meloni 2018b). This reductionist move is, according to several (Meloni and Testa 2014; Meloni and Müller 2018), not devoid of consequences since the "social and political imaginaries" inspired by epigenetics are often oriented towards individual-based and pharmacological interventions (Richardson 2017, pp.29-30). As argued by Jörg Niewöhner (2011), practices of knowledge production in epigenetics are in fact taken in a fundamental tension. On the one hand, epigenetic scientists produce what he calls an 'embedded

body'; namely, a body that "is heavily impregnated by its own past and by the social and material environment in which it dwells" (Niewöhner 2011, pp.289-290). On the other hand, the epistemic tools of the life sciences also entail that the researchers' work results in a systematic attempt to "operationalize instances of social change" responding to "criteria taken directly from the practice of molecular biology" (Niewöhner 2011, p. 291). This is what the author calls "*the molecularisation of biography and milieu*"; namely, the translation of everyday social contexts and significant biographical events into a matter to be described, understood and dealt with at the physiological and molecular level (Niewöhner 2011, p. 291; original emphasis).

This article builds upon these observations in science studies and engages with the openings towards biosocial thinking in one behavioural epigenetics lab. Specifically, the article details the different experimental steps that lead scientists to produce a biosocial account of "early-life stress"; namely, an understanding of this phenomenon as a nexus of molecules and experiences, biological and biographical events. The work towards the construction of a biosocial account of "early-life stress" is, I show, characterised by an intricate factual and value-laden labour that alternates and aligns elements of the social and biological orders. In line with the constructionist tradition in Science and Technology Studies (STS) (cf. Latour 1987; Fujimura 1996), below I detail three distinct articulations of techno-scientific means, moral standards of research practice, biological knowledge and socio-political thinking about the role of epigenetics in our societies. These articulations provide insights into the intricate sociotechnical systems that give rise to accounts of the entanglement between biology and experiences in epigenetic biosciences.

First, I focus on the production of the biological traces of early-life experiences through behavioural conditioning experiments. This initial experimental stage, connecting experiences to biological functioning, rests upon a highly choreographed experimental process that results from the negotiation of elements from distinct ontological orders (cf. Thompson 2005). Technical, epistemic and moral considerations have in fact to be carefully poised to produce the embodiment of "early-life stress" in this type of laboratory research. *Second*, I describe the purification of the epigenetic signatures of "early-life stress" into specific tissues and genetic loci that can be linked to an organic and physiological explanation of the health-related effects of these experiences. This stage of knowledge-production, I show, forecloses the body-environment continuities that were crucial to the first step of experimentation (i.e. behavioural conditioning). The articulation of this task in the lab rather produces a disembodied molecular explanation of the effects of stress that travels across organs, individuals and species (cf. Rose 2007; Zwart 2016). *Finally*, the article focuses on how constructing a material, organic continuum between molecules and experiences in the lab gives rise

to strategies of intervention into such complex biosocial entanglements. Regarding this, the paper reports on the protocol of Environmental Enrichment (EE), which this lab employs to modulate the "aberrant" epigenetic marks of early-life experiences and prevent their transmission across generations. Notwithstanding its long history in neuropsychology and cognitive sciences (APA 1947), EE is gaining traction in epigenetics with some labs starting to employ this technique (McCreary and Metz 2016). EE consists of an intervention into the housing conditions of laboratory animals, which is directed at stimulating their cognitive, sensory and motor capacities (Hannan 2014). This technique has been shown to reverse different behavioural, physiological and neural deficits in animal models, including the adverse epigenetic effects of stress-related conditioning (Clemenson, Deng, and Gage 2015). Importantly, I show, scientists in the lab justify their choice of EE on both epistemic and socio-political grounds. On the one hand, they regard EE as restoring, at an experimental level, the importance of considering "stress" as simultaneously affecting multiple pathways in the body. In this respect, EE enables them to distance their approach from widely employed pharmacological treatments of stress-related epigenetic modifications (cf. Szyf 2009). On the other hand, EE provides them the opportunity to scaffold a specific socio-political imaginary from their research (Jasanoff and Kim 2015; Richardson 2017; Chiapperino and Panese 2018). By acting on the social and material environments to correct the biological effects of "stress", EE allows these scientists to strategically claim that their experimental practices elevate forms of political and collective intervention – instead of individual and molecular ones – into the long-term epigenetic effects of stressful experiences.

Taken together, these observations suggest that the epistemic object (Rheinberger 1997) of stress as biosocial phenomenon gets articulated differently across distinct experimental stages in the lab. Specifically, the research group functions under the assumption that the complexity of these biosocial entanglements must be broken down into distinct experimental stages – each subject to its own work of articulation one might add. Following this coming together of techniques, methods, norms, values and knowledge reveals how the lab's practices *oscillate* between an engagement with, and a remarkable obliteration of the biosocial entanglements producing the phenomenon of "stress". At the same time, the specific sociotechnical configuration of this lab offers the opportunity to underline the design flexibility (Pinch and Bijker 1984) that characterises experimental engagements with biosocial thinking in the life sciences. While these scientists' work largely overlaps with customary reductions of "stress" to its molecular effects in epigenetics (Meloni and Müller 2018), their use of the EE protocol exemplifies how epistemic practices can be articulated to problematise mainstream research agendas in this field. EE is in fact a local configuration of techniques and

resources, as well as skills and beliefs of the involved scientists, that is meant to produce the distinctiveness of the lab's work. First, EE allows these scientists to distinguish themselves from other approaches in the field and to instrumentally construct the narrative of a lab tangibly breaking with molecular reductionism and interventions (Fox Keller 2016). Second, EE enables them to navigate the tension between social/infrastructural interventions and molecular/individual interventions (Chiapperino and Testa 2016). In a nutshell, EE is an experimental design that, in the lab's view, avoids the reductionist tendencies in epigenetics, and shifts the public relevance of this knowledge to the level of social/collective interventions into the material and social environments. Needless to say, also the experimental outcomes of EE are limited in several respects and demand further scrutiny to assess their potential contribution to a thick biosocial science of disease and illness (cf. Meloni, Williams, and Martin 2016). Yet, the observations I report here suggest that there is flexibility not only in how epigenetic scientists think of, or interpret the artefacts of their research (Tolwinski 2013). Rather, flexibility lies also in how these artefacts can be designed and produced to tentatively engage with ideas of a biosocial body as entangled with its material and social environment (cf. Pinch and Bijker 1984).

By doing so, the present paper complements existing socio-political analyses of epigenetics in STS and provides empirical insights into debates on the experimental entanglements across social and natural sciences in the post-genomic age (Callard and Fitzgerald 2015). Close scrutiny of the construct of EE, I argue, illustrates how epigenetic scientists can problematise the opening towards biosocial thinking *from the standpoint of their epistemic work* (Meloni, Williams, and Martin 2016; Meloni et al. 2018a). Rather than being simply molecular instead of environmental, "biological" as opposed to "social", knowledge on the embodiment of "stress" produced by this lab moves across these dichotomies to strategically entangle them and produce its different socio-political positioning. As detailed below, this commitment is clear in the declared intent of the principal investigator to overcome resistances, assumptions and inherently limited approaches in the life sciences that treat the porous frontier between biological and social existence as a matter of molecular intervention. For this reason, I conclude, EE is of interest to the debate around the biosocial in social studies of post-genomics (Meloni, Williams, and Martin 2016; Meloni et al. 2018). This technique does not certainly resolve the conceptual and methodological issues that have hitherto made incompatible the natural and social sciences (Lloyd and Müller 2018). Yet, it provides to STS scholarship a case study of how molecular biologists attempt to complexify the reductionist properties of the small-science they practice (cf. Knorr-Cetina 1999).

An important aspect of the practices I describe here certainly lies in the status of the laboratory itself. The lab is a specific environment and cultural construct where research objects such as "stress" are far from being approached in the way they manifest in everyday life (Knorr-Cetina 1995; Knorr-Cetina 1999). The lab is rather an epistemic and social organisation that renders visible natural phenomena through highly artificial streams of interaction among equipments, tools, humans and non-human animals (Knorr-Cetina 1999, ch.2 and 4). Furthermore, another important feature of the research I follow here lies in the role animal models play in knowledge production. As shown extensively by studies on research involving animal models (Berger 2009; Despret 2004; Davies 2010; Nelson 2016), laboratory animals get used as "symbols, as companions, and as spectacles" for humans (Nelson 2018, p. 3). Similarity and diversity among human and non-human animals are eminently at play also in the practices I describe here. This type of epigenetic research strikingly displays the extent to which instruments, equipments and experiences – both of scientists and non-human animals – need to be cultured and taken care of, to conduct successful experiments (Chung et al. 2016; Kirk 2016; Lappé 2018). *A fortiori*, the plasticity and sensitivity to environmental stimuli of the epigenome require that culturing and care of laboratory animals (usually rodents) is highly controlled to produce reliable knowledge of the molecular effects of "early-life stress". Yet, a focus on the situated practices of these scientists shows an additional element at play in this type of laboratory science. As argued by Nicole Nelson (2018), scientists working with animals in behavioural research are aware of the artificiality and precariousness of their factual claims. More than being concerned with the establishment of specific evidentiary chains for the explanation of a given phenomenon in humans, their work is best captured as the construction of 'epistemic scaffoldings' (Nelson 2018, pp.81-111) connecting knowledge about animals and humans under the assumption that the lab's complexity is *different* and its artificiality *intense*. Otherwise stated, these practices are best described as scientists' cultivation of distinct layers of complexity (Müller and Samaras 2018; Lappé 2018), which define their specific style of knowledge-making.

Following these suggestions, my aim here will not be to describe to what extent, with what merits and limitations these epigenetic researchers claim to thin down the distance between the biosocial processes producing the embodiment of stress (*qua* human, psycho-social phenomenon) and "stress" (*qua* technologically intensive epistemic object of a lab)[3]. Rather, as mentioned above, the paper will engage extensively with the ways scientists articulate the continuum between the

[3] To mark the importance of this premise for the remaining, I have decided to use the word "stress" within quotation marks throughout the text when referring to the work of the laboratory. This allows reminding the reader of the contentious nature of scientists' use of the term stress (intended here as embodied, psycho-social human phenomenon) in the artificial environment of the lab.

material and experiential traces of "stress" in their experimental practices. As shown below, much of this epistemic work goes into the crafting of openings and closures of body-environment continuities, the highlighting and deleting of the biosocial entanglements of "stress" through different experimental steps.

Situating the Lab: Transgenerational Epigenetic Inheritance of "Early-Life Stress"

The data for this article derive from a three-years project exploring epigenetic knowledge as factual resource to actively shape normative claims about parental and intergenerational responsibilities. The experiments I observed varied considerably due to the plurality of views animating this field (Meloni and Testa 2014). Researchers work on mechanisms of so-called intergenerational and transgenerational epigenetic inheritance (Bošković and Rando 2018; Perez and Lehner 2019) from a variety of disciplinary perspectives such as epigenomics, behavioural epigenetics, epigenetic epidemiology, paediatric medicine, and gestational medicine. The fieldwork I conducted includes multiple observations of laboratory practices, the attendance of lab meetings and public conferences, as well as a series of interviews with scientists and practitioners working in these domains (N=22). The specific questions I explore here are part of this dataset and concentrate on the practices of one specific lab located at (what I shall call) the "University of Switzerland" (henceforth UoS). To further document the informants' work, I devised an additional round of data collection tailored to the specific practices of this laboratory. After an in-depth analysis of the lab's publications and of the literature on their techniques (e.g. behavioural experiments protocols, enriched housing, and laboratory environments), I arranged several visits for both informal and formal observations of laboratory procedures, experiments and meetings. These were iteratively integrated by exchanges with lab members and the principal investigator (PI), as well as a final in-depth interview with the PI exploring themes emerging from previous interviews, observations, and analyses of the lab's work.

The UoS lab is a renowned research group in the field of behavioural epigenetics. Similarly to other labs (Powledge 2011; Sandi and Haller 2015), these scientists aim to understand how differences in early-life experiences (e.g. maternal care, exposures to stress) produce distinct behavioural patterns that correlate with variations in the conformation and molecular marks of brain cells. In addition, this lab has been a forerunner for experiments showing the transgenerational transmission via the gametes of epigenetic effects of early-life experiences. Although the lab is now well-established, its research has initially been met with scepticism in the life sciences community (Daxinger and Whitelaw 2010; Isbel and Whitelaw 2015). During one interview, Marie (the PI) was open about the limitations of their work and the struggles their science had to face to get recognition:

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> The first paper we published took us five years. All the data on transgenerational inheritance, we had them in 2004. First time we submitted in 2005, and the paper was published in 2010. In 2005 it was way too early…We went first with [a prestigious journal]; after two years they asked us more experiments. They all worked. At the end the decision was left to one reviewer, as the other ones went missing in the meantime, or they agreed to publication. The last reviewer said "*I don't believe it*", and then [the journal] rejected our work (*Interview 1, Marie, PI*).

These struggles can better situate the UoS lab within contemporary epigenetics (Deichmann 2016). On the one hand, their research is subject to the common limitations of behavioural epigenetics. These include concerns about reliability of the tissues and time points examined, specificity of modifications across tissue- and cell-types and the functional implications of the variations observed (Roth 2013). On the other hand, this lab also faces a great deal of doubts for having extended claims about the traffic between experiences and the body to the temporalities of biological inheritance (Mitchell 2018; Perez and Lehner 2019). Evidence of transgenerational epigenetic inheritance has in fact been conflated with a revival of Lamarckism that is deemed problematic on the grounds of current neo-Darwinian evolutionary theories (see Loison 2018 for a critique of the association between Lamarckism and epigenetics). Other critics have instead focused on internal flaws attributed to this strand of epigenetic research. Some have pointed to the lack of evidence showing how an exposure affecting epigenetically a given tissue (e.g. the nervous system and the brain) could then travel to the gametes (e.g. sperm) to be transmitted to the progeny (Isbel and Whitelaw 2015). Others have instead called for further investigations of the link between epigenetic marks, genetic variability and complex behaviours both in animal models and humans (Heard and Martienssen 2014).

An appreciation of the complexities characterising research practices in the UoS lab was ubiquitous in my interactions with its members. Far from constituting an unspoken feature of their research, the status of the "knowledge" they produce was an acknowledged element with repercussion on the design, conduct and interpretation of their experiments. Similarly to what Martine Lappé (2018) has observed in a different behavioural epigenetics laboratory, scientists at UoS interpreted the limitations inherent to their research as a pragmatic slant throughout their experimental work, which allowed them to produce "reliable" and "reproducible" results on the mechanisms of embodiment of "early-life stress".

Step one: the 'ontological choreography' producing "stressful experiences" in the lab

The group's research is conducted in a widely used mouse strain. Their studies of the influence of life experiences on mental and physical health across generations resorts to a model of induced "early-life stress" established by the lab. The model consists of a protocol for repeated and aleatory three-

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hours-per-day separation of the dam (F0 generation) from its pups (F1 generation) during the weaning period (the first twenty-one days of a mouse's life), coupled with stress conditioning procedures exerted on the dam during the same period. During separation, dams and pups are placed in separate compartments: the dams stay in the standard cages, while the pups are placed in a plastic container on top of the cage itself. Dams and litters, during separation, are close enough to maintain olfactory if not visual contact. Stress conditioning procedures exerted on the mother include either a twenty-minutes restraint in a Plexiglas tube or a six-minutes forced swim in cold water (18°C) applied unpredictably and randomly during the daily separations. These practices of separation and stress induce behavioural alterations in the parenting of the dam (e.g. nursing, licking and grooming) and, in turn, produce behavioural patterns and molecular/metabolic (epigenetic) alterations in the pups. These alterations, the lab has shown, can be transmitted across several generations (down to the F5 generation during observations) through the germline.

The researchers at UoS employ a variety of techniques to produce and document the inheritance of early-life experiences. Some are behavioural measures of the patterns of "care" the dams provide to the litter – such as the time they spend licking and grooming their pups, or the time they spend off-nest (i.e. away from the pups in the cage after separation). Variations in these behaviours occur naturally in rodents, but they have become a conventional measure for nurturing in animal models and for how nurturing variations produce diverse stress-coping patterns in the offspring (e.g. F1, F2 and F3 generations) (see Stern 1997). Other behavioural measures apply to the pups and their offspring and include a repertoire of tests (conducted when these animals are ninety days old) measuring what the researchers call "depressive-like behaviours" in rodents. During one visit to the lab, Grazia (a lab technician) is accompanied by a master's student, Anna, who is visiting the lab for an apprenticeship. Grazia is a highly-skilled technician working with mice since a decade and is the pillar on which the group relies to obtain samples for molecular analyses. The agenda of the day entails carrying out the so-called "forced swim test", an experimental technique routinely used in this lab not just as conditioning measure "stressing" the dam (as mentioned above), but also as measure of "depressive-like behaviours" (i.e. swimming vs. floating) in the offspring of the conditioned mice. Known also as the "behavioural despair test" (Porsolt, Le Pichon, and Jalfre 1977) this method consists of placing rodents in an escape-proof cylinder filled with cold water (18°C). The rodent will initially engage in vigorous escape-oriented movements, but then within minutes (usually just a couple of minutes) those understood to have more "depression-prone" behaviours exhibit increasing times of immobility and floating with respect to controls. Although the forced swim test is of widespread use in behavioural epigenetics, several epistemological critiques have been moved

to this technique (Davies 2010). Critics have questioned the value of the test in terms of its capacity to measure effectively depression in mouse (i.e. internal value), and in terms of its utility to better approach depression in humans (i.e. representational value) (Tecott 2003; Molendijk and de Kloet 2015). Although the forced swim test is widely employed to measure the efficacy of anti-depressant drugs (in terms of their reduction of immobility and floating time), critics argue that the drug action and brain pathways involved in this highly stressful situation may not necessarily be the same required to treat chronic depression in humans (Cryan and Holmes 2005). On the day of my observations,

> Anna is operating the software for measuring the floating vs. escaping time of F5 mice under the attentive guidance of Grazia. It's a push and hold system through which Anna can record floating time, aided by a camera placed on top of the plastic jar in which the mouse was tossed. The software detects floating vs. escaping time also automatically, thus providing a control for any potential experimenter's failure. We silently assist to this operation lasting six minutes for each mouse (twenty on this round) sitting in a dark computer room contiguous to the animal house. Silence is a key feature of the handling of these animals. Grazia is enthusiastically whispering though about the potential breakthrough of showing behavioural and epigenetic variations in the F5 generation, but she regularly cuts her speech when she notices a mouse on the screen struggling, or exhibiting despair (i.e. floating). Anna is blind with respect to whether the mouse being observed issued from a litter whose ancestors were stressed, or whether it is a control. Grazia has arranged the protocol for her a few days in advance so that Anna cannot know the origin of the mouse being tested. Once the six minutes are over, we leave the computer room to go bring back the tested mouse into the cage. Grazia wants to teach Anna how to handle the mouse after this test. She picks up a tissue and gently dries the animal by caressing its fur. "This helps bringing them back to normal temperature rapidly: *I do not want to stress them*", says Grazia. (***Vignette 1***)

The first element of my observations relates to what Nicole Nelson (2018, p. 107) calls the "extra-factual work" scientists invest in laboratory research. As she argued extensively (Nelson 2016; Nelson 2018), an understanding of behavioural studies in molecular biology cannot ignore the environment of the laboratory itself as a complex bundle of practices going beyond knowledge-production. Far from being only concerned with the stabilisation of facts (Latour 1987), researchers working on behaviours with animal models treat their practices as a thoroughly unstable process. The subjects, objects, environments, apparatuses, materialities and truth-claims populating these labs are fundamentally precarious and easily perturbed, Nelson argues. Thus, this way of knowledge-making is better understood through the central role played by the care invested by researchers in their daily activities to mitigate the permanent uncertainties surrounding this type of work (see also Lappé 2018).

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Vignette 1 offers the possibility to illustrate how the practices at UoS align with this reading. The protocol of the forced swim test is characterised by an extended network of actors that need thoughtful coordination to produce knowledge on the differences between "stressed" and "non-stressed" animals. The mouse, the water at a given temperature, the shape of the jar, the camera connecting digitally the animal house with the computer room, the timer, the software detecting floating/swimming and the silently focused researcher all participate to a process that must be carefully carried out to produce a meaningful experience of "stress" from the experimental point of view. This articulation of machines and animals – both human and non-human – has to be standardized and consistent to produce (and reproduce) adversities in the early-life environment of these mice and their consequences on adult behaviours (as well as the epigenetic mechanisms mediating this continuity, as we shall see in the next section).

Yet, Grazia's conclusive remarks about the need to "avoid stressing these mice" – which are just one telling instance of several she made – unveil a further dimension of the extra-factual work of these researchers (Nelson 2018). This consists of a specific moral work performed to demarcate knowledge-production on the embodiment of "early-life stress" from the need to consider the welfare of the tested animals. Producing the embodiment of stress – I learnt during my visits – rests upon a specific order internal to the lab that balances and separates the experimental objectives with moral justification of these practices. Performing the forced swim test is considered, according to EU and Swiss regulation (Confederation Suisse 2008; European Parliament and European Council 2010), as one of the procedures exposing the animals to the most severe suffering allowed by legal standards. For this reason, the researchers must hold a clear distinction between what counts as workable "stress" from an epistemic point of view and what instead falls under the injunction to avoid stressing these animals for ethical reasons. This moral, extra-factual component of Grazia and Anna's work is thus another set of practices, behaviours, and situations that needs to be cultured in the lab (Greenhough and Roe 2018). This extra-factual culturing of the animals is necessary to align the natural order of "stress" investigated in the lab with the social order norming the lab practices (e.g. compliance with regulation, renewal of licences, deontology; see Kirk 2016).

The term "ontological choreography" refers in Charis Thompson's work (2005) to "the dynamic coordination of the technical, scientific, kinship, gender, emotional, legal, political, and financial aspects" in assisted reproduction clinics. This notion highlights how the supposedly "undifferentiated hybrid mess" of people, objects, values, facts that partake in assisted reproduction is actually a "deftly balanced coming together" of matters that fall into different ontological orders (p.8). These natural, technical, moral and social elements – I argue – must be coordinated in highly

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staged ways also in the daily practices of the UoS lab to produce a meaningful biosocial understanding of "early-life stress". On the one hand, the environment of the lab has to be materially arranged and operated to create "stressful" environments that matter for knowledge-production. The choreographed performance of the forced swim test is, in the context at issue here, what produces an experience of "stress" that is epistemically valid and relevant. On the other hand, acting on the same environment responds also the moral injunction of mitigating its stressful features when the procedures, machines and gestures fall into the extra-factual work of protecting animal welfare (i.e. avoiding stressing the animals in vain). This double movement of articulating epistemically and morally the relevance of the environment of the lab provides insights into scientists' production of a biosocial account of "stress". Experimental practices like the forced swim test show how post-genomic biosciences construct *an ontological continuum* from environments and experiences to bodies and biology. Such biosocial complexity is dealt with in ways that demand the choreographed attunement (Despret 2004) of different kinds of things, animals, norms and values that are deemed capable of producing a stable version of the traffic between two conventional ontological orders of life: life as a biological and as a psycho-social phenomenon. Next is the description of how these scientists translate such complex biosocial entanglements into the epigenetic traces of "early-life stress".

Step two: materialising the biosocial continuum into epigenetic modifications

Another set of techniques characterising the UoS lab consists of molecular measures of the epigenetic marks of the "early-life stress". The UoS lab's publications invest a diverse array of tissues with the potential to carry the material traces of early-life experiences. Chiefly, their publications focus on brain regions involved in the processing of decision-making and emotional responses, such as the amygdala, the hypothalamus and the pre-frontal cortex. Although the consequences of early-life adversities implicate several pathways in the body (McEwen 2005), the reason to concentrate on these brain regions is that, conventionally, these play a key role in pathological dysregulations of stress-coping (Buijs and Van Eden 2000). The same goes with the tissues that are regarded as vectors for the transgenerational transmission of these marks. The possibility to inherit these predispositions (in the absence of the experience producing them) requires that germ cells (such as sperm) are the material carriers of epigenetically-acquired marks across generations (Horsthemke 2018). Crafting the biological traces of stress, in a way that is meaningful to an established literature on their localisation and physiological role, comes therefore at the price of excluding a complex uptake of the embodiment of such experiences. As argued by Marie (the PI):

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> Our model of postnatal trauma tried to identify factors that could access the circulation in the body. If you think about it: when a pup or a baby is exposed to trauma it activates stress pathways, many pathways in different organs. However, we know that most of them are controlled by, for instance, the hypothalamus. If you are interested in memory, you should look at the hippocampus. If you are interested in decision-making, or goal-directed behaviour, then you should look at the pre-frontal cortex. Emotions in the amygdala, and so on and so forth. But the premise of this is always that these modifications happen and travel from tissue to tissue. These factors go through the body: they have to access germ cells in testis, get to the ovaries, etc. They must get through several barriers. It is perhaps easier earlier in life, as these barriers are not formed since the beginning. *But to get the full story working*, we will have to show how these barriers are overcome. (*Interview 1, Marie, PI*)

While researchers know that the "wear and tear effects" of stress affect both the brain and the body (McEwen 2005, p.317), their studies do not fully account for how these experiences transit in the body, how they get inscribed in the brain, and how they then turn into molecular predispositions localised in the gametes. Within the context of my observations, the reason to restrict the lab's focus on a few cell types responds therefore to a precise strategy of valorisation of the group's research. The exclusion of the multiple organs and tissues involved in the embodiment of early-life stress depends on the possibility to make one's science legible and pertinent to a specific scientific community.

Marie further elaborated on this point when detailing their choice to concentrate only on some molecular mechanisms in these tissues. Not all genetic loci are in fact taken into account when researchers look for the potential biological mechanisms linking "early-life stress" with adult behaviours and transgenerational transmission. In particular, the lab has identified epigenetic modifications (i.e. DNA methylation and non-coding RNAs) as mediators of the expression of some candidate genes whose function in the literature points to a role in depressive behaviours and stress-coping failures (e.g. serotonin receptor genes, glucocorticoid receptor gene). There exist, in other words, several conceptual, academic, technical, and material constraints that scientists have to deal with in the production of knowledge on the embodiment and transmission of "early-life stress":

> The literature on the glucocorticoid receptor is quite well developed and so we decided for a pilot study to go for this gene. It's a proof of principle study. We made it easy for us! But it is worth stressing that the role of the glucocorticoid receptor gene is over-inflated. I don't like doing this type of things: using a candidate gene that everyone else is using just because it's in the mainstream literature. It biases the thinking of people, everyone focuses on that and ignores the rest. So, I would like not to reinforce the idea that glucocorticoid receptor is the main receptor involved. *It's just that there is a lot of literature on that*. […] You know how science works. It's easier to surf on the wave, rather than scratch your head and find something else. Indeed, in our model we did a lot of

> metabolomics analysis, and we found that the effects of the model are completely outside of the glucocorticoid receptor. There are other receptors that function like it. (*Interview 2, Marie, PI*)

These excerpts show how identifying the epigenetic marks of "early-life stress" rests upon several assumptions about the localisation and the candidate mechanisms that could function as "molecular conduit" (Landecker and Panofsky 2013, p.341) between experiences and biology. Within the UoS lab, the embodiment of stressful experiences gets measured in those regions of the brain (e.g. the amygdala, the hypothalamus) and in those genetic pathways (e.g. serotonin receptor genes, glucocorticoid receptor gene) that have already been invested as key mediators of such processes. These scientists know that stress is a phenomenon affecting multiple pathways, organs and regulatory systems of the body at once, including multiple loci of the genome. Indeed, how epigenetic modifications travel from tissue to tissue is an open controversy in the behavioural epigenetics literature (Sabour and Schöler 2012; Horsthemke 2018). Yet, the possibility of seeing one's work recognised in the specific literature on the molecular basis of stress-related conditions drives scientists to intentionally isolate certain tissues and genetic loci as the mediators of body-environment relationships.

In this respect, the construction of a biosocial account of "stress" in the lab does not consist solely of the choreographed embodiment of experiences illustrated above. Rather, the molecular techniques in the lab allow scientists to produce a further layer of understanding of these biosocial entanglements, which resides in the materialisation of the continuum between biography and biology within specific biological pathways. In the case at issue, the percentage of methylation in (for instance) a promoter of the glucocorticoid receptor gene in the hippocampus or in the sperm of a mouse constitutes the material instantiation of the "trauma" lived by the pups. The composite environments of the lab, the "stressful" experiences of the mice, the work scientists perform on themselves and on the animals is – at this stage of knowledge-production – articulated into molecular effects on the functioning of specific genetic regions of brain and germ cells.

The epistemic practices of the UoS lab exemplify therefore how post-genomic biosciences turn complex, embodied biosocial experiences (however staged they may be) into their quantifiable molecular traces. This "molecularisation of biography and milieu" (Niewöhner 2011, p.13) is part and parcel with the *regime of perceptibility* that permeates epigenetics; namely, "the way [this] discipline or epistemological tradition perceives and does not perceive" these phenomena (Murphy 2006, p.10). This obliteration of the embodied complexities of "stress" has however consequences for the meaning it assigns to the biosocial continuum between experiences and biology. First, we witness here the reduction of the complex coming together of natural, technical, moral and social

elements of behavioural experiments to putative epigenetic endpoints that account for these entangled social and biological processes. Sociologists of science and technology have long observed how the style of reasoning of molecular biology entails the reduction of social relations and cultural patterns to laboratory manipulability (Hacking 1992; Knorr-Cetina 1995). Unsurprisingly, this critique has found expression also in the STS appraisals of epigenetics, with several scholars pointing to the multiple ways in which such molecularisation inscribes the effects – and underlines the relevance – of social phenomena as they are made sense of at the level of epigenetic marks (Niewöhner 2011; Meloni and Testa 2014; Meloni 2014). The lab at UoS is, in this respect, no different from what scholars have observed in other situated practices. The complex social environments of mice and humans get supplanted, at this stage of knowledge-production, by the chemical modifications of DNA and their scattered cellular localisations.

Second, the practices of the lab at UoS provide also the opportunity to underline how this obliteration does not pertain only to body-environment traffic, but operates also at the level of the inner functionings of the body (cf. Rose 2007; Zwart 2016). Researchers at UoS are unable to account for the whole epigenetic, metabolic and hormonal patterning of these experiences in bodily functions. In producing the material instantiations of the embodiment of early life adversities, they build upon a scientific literature and consequently focus on well-known molecular pathways for body-environment interactions and their effects on physiology. This strategic choice allows them to contribute to 'normal science' (Kuhn 1996) on the neurobiological basis of psychiatric illnesses. In doing so, however, their practices strip away from the biosocial continuum those organs, tissues, cells, proteins and molecules that do not display already known affinities to the diseases and organs they examine. Brushing over such a complex, holistic science of the embodiment of social experiences enables them to extrapolate meaningful and legible material traces of such biosocial nexus for their reference community (Murphy 2006). Yet, this practice has also the corresponding effect of turning an embodied phenomenon into manipulable and transferable elements that are isolated from the organism and, as such, can travel from one organism to another, from the behaviours of mice to those of humans, as well as from one generation to another. The materialization of the epigenetic traces of life experiences means, in brief, introducing a critical hiatus in the biosocial continuum *between* the body and its social situatedness, as well as *within* the body as unified living entity.

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Step three: articulating biosocial interventions through Environmental Enrichment

Producing the material instantiations of "stress" is not limited to the objective of identifying the molecular traces of one's experiences. As argued by Paul Rabinow (1996), contemporary biology rests upon a genuinely technoscientific rationality, which consists of turning the objects of scientific knowledge into objects on which technologies can possibly *intervene*. This dimension of contemporary biology means that "representing and intervening, knowledge and power, understanding and reform, are built in, from the start, as simultaneous goals and means" (Rabinow 1996, p.93). Regarding strategies of intervention on the biosocial nexus of "stress", scientists at UoS have developed the following approach:

> We did a proof of principle study showing that an enriched environment – more toys, more activities, more food – for the father could remedy to its trauma and prevent the transmission in the progeny. A phenotype that was reversed in a couple of weeks, from weaning to adulthood. (*Interview 1, Marie, PI*).

Protocols for Environmental Enrichment (EE) are certainly no novelty in research involving animals. EE has a long-standing history in cognitive and neuro-sciences, which only recently has come to intersect the domain of behavioural epigenetics (Nithianantharajah and Hannan 2006; Hannan 2014; Clemenson, Deng, and Gage 2015). The first description of the effects of EE in experimental animals goes back to one of the founders of neuropsychology, Donald O. Hebb (1904-1985). At the 1947 Meeting of the American Psychological Association (APA 1947), Hebb's contribution included data about the different performances in problem-solving between rats reared in standard laboratory cages and rats "reared at home as pets with much of their time spent outside their cages" (APA 1947, p. 307). These results, Hebb argued, pointed to the effects of cognitive, physical and social stimuli on the development of brain structure and functions. Starting from this pioneering experiment, protocols of EE have gradually become standard practice in two strands of neurological and psychiatric research involving test animals[4]. On the one hand, EE has been widely used in studies on neurogenesis and developmental plasticity, allowing researchers to show the effects of the combined effects of social, physical and sensory stimulation on the animal's development (Clemenson, Deng, and Gage 2015). With the development – from the 1970s onward – of animal models carrying genetic predispositions

[4] This categorisation does not capture the diversity *internal* to the two main streams of EE-related research (i.e. neurodevelopmental plasticity and animal welfare), which is due to the different disciplinary approaches each of them encompasses. Reconstructing in detail these disciplinary uses – from developmental psychology, neurosciences and populational health, to animal welfare and animal captivity studies – goes beyond the scope of this article. Few studies exist, however, that provide a historical perspective on EE (see: Mellen and Sevenich MacPhee 2001; Young 2007), as well as a few accounts of other contemporary uses of EE in the life sciences (Davies 2010; Nelson 2016).

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for neurodegenerative diseases, EE has moreover become a technique of extensive use in studies on "brain repair" (Hannan 2014). EE has been shown to dramatically delay the onset and reduce the severity of motor, cognitive and behavioural deficits (both in studies on test animals and humans) for several conditions, such as Huntington's, Alzheimer's, and Parkinson's disease (Nithianantharajah and Hannan 2006). On the other hand, the support given by EE to the importance of living conditions of animals lent legitimacy to the nascent field of animal welfare studies in the 1960s and 70s. As argued by Nicole Nelson (Nelson 2016), "enriching the environments of laboratory mice" became common currency in "the world of animal welfare" and shifted regulatory understandings of animal suffering "from narrow conceptions of post-operative pain to more encompassing notions of mental suffering and well-being" (Nelson 2016, p.11).

While touring the lab, Grazia (the lab technician) illustrates how EE works at UoS:

> Grazia opens the cage for EE. It is a multi-modular object, divided into two floors, far bigger than the standard cage. She removes, one by one the different elements, after having split the two floors on the table. "The wheels provide a type of physical exercise that would be impossible in the standard cage", she says. Then, she explains how usually the cage contains six mice, which have been subjected to stressful conditions in early life. "The cage allows the mice to enjoy a type of sociality that does not belong to standard caging of these animals in laboratory sciences", Grazia affirms. She goes on with a detailed description of the activities that the mice can perform in the EE cage: "they have to climb up a staircase and figure out a maze, before going downstairs again on the other side of the ground floor in the compartment with food". The maze, she continues, gets changed every few days "in order to stimulate the mice cognitively". The food compartment is separated from the other half of the ground floor by a tilting door that can be used only to join back the compartment where the nest and wheels are placed. The mice cannot use this door to go back to the food compartment. "Every time they want to eat, they have to learn the path again. It's very much like the situations with which they are confronted into the wild", she says. Then, she concludes: "this is our own way of doing it, but of course every lab has its own approach. The idea is to exploit the tool and see what happens, since we know that exposure to this environment can correct the behavioural and molecular marks of early-life stress. Yet, differently from pharmacological treatments, we don't know *what the mechanism is, nor whether it can be found, or whether we want to find one*." (***Vignette 2***)

Starting from Vignette 2, it is possible to describe how scientists at the UoS lab perform three kinds of work through the use of EE: (i) EE is an experimental setup that fuels the lab's own narrative of distinctiveness in the field of behavioural epigenetics; (ii) EE allows the lab to claim that the intervention they crafted symmetrically accounts for the biological and socio-environmental factors

of stress-related health effects; (iii) EE enables UoS scientists to construct a specific imaginary of public health intervention on stress-related illnesses to be associated with their laboratory research.

First, UoS scientists emphasize how EE positions the lab in discontinuity to widely used pharmacological approaches to the reversal of these epigenetic marks. Research on the reversal of these effects typically resorts to classes of drugs that are known to act on the epigenetic machinery, such as DNA methyltransferases (DNMTs) and histone deacetylases (HDACs) inhibitors (Szyf 2009; Day 2014). DNMTs and HDACs have proven to be effective to correct epigenetic modifications in animal models and have become an important element for current developments of targeted therapies in humans (Szyf 2009; Schroeder et al. 2010). Commonly used protocols to test the efficacy of an epi-drug consist of a series of organised steps directed at mastering the molecular processes triggered by "early-life stress": identify which mechanisms to join in chemical reaction, determine how long and with what doses these ought to be subjected to a treatment, verify the erasure of the mark through the isolation and analysis of the relevant tissue. The most problematic feature of this approach, Marie argues while interviewed (Interview 2; excerpt below), is that this mechanistic reasoning takes away attention from a "global" perspective on stress. Treating only some of the material instantiations of stress with drugs may in fact "not be totally effective" to address the environmental factors producing it and its effects on multiple physiological systems of the body.

This is why, in her view, EE renders the UoS lab radically different from others in the field. The cage for EE is – as Vignette 2 illustrates – composed of different elements that produce sensorial, cognitive, spatial, physical and social stimulation for the animals. The mice enjoy "a type of sociality" and interactions, Grazia affirms, that do not belong to standard caging due to the limited number of specimens these can house. The running wheels entertain physical stimulation, which is normally unavailable in standard caging. The maze puts the animals on a quest that is supposed to mimic the "natural" occurrence of food hunting. Besides raising the question as to what extent EE recasts standard animal housing as a form of sensorimotor deprivation (Davies 2010), this staged composition of stimuli testifies how EE produces the claimed distinctiveness of the UoS experimental configuration. This lab can fuel the self-narrative of breaking with the mainstream acceptance of epi-drugs because EE reshuffles and realigns some of the core methods and assumptions that dominate their own field. The claimed distinctiveness of their approach gets performed as the scaling up of intervention to the reconfigurations of "standard", "adverse" and "enriched" living conditions, which is meant to remediate to the flaws intrinsic to the scaling down of these interventions at the level of biochemical manipulations.

This leads to a second type of work the UoS lab performs through EE. By shifting action to an environment-based treatment of the effects of "stress", the actors frame the use of EE as restoring a symmetrical uptake of "stress" as an entangled biological and socio-environmental phenomenon. As shown in the previous section, materialising the epigenetic traces of "early-life stress" introduces a critical hiatus between the body and its environmental situatedness, as well as within the body as unified living entity. The specific form of intervention through EE gets instead talked about in the lab as an attempt to depart from this skewed focus on molecules (cf. Niewöhner 2011; Landecker 2016). The type of manipulations characterising this experimental stage are meant to produce precisely a fundamental unity of biological substrates and environments, as well as of different physiological systems of the body.

This is evident in Grazia's remarks about the functional properties of the EE cage. Firstly, she expresses doubts about whether a mechanism for the therapeutic action of EE "can be found", or whether they "want to find one" (Vignette 2). The reason for this remark lies in the fact that the various elements of the cage are disposable tools usable in combination, in sequence, or separately. Some labs use only physical enrichment as this stimulation produces documented neuromorphological, cognitive and sensorial improvements. Other scientists resort instead to a combination of physical and interactional stimulation to promote beneficial behavioural outcomes, such as playfulness among the animals. Still others focus on cognitive stimulation by tinkering with different types of toys, mazes and foraging systems encouraging explorative behaviours (see Hannan 2014; Clemenson, Deng, and Gage 2015; McCreary and Metz 2016 for an overview). The lab's choice to resort to all of them at once is meant to affirm instead that, more than being a matter of which particular stimulus produces a given outcome, it is the complexity and exploration of the cage itself that benefit the mice. Finding one mechanism accounting for each physical, sensorial, cognitive, or social stimulation may thus prove an arduous, if not impossible task to these scientists: simply put, the experimental setup of EE does not permit to control for the effect of each variable. For this reason, Grazia considers dissecting mechanistically EE's action an objective impossible to achieve, or one they may not even want to pursue. Combining these different manipulations highlights, in their view, how it is possible to treat "stress" and its aberrant epigenetic effects in ways that fundamentally combine elements that are part of physiology (e.g. organic substrates), part of the material environment (e.g. physical stimulation, food hunting), and part of psycho-sociality (e.g. cognitive stimulation, playfulness).

Secondly, Grazia's remarks culminate in the affirmation of the difficulty to identify on what biological mechanisms within the body EE may precisely act. The reason to affirm this is that UoS

scientists claim to restore, through EE, the importance of "stress" as a phenomenon that is not reducible to isolated tissue- and gene-specific modifications (Zwart 2016). As better explained by Marie, the intervention enacted through EE has "global" effects on multiple physiological systems of the mice. Dissecting how each of these systems is affected by this intervention constitutes a major challenge ahead of the lab for a thorough exploitation of the complexity of this approach:

> The thing is that *it is difficult to determine what are the benefits of EE globally*. Our first study was only a pilot, but we just obtained a grant to reproduce it on a larger scale and at different timepoints. The problem is that we looked at one or two behaviours and we looked at one gene. We need really to extend this to see what levels, what marks and what symptoms are affected, to exploit the potential of the approach. We know that there is a reversal of behaviours and the epigenetic mark we looked for, but not how it works, what are the other pathways involved, etc. (*Interview 2, Marie, PI*).

The complexity of the cage is, in other words, deemed capable not only of combining different kinds of material and psycho-social stimuli, but also to induce physiological, cognitive and sensorial changes that affect multiple pathways and organs at the same time (Clemenson, Deng, and Gage 2015). Discerning how brain structures, general metabolism, different organs and behaviours are all impacted by an intervention into living conditions is however a task that may prove extremely difficult to these scientists. These excerpts show therefore also how challenging it is to recover a centrality of the lived body in the small-science style of molecular biology. Accounting for the complexities of an environment that endlessly modifies the bodies of the involved mice is indeed an experiment that may fail in some important respects. The traffic between the external (i.e. social interactions, physical activity, cognitive stimulation) and the internal (i.e. the body), as well as the interplays within the organism (i.e. different organs, genes) require a deliberate and articulate effort on the part of researchers that is still lacking for a full exploitation of this tool. In this respect, we can see how UoS scientists are aware that EE constitutes only an attempt to counter those practices – also internal to the lab – producing a miniaturised version of the environment in specific molecular modifications (Lock 2015). While their pilot study on EE has established that *in principle* it is possible to correct the traces of "stress" by acting at the crossroad of the body and its surroundings, this technique also presents scientists with the difficulty to research the body as a complex, multi-layered biological and socially situated entity.

Finally, the UoS lab performs a last type of work with the use of EE. Whether fully exploited in its epistemic potential or not, this technique offers them also the possibility to construct a specific social and political imaginary to be associated to their science in the wider society (Jasanoff and Kim

2015; Richardson 2017; Chiapperino and Panese 2018). As maintained by Marie, articulating the construct of EE finds its justification on mixed epistemic and socio-political grounds:

> I don't remember exactly the chronology or the logics behind our study, but it's always been important to us to know whether the consequences of traumatic experiences on the epigenome are reversible. Otherwise it's depressing! And also conceptually, since the epigenome is plastic. So, if you want to explore this plasticity, EE seems to me the most logical way to proceed. But it also reflects the way I think, and my beliefs, or my personality as well…I was never a fan of big pharma companies. I myself rarely take any drug, and if there is another option for betterment, or prevention I tend to use it. […] With this approach to life in mind, and in reaction to all the financial lobbying around pharma companies, as a researcher I am not interested in creating profit for a company and in promoting this type of logics. I actually could never work in the private sector. *The point for me is acting on the broader causes of sickness*. (*Interview 2, Marie, Principal Investigator*).

According to Marie, the deployment of EE as an alternative to pharmacological treatments is intended also to structure the socio-political circulation of epigenetic knowledge. This approach does not stand only, in her view, for an appreciation of how epigenetic marks can be reversed by tweaking with the environment and with multiple physiological systems at once. Rather, EE represents also a way to imagine socially recognised ways to act on the biosocial nexus linking "early-life stress" and mental health. Marie characterises EE as shifting the relevance of epigenetic knowledge away from the domain of pharmacological interventions and, as such, also from the social control of these processes by pharmaceutical companies. During the same interview, she repeatedly insisted on the complementary epistemic and socio-political dimensions of EE in the lab:

> If you are realistic, and you look at data like ours, it cannot be possible that a drug can fix everything. […] The consequences of traumatic experiences on the epigenome are vast, but reversible. The epigenome is plastic and there are other approaches to modify it: it might be much less realistic and much more complicated to think of a more global approach to health like with the principle of EE. But it is probably the best way to go. Finding a drug that has an effect is a much easier scientific task: you can control for the variables, you can test the effects. […] The problem is the social interactions that are behind relationships in our societies, and that have consequences on all of us. Many people are suffering also from mild abusive interactions, and the problems they may face are not necessarily pathological. *EE means thinking systemically about portions of our society that are regularly frustrated because of jobs, educational system, lack of opportunities*. (*Interview 2, Marie, PI*)

This brief excerpt illustrates the specific set of values, norms and obligations scientists in the UoS lab claim to forge through their experiments involving EE. In Marie's opinion, EE means affirming the importance of an intervention at the level of the social environment – as structured configuration of

physical, social, and political settings in which people live – to correct and prevent the aberrant consequences of stressful experiences. In her view, EE enables epigenetic biosciences to displace actionability away from molecular instantiations of "early-life stress" into domains of agency that pertain to institutions and collectives. Certainly, she argues, within the epistemic culture of the life sciences (Knorr-Cetina 1999), a drug can be conceived as a potential manipulator if not a cure for the organic and behavioural effects of "early-life stress". However, the socially embedded nature of the epigenome points to the importance of taking into account how these effects get produced (and re-produced) by the material, institutional, as well as political configurations of our societies.

These different types of work performed through EE can be interpreted in different ways. A critical scrutiny of these practices demands, first of all, questioning the different claims of UoS scientists; namely, (i) whether EE constitutes a break with the experimental culture of behavioural epigenetics, (ii) whether it restores a notion of the body as situated biosocial entity in the lab, and (iii) whether it does lend legitimacy to structural social interventions into the configurations that re-produce the aberrant consequences of stress in our societies. As to the first claim, it is worth noting that experimental systems are ramified ensembles that are taken into a peculiar tension (Rheinberger 1994; 2011). On the one hand, they need to inscribe themselves into an epistemic culture (i.e. material and theoretical contrivances into which knowledge must fit to earn scientific credit). On the other hand, these systems get also articulated to transgress the boundaries within which one's science seems to confined, in order to produce a narrative (and material configuration) of scientific novelty. Through this lens, it is possible to shed a critical gaze on the ways scientists at the UoS lab construct the narrative of their science being fundamentally different from typical behavioural epigenetics. Far from breaking with the others, the lab is rather digressing and transgressing from mainstream forms of knowledge-making, while at the same time staying within the limits of its discipline. Think of the articulation of EE as a novelty within the landscape of behavioural epigenetics, which the UoS scientists have repeatedly emphasised. This construct is only a novelty if we confine our view to the literature on rodents, offspring nurturing and epigenetic transgenerational inheritance (McCreary and Metz 2016). Interventions in the (social and material) environment to induce epigenetic changes in physiological and behavioural phenotypes are however common currency in similar research on insects (Herb et al. 2012; Lockett, Kucharski, and Maleszka 2012). EE protocols are, as mentioned above, an established experimental approach in research outside epigenetics on neurodevelopment, neurodegenerative diseases and cognitive decline (Nithianantharajah and Hannan 2006; Hannan 2014; Clemenson, Deng, and Gage 2015). In a nutshell, attention should be paid to the fact that the displacement of EE into the behavioural epigenetics setting of the UoS lab generates a narrative of

novelty partly because it is an experimental system that gets quickly deployed from neighbouring fields to create such effect in another sub-disciplinary ensemble.

Furthermore, it is also possible to deconstruct the claim according to which EE restores the centrality of the body as multi-layered, biological and environmentally situated entity in the research setting of the lab. While the composite configuration of this experiment certainly engages with a hybrid ontology of "stress" that is biological as well as relational and environmental, the explanatory framework for assessing the effects of this intervention is still heavily linked to a molecularising gaze (Pinel, Prainsack, and McKevitt 2017). Framed as the mediators of the interaction between the cage and the inner bodies of the tested mice, only "two behaviours" and the epigenetic modifications of "one gene" (Marie, Interview 2) get in fact purified as the read-outs of the "global" effects of the cage in the pilot study published by the group. More than being therefore set in contrast to molecular reductions of "stress" to epigenetic modifications, the activities of this lab rather seem to get recognition precisely by aligning EE to those translations into and out of the molecular that several scholars have observed in epigenetic research (Niewöhner 2011; Lock 2015; Chung et al. 2016; Landecker 2016).

Finally, close attention should be paid also to the ways EE "operationalise[s] instances of social change according to criteria taken from the practice of molecular biological research" (Niewöhner 2011, p.13). For all the socio-political potential the lab attaches to this construct, it is indeed an open question whether EE does more to advance a socially situated view of our biology (Niewöhner and Lock 2018) than other typical strategies of intervention in molecular biology (e.g. drugs, lifestyle changes, etc.). Knowledge-production of the social origins of stress-related health conditions has in fact a longer history than epigenetics. Medical formulations of stress display since their onset the confrontation among bio-physiological and psycho-social explanations concerning its aetiology, its significance, as well as the potential strategies for its prevention (Cantor and Ramsden 2014). Numerous epidemiological studies have also shown the relationship between stressful experiences and health across distinct historical periods (Susser 1981; Turner, Wheaton, and Lloyd 1995; Turner and Lloyd 1999), as well as in relation to gender (Kessler 2003) and race/ethnicity (Riolo et al. 2005). Yet, a wide body of social science scholarship has also mapped how these findings often get translated into matters to be addressed at the level of individual behaviours and lifestyles (Prainsack and Buyx 2011; Venkatapuram 2011). As shown also in the case of the epigenetic effects of socially determined racial disparities (Kuzawa and Sweet 2009; Mansfield 2012), the social dimensions of health are often obscured in public health translations of biomedical knowledge to leave room to a policy emphasis on individual responsibilities. On this basis, it is not hard to see how

the construct of EE may as well be translated into an injunction towards personal responsibility to improve living conditions in early-life. As Maurizio Meloni has argued (2016), the relationship between biology and politics is one of fundamental underdetermination: epistemic statements combine with different political values and adversarial uses of the same evidence in the social arena. Whether EE can tip the balance in favour of biosocial strategies of health promotion through socio-political measures, or whether it can succeed in promoting a social aetiology of the molecular traces of stress is not a matter that the situated practices and socio-political imaginings of the UoS lab can settle. The lab's emphasis given to "social" interventions on the biosocial nexus of "stress" and health does not suffice to determine the exercises of biopower (Rabinow and Rose 2006) this type of science will inspire.

This notwithstanding, it is also worth elaborating upon the openings towards biosocial thinking (Meloni, Williams, and Martin 2016) offered by the specific sociotechnical configuration of EE in the UoS. While limited in several respects, what I witnessed in the lab constitutes a situated attempt of life scientists to produce a repertoire of facts, mechanisms and technologies of intervention that concretely problematises the disembodied and individualistic narratives spreading out of epigenetics (Richardson and Stevens 2015; Kenney and Müller 2017). Although the group's views are certainly not informed by STS analyses of the drastic molecular biopolitics of the embedded body in epigenetics (Niewöhner 2011), scientists at UoS invest a lot of work to mitigate notions of the body in their science as a self-contained, decomposed and molecular entity (Rose 2007; Zwart 2016). And they do so not only through the discursive representations of their work delivered to the social scientist interrogating their practice. Rather, the group's attempt goes at the core of the experimental systems it employs. Without the need to claim that they succeed in escaping the dominant logic of their field, uses of EE in this lab suggest that there exists a certain design flexibility (Pinch and Bijker 1984) among the experimental engagements with biosocial thinking in the life sciences. The scientists I followed profit from the "digressions and transgressions" (Rheinberger 2011, p.315) they can afford to navigate the mutual constitution of the reductionist episteme and individualizing socio-political positioning of their science. From a critical perspective, this may not make much of a difference. Indeed, as shown above, critique provides different avenues to detect the strategic and over-inflated narratives hidden behind their declared engagements with the epistemic shortcomings and problematic figurations of agency coming out of epigenetics. Yet, a different outlook on these practices may focus on "how they think through, and work on, the tangled imbrication of bodies, brains, minds, subjectivities, lives and machines" in their practices (Fitzgerald and Callard 2015, p.11). To this reading, the UoS lab rather provides an example of how the artefacts of epigenetic

science can be produced to tentatively engage with ideas of a situated biology (Niewöhner and Lock 2018), as well as with the tension between collective and molecular/individual interventions at the core of epigenetics' biopolitics (Chiapperino and Testa 2016). To this view, the use of EE in the UoS lab suggests therefore that different degrees of imbrication between bodies and their (material and social) environments co-exist within practices of epigenetic biosciences. This diversity of approaches may certainly be limited – as I have shown in the case of the UoS lab – but it demands a thorough empirical scrutiny for the sake of unpacking epigenetics' conceptual, factual and normative contributions to a thick biosocial approach to health in our societies (Meloni, Williams, and Martin 2016).

Conclusions

The production of a biosocial account of "early-life stress" in the UoS lab emerges from processes straddling the technical and normative, the factual and the value-laden, the biological and social orders of scientific activity. The work of UoS scientists is characterised by a carefully attuned articulation (cf. Latour 1987; Fujimura 1996) of equipments, technologies, environments, interactions, behaviours, norms, academic injunctions, humans and non-human animals. The alignment of these different dimensions runs throughout the experimental pipeline I followed: from stress conditioning, to measurement of its epigenetic effects, and therapeutic interventions into these molecular marks.

Crafting a biosocial understanding of "stress" in the lab, I showed, oscillates between an emphasis on the material, organic and molecular traces of experiences and circumscribed attempts to deal with the biosocial complexities of this phenomenon in experimentation. First, the ontological choreography (Thompson 2005) of machines, mice and humans in conditioning experiments rests upon a mixed "extra-factual" (Nelson 2018, p.12) and epistemic work to produce certain experiences of mice (e.g. maternal separation, forced swim) to be considered "early-life stress". "Stress" comes to matter, at this stage of knowledge-production, as embodiment of experiences through the alignment of laboratory protocols with ethical and regulatory standards of animal welfare. Second, the continuum between (material and social) environments and bodies is also experimented with as material/biological traces. This happens when academic constraints and the dominant molecular episteme of epigenetics come into play. In order to contribute to the specialised literature on the molecular effects of "stress", this step of the research process consists in the purification of the epigenetic marks of early-life experiences into specific tissues and genetic loci. Here, we witness a (widely acknowledged) specificity of the experimental system of molecular epigenetics. Isolation of

the traces of "early-life stress" obliterates the continuities between the body and its socio-environmental situatedness (Niewöhner 2011; Landecker 2016), as well as within the body as unified, whole living entity (Rose 2007; Zwart 2016). Third, intervention into the epigenetic traces of "early-life stress" through EE shows how scientists at UoS attempt to re-position their science vis à vis the complexities of a biosocial account of "stress". EE is a composite technique acting on the organic traces of "early-life stress" through material, physical, cognitive and social stimulations. This epistemic machinery (Knorr-Cetina 1999) gets narrated as a distinctive approach in the field, and as a technoscientific approach restoring an uptake of the body as hybrid biological and socio-environmental entity in the lab. For this reason, scientists at UoS also lean on this technique to imagine their science as lending legitimacy to structural interventions into the socio-political determinants of stress-related illnesses (Jasanoff and Kim 2015; Richardson 2017; Chiapperino and Panese 2018).

The ways the UoS lab moves across scales and ontological orders, episteme and socio-political imaginings to make the body a porous and sensitive entity is far from being compatible with the ways "the social sciences […] *narrate* the material body and its environment" (Niewöhner 2015, p.231; original emphasis). Indeed, while this experimental system embeds the body in its (material and social) environments, its biosocial constructions are not the same as social scientists' call for a thick biosocial science (Meloni et al. 2018b). This task certainly falls outside the reach of benchwork science conducted with animal models (Lloyd and Müller 2018). Nonetheless, following the practices of this lab provides insights into the ways epigenetic scientists currently problematise openings towards biosocial thinking as matter *internal* to the designs and configurations of their epistemic work. As such, the case study presented here may contribute to current debates on the experimental entanglements across social and natural sciences in the post-genomic age (Callard and Fitzgerald 2015). Close scrutiny of how life scientists attempt to articulate a biosocial complexity of life through experimental adjustments helps us to understand how they can foray into complex thinking of the entanglements of our bodies with their environments. The UoS lab affords us an entry into the limitations that are intrinsic to the determinist and reductionist thinking of post-genomic life sciences (Waggoner and Uller 2015). While declaring itself a science of genome's plasticity and malleability, epigenetics is widely dominated by approaches that are not suitable to a thorough appreciation of the traffic between nature and nurture (Fox Keller 2015; 2016). The practices I described offer therefore a glimpse of the type of work the life sciences may have to perform to move closer their style of knowledge-production to the complexity thinking required by an appreciation of our situated biologies (Niewöhner and Lock 2018). To the social scientists interested in such an approach, this

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immersion into post-genomic science may indicate where reflexivity on a symmetrical appraisal of the biological and social dimensions of health is needed. There is still a long way to go before the life and social sciences are capable to participate together to such an ambitious project.

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