

Tracing Uncertainties in New Prognostics of Consciousness

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Uncertainty is a basic condition of medicine - in research, in the clinic and in the intersection between the two domains. Prognostics is in its very nature an attempt to address and manage the uncertainty of the future. New technologies are continuously developed in order to make prognostics more precise and hence make the future more predictable. However, such technologies may not always serve to decrease uncertainty, but rather enhance or introduce new uncertainties, and thereby open other futures than those imagined. Our study follows an interdisciplinary Danish research group currently seeking to advance methods of neuroimaging in prognostics for unresponsive patients with uncertain consciousness due to anoxic brain injury after an out-of-hospital cardiac arrest. Applying an interdisciplinary approach combining ethnographic methods and philosophical analysis we trace the experience of uncertainty in this context of tool development at the intersection of scientific and clinical reasoning around disorders of consciousness. Specifically, we employ and develop the three-dimensional framework of uncertainty developed by Han, Klein and Arora (2011). We identify salient uncertainties from the perspective of the researchers and show how these lead to different uncertainties experienced by the clinicians. Additionally,

we show that while ambiguity may be the source of different kinds of uncertainty, the context determines the nature of the source. Our investigation has a descriptive and theoretical focus, however, uncovering these details may serve as a basis for normative discussions of strategies for uncertainty management, as well as evidence evaluation in research and the clinic in the future.

Introduction

»He [the physician] is noticeably moved by the fact that it was possible to locate something after all, a response. He says that he had a hunch all along that she [the patient] reacted to sound. As an example, he mentions that one day, when he had been in to see her, had stirred a teaspoon in a cup by her head and then the patient had moved her eyes as if to see where the sound came from. Peter [MR-physicist and researcher] repeats that he cannot say anything about whether the response indicates life, consciousness or anything to which hope may be attached, but the normal MR-scan is completely unchanged and she is clearly anoxic.« (Fieldnotes from report to clinician following fMRI scan of patient with anoxic brain injury clinically diagnosed as vegetative).

Most people who have survived an out-of-hospital cardiac arrest (OHCA) are initially comatose. While some may gain capacity of functional communication to different degrees, others never recover. The prognosis for recovery is radically different depending on whether the patient develops to a vegetative state (VS)¹ or a minimally conscious state (MCS) (Giacino et al. 2018). Patients in VS are regarded as lacking the capacity for consciousness entirely, while patients in MCS are considered to have some minimal capacity for consciousness. Currently the standard method for determining consciousness is the JFK Coma Recovery Scale–Revised (CRS-R) (Giacino, Kalmar, and Whyte 2004). CRS-R relies on behavioral cues and is ordered by degree of complexity from the purely reflexive to behaviors mediated by cognition. It is comprised of six subscales: auditory, visual, motor, oromotor and verbal functions, communication and level of arousal (Giacino, Kalmar and Whyte 2004). Researchers have argued that this method is conceptually flawed, as it equates behavior with consciousness, and that the rate of misdiagnosis and the related problem of prognosis is unacceptable (Overgaard 2009). Misdiagnosis of VS has received a lot of attention, both in the public and in medical research. Case descriptions of sudden awakening and discovery of consciousness after years of misdiagnosis trail through medical and critical care literature (Vanhaudenhuyse

et al. 2018; Bruno et al. 2011). This has led to a wish for new tools of diagnostics and thereby more accurate prognostics for this subgroup of patients. The hope for such new tools in the future is that more precise assessments of the level of consciousness may enhance predictions of who may potentially benefit from better treatments (i.e. Stender et al. 2014; Skibsted et al. 2018). Thereby, also providing better support for decisions on withdrawal of treatment.

To the individual a prognosis concerns the possible futures of a life. A prognosis is a prediction of an outcome conditional on the characteristics of the patient and a considered medical action (Hilden and Habbema 1987). Prognostication in unresponsive OHCA patients is highly complex, as information from several clinical and epidemiological studies, as well as observations of the individual patient and considerations about plasticity of the brain must be integrated in a single outcome. Prognosis often has the form of a probability of an outcome within a time-frame (Hilden and Habbema 1987). Thus, the prognosis is itself an expression of uncertainty. The prognostic tool serves as a technology for making the prognosis. Developing a new prognostic tool is an attempt to reduce uncertainty, making it possible to outline discrete scenarios that provide more coherent support for the necessary decisions in individual cases (Hilden and Habbema 1987).

Our ongoing study follows the work of a research group behind a current experimental protocol at a Danish hospital, working to implement fMRI scans and EEG measurements in the diagnostics and prognostics of OHCA patients with ambiguous consciousness. We explore the experience, negotiation and management of uncertainty specifically in relation to the introduction of the new neuroimaging tools. In this paper, we focus on the fMRI tools, as this part of the protocol is more advanced in terms of integrating the research in the clinic.

Our aim is to explore the uncertainties involved, as well as take an important step towards developing our interdisciplinary research methodology. The study is novel, as it traces uncertainties by simultaneously working from empirical material produced in the ethnographic field and from an abstract theoretical framework towards a characterization of the salient uncertainties. Others have tried to outline the sources of uncertainty in disorders of consciousness (DOC) from a philosophical perspective (Lazaridis and Johnson 2018). However, our analysis is novel as it integrates empirical material and offers a structured framework for the uncertainty. We employ and critically discuss a three-dimensional conceptual framework for characterizing uncertainty in medicine developed by Han, Klein and Arora (2011), designed to encompass all (possible) manifestations of uncertainty in health care. We outline their framework and critically discuss its application to the

case of the development of the neuroscientific tools, as prognostic tools of the future in assessing disorders of consciousness. Employing this framework provides a possibility to distinguish different kinds of uncertainties and aspects of uncertainties. It thus makes it possible to describe the detailed landscape of uncertainty. Our investigation has a descriptive focus, however uncovering these details may serve as a basis for discussions of normative and ethical considerations, in relation to selecting strategies for management of uncertainties, as well as in an evaluation of evidence in research and the clinic in the future.

Methods and Ethnographic Setting

The study employs a blend of methods from analytic philosophy and medical anthropology seeking to harvest the potential of theoretical reasoning situated in a specific ethnographic context. Utilizing the theoretical tool of conceptual analysis from analytic philosophy we seek to clarify key concepts and explore the logical space of uncertainties in relation to the setting. The comprehensive ethnographic material of the study is a combination of interviews, participant observation and relevant documents. Specifically, we include material from six semi-structured interviews with researchers and clinicians engaged in the development of the experimental protocol. Further, fieldnotes are included from ongoing participant observation in a highly specialized intensive care, early neuro-rehabilitation hospital setting (since May 2019). As well as participant observation in a related research context, specifically concerned with the experimental fMRI, including fieldwork in two experimental fMRI scans (September 2017) and the clinical interaction around these. Also, email correspondence in relation to fMRI scans, as well as relevant documents related to the experimental protocol, such as information for participants and surrogates about the fMRI scan, clinical guidelines and descriptions of treatment trajectories constitutes part of the material. The field in this study is as such multi-sited, encompassing a constant movement between the clinic and research settings, and the transfer of knowledge constituted between these. The analytical work in this study is framed abductively (Timmermans and Tavory 2012; Brinkmann 2014) as a movement between the theoretical model of uncertainty (Han et. al 2011) and the empirical hesitations and uncertainties introduced to this model from the ethnographic work. Research always involves an ethical relation with the world we are studying (Hastrup 2004), which directs the representations and authority claimed by our work. This project holds ap-

parent ethical challenges, as the research is carried out in very sensitive settings. Approaches to ethics and informed consent has been thoroughly discussed with participants and gatekeepers to the ethnographic settings. Specifically, all participants in interviews have provided written, informed consent and for the participant observation the management at the hospital and clinic have consented to the work. All staff, relatives and others we have interacted with in the field have been informed of the work and asked permission for our presence in the specific situations. Patients were informed about our presence in field but were not able to respond to this information. The study is registered with Aarhus University, Denmark and the Central Denmark Research Ethics Committee has been notified of the project (Case number: 1-10-72-1-19). In accordance with Danish research regulations they do not require ethical approval for this research.

The Three-Dimensional Framework

Han, Klein and Arora (2011) define uncertainty as an experience of ignorance and argue that each particular experience of uncertainty in medicine is characterized by three dimensions. The first dimension is the source of the uncertainty – the primary cause of the uncertainty. The second dimension is the issue – what the uncertainty is about. The third dimension is the locus of the experience – the subject who experience the uncertainty. Below we outline their framework and discuss how it applies in our field. During the outline we provide relevant examples, however as each instance of uncertainty is characterized by all three dimensions the initial exposition will focus on the conceptual boundaries of the framework. In our exposition we develop the framework, where things have been left unclear by Han and colleagues (2011 and 2017). For an overview of dimensions see also Figure 1.

Sources

The source of uncertainty is that which causes the specific uncertainty. Han, Klein and Arora (2011) distinguish between three main sources 1. *Probability* 2. *Ambiguity* and 3. *Complexity*. Below we explain each category.

Probability

Concerns the fundamental indeterminacy or stochastic nature of future outcomes. This is what Hacking (2006) has termed aleatory probability. For example, we may know from a study that 50 % of subjects who are initially diagnosed as being in a MCS has no to moderate disabilities after 12 months (Giacino and Kalmar 1997). However, with respect to the individual patient in the clinic we have no knowledge of which outcome will result. What we do know, is the probabilities of these outcomes. This is similar to knowing the probabilities in a game of heads and tails with a fair coin. Uncertainties stemming from probability are sometimes labeled 'irreducible' as they cannot be reduced by the mere acquisition of more knowledge.

Ambiguity

This source of uncertainty concerns the nature of available information about probabilities. Examples are lack of reliability, credibility and adequacy of information. This is also called epistemic uncertainty, as it relates to the knowledge, or lack of such, about the probability of nature (Djulgovic, Hozo, and Greenland 2011). Ambiguity can arise as the result of imprecisions, conflicting or insufficient evidence. One way of managing this in science is by stating a confidence interval, which reflects the reliability of the statistical estimate.

Complexity

Han, Klein and Arora (2011) characterizes complexity as "aspects of the phenomenon that make it difficult to comprehend" (p. 833). In this way complexity is defined by both ontological and epistemological aspects, as it depends on the character of the phenomenon as well as ability to comprehend. Examples provided are conditional probabilities or multiplicity in causal factors, outcomes or choice options, which may diminish comprehensibility and/or produce information overload. As complexity has an epistemological aspect it may be remedied to some extent, for example it may be managed through the use of algorithmic tools in prognostics.

Issues

The issues of uncertainties concern what the person is uncertain about. Han, Klein and Arora (2011) divide issues into three main categories: 1. *Scientific uncertainty*. 2. *Practical uncertainty* 3. *Personal uncertainty*. Each focus on specific parts of the medical situation. Scientific uncertainty is disease-centered, whereas practical uncertainty is centered around the medical system and finally personal uncertainty is centered around the patient.

Scientific Uncertainty

Scientific uncertainty concerns uncertainties about scientific entities and activities such as models, measurements and sampling. Han, Klein and Arora (2011) distinguish between four issues: diagnosis, prognosis, causal explanations of the illness and treatment recommendations. Our focus is prognosis. However, in practice these issues are highly entangled and we take diagnosis to be an important step in the process of prognosis (Wilkinson 2013). Depending on the locus the issues of prognosis may take different forms. A clinician may be uncertain about the prognosis of an individual patient, whereas a researcher may focus on uncertainties about the capacities of the prognostic tool.

Depending on the sources, the scientific uncertainties may also be of different nature. From probability we encounter uncertainties tied to applying class probability (the frequency) to individual case probability. In theory, this may not be remedied by more information. However, in practice what can be done to aid such a generalizations, is to have high awareness of differences between patients in the test group, as well as the setting under which the result was obtained (Djulgovic, Hozo, and Greenland 2011). When the source is ambiguity, we may distinguish between *conceptual* and *methodological uncertainty* (Han et al. 2017). *Conceptual uncertainty* may have two main sources namely model inadequacy (in our setting this could relate to general models of consciousness or models relating cognitive abilities to brain activation) and taxonomical inadequacy: limitations presented by the taxonomical system used to classify the illness i.e. the definitions of categories. *Methodological ambiguity* concerns uncertainty about test or research methods such as: 1. Problems with the integrity of sample or data (i.e. bias) 2. Limitations of test methods (i.e. precision and accuracy in instruments) 3. Unmeasured factors 4. Error or variance in the procedure 5. Misinterpretations of test (i.e. failure to analyze test results).

In prognostics, complexity is also regularly a source of uncertainty as the process of prognosis involves taking into account information about how different causal models interact, as well as the results of tests and clinical studies.

Practical Uncertainty

Concerns experience of lack of knowledge of structures of the health care system, such as facilities, resources and expected quality of care, as well as processes for actions in this system. The examples included by Han, Klein and Arora (2011) are exclusively focused on the patient and relates to uncertainties about the competence of one's physician, how to identify and access the right services, the responsibilities and procedures that one must undertake to receive care. However, practical uncertainty understood as uncertainty regarding which practical actions to perform and how to navigate the health care system are also part of the world of the clinicians and researchers. A clinician may face uncertainties related to patient care (i.e. where in the system does this patient get the best possible treatment or which unit can I discharge the patient to?). Similarly, researchers may experience uncertainties in relation to the development of the new prognostic tool (i.e. How do we recruit enough patients for the trials?).

Personal Uncertainty

Personal uncertainty, according to Han, Klein and Arora (2011), concerns psychosocial and existential issues such as the effect of treatment or illness on one's goals in life and one's personal relationships. They particularly mention issues identified by Kasper et al. (2008) such as social integration and uncertainties about mastering of requirements. The categorization by issue does not in itself determine the locus of uncertainty, however, the only appropriate locus of the examples of personal uncertainty mentioned in Han, Klein and Arora (2011) is the patient.

Locus

Establishing the locus of uncertainty always requires reference to a specific situation or given circumstance. In a specific situation uncertainty can exist in several loci at the same time or be manifested exclusively in one of the subjects partaking in the situation. According to Han et. al. (2017) uncertainty may sometimes be

shared, as when a physician effectively educates the patient about scientific uncertainties relating to the benefits and harms of a treatment. However, if we are to take at face value Han et al.'s definition of uncertainty as a subjective experience, then uncertainty is difficult to truly share, as one dimension will differ, namely the locus. That is, the uncertainty experienced by the physician and the patient are not two different *instances* of the *same* uncertainty, but rather two *kinds* of uncertainty. What is shared is the issue and the source of the uncertainty. This is a more precise characterization as it highlights that the locus of the experience makes a fundamental difference to the nature of the uncertainty. Uncertainties sharing both source and issue may differ greatly in salience and related feeling of urgency depending on the locus. After all the patient will be the one suffering both harms and benefits of the treatment in question. Further, different people are likely, due to different cognitive capacities and extent of knowledge, to experience different degrees of uncertainty, even when the source and issue are shared. We may also expect that uncertainties may be experienced differently depending on wider social and socio-economic context (Løvschal-Nielsen, Andersen, and Meinert 2018). It is exactly because the context of the individual person matters that it makes sense to include locus as a separate dimension in the framework. In the case of unresponsive OCHA patients, a key question is exactly whether the individual patient may be the locus for uncertainty at all. However, as our focus here is the process of the development of the new prognostic tools, we focus exclusively on the loci of the clinical and research staff.

Tracing Uncertainty in the OCHA Case

In this section, we employ the three-dimensional framework in tracing and categorizing uncertainties in the case of the development of a new neuroscientific prognostic tool for nonresponsive OCHA patients, while at the same time using examples from the empirical investigation to elucidate how the conceptual framework could be developed. Working from the three-dimensional framework there are several possible ways to begin to trace the uncertainties as each dimension provides a possible point of departure. In this paper, we take point of departure in the loci of researchers and clinicians and then consider salient uncertainties experienced in each locus in turn. However, before outlining the uncertainties we briefly introduce the technology and methods behind the fMRI protocol.

Introduction to the Technology and the Aim of the Protocol

The fMRI method measures activity by measuring blood circulation in the brain and the difference in magnetic properties of oxygenated and non-oxygenated blood. The stimuli in the test of the experimental protocol are auditory and the tasks are passive and require no action on part of the participant. Patients are tested twice during the 8-10 weeks period of assessment. The results of the fMRI are presented as images where the average of several measurements is projected onto a model of the standard brain. In the protocol, the technology is envisioned as a means for assessment of the individual patient: *»the recorded images are employed for detection and assessment of the level of consciousness of the patients«*. It is a stated ambition of the protocol to share the results of the individual tests with the surrogates of the patient participant. This is also outlined in the information material provided to surrogates prior to study enrolment: *»Your relative will be able to directly benefit from the examination (test), as the results will be included in the overall assessment of the prognosis and the future process of treatment«*.

The Researcher's Perspective Scientific (Methodological) Uncertainties

Some of the scientific uncertainties related to the new tools are disclosed in the procedure of the fMRI scans. Even patients assumed to be in VS have involuntary spasms, head movement, or irregular breathing. At one of the first scans, the very disruptive and irregular breathing pattern of the patient, causing sudden bursts of movement, created some methodological uncertainties with respect to the possibility of using the data for analysis.

»The images look like crap“, the researcher says, “even the most creative analysis won't tell if that was a response, or he just moved« (fieldnotes, August 30, 2017)

The source of this uncertainty was ambiguity about the quality of the data. The patient in the scanner was relatively still compared to what may in general be expected which made the researchers worry that they would have to give up the study altogether. As a way of controlling this uncertainty, the researchers subsequently introduced a light sedative drug into the protocol. However, this drug reduces the activity in the brain area of interest for the test. The activity of this area

is, according to research, already reduced in this type of patients, so the sedation adds uncertainties on its own. Also, this second uncertainty arises from the ambiguity involved in the possibility of measurement error. These uncertainties are particularly salient for the researchers as it is their responsibility to try to remedy these by further modifications of the method. In the end, the researchers, despite the poor quality of the data, were indeed able to locate a response in this particular patient. As the patient was considered vegetative by clinical observations this was a surprising result. Though the researchers considered the result to be certain, the clinician chose in the end not to include the finding in the prognosis. We will return to this issue when considering the uncertainties experienced by the clinician.

Uncertainties Surrounding the Stimuli and Paradigm

It was the original intention that the fMRI part of the protocol should share the experimental paradigm of the already ongoing EEG study. This paradigm was quite complex and developed to track a hierarchy of different levels of language processing from *»automatic sound processing to the tentative language processing and to the full-on difference in meanings«* (Interview with researcher). It was designed as an oddball paradigm. This kind of paradigm consists of a sequence of the same repetitive stimuli (the standard) which is randomly interrupted by a different stimulus (the deviant). However, in the process of testing the paradigm in the fMRI scanner with a healthy control, the researchers identified some salient methodological uncertainties with respect to the stimuli and its interaction with people in the scanner. People in the fMRI scanner are lying down and the noise is quite high. This means that even for healthy subjects the person is more likely to fall asleep than in the EEG study where people are seated in a chair. Also, the fMRI researcher indicated that it had been a concern to them that the OCHA patients, who they would be examining in the scanner, were likely to fluctuate in and out of consciousness. Given the state of the patients, it was of concern whether they were able to get through to the person at all and they were less concerned about more complex cognitive functions. Even the structure of the oddball paradigm was considered to be too complex for the purpose:

»[...]there were some studies about how one could mix these [the stimuli], [...] then there was something about, that we should run two times instrumental and then

three times with lyrics and so on...but again, it got too... as long as we could see anything at all.» (Interview, MR-physicist/ researcher on design of the stimuli).

Thus, a simpler or less nuanced paradigm seemed not only sufficient but also more appropriate. By chance, the fMRI researchers happened to discuss this while being overheard by another neuroscience researcher not engaged in the particular project. This person suggested to them to use the difference between instrumental music and music with lyrics for the paradigm, based on the success of another research group with such studies. Satisfied with this suggestion the researchers opted to develop a new paradigm including musical stimuli which could be played »at full blast« and which could be heard by the participant in the scanner. The selected music was a well-known, popular song supposedly familiar to most future patients. The stimuli were made out of two 15 sec cut-outs of this song, one instrumental and one with lyrics. The two music cut-outs were played in sequence with a 15 pause after each and followed the same rhythm through all 15 minutes of the scan. The paradigm was not tested on healthy subjects previous to the fMRI scans involving patients.

It is possible to interpret the situation in at least two ways. One is to see this as a lack of respect for the normal standard of such research, that stimuli should be tested on healthy subjects first. A recent national clinical guideline from the UK warns of uncertainties related to the standard of the experimental paradigms for neuroscientific research in relation to disorders of consciousness (Turner-Stokes and Royal College of Physicians 2013). Similar concerns were raised in interviews about this project on the appropriateness of developing stimuli in this way. On the other hand, the choices made by the fMRI researchers can be interpreted as a weighing of uncertainties in light of real-life conditions revealed only in the clinical setting. In this light, the situation can be described in the following way: Everything is set up for the experiment, ethics have been approved, the scanner has been updated, and so on, but the paradigm seems at risk of making people fall asleep in the scanner. It also appears unnecessarily complex to the researcher and something needs to be done. There are three options. The first is to stop the research, the second is to go ahead with the paradigm anyway and the third is to make something new. There was no time to conduct initial (statistically significant) research on healthy subjects. This is a matter of weighing uncertainties. There are uncertainties tied to the original stimuli which seem very salient to the fMRI researcher and which is not something that would have come up as a problem in the original EEG study on healthy subjects. In the EEG study all parti-

cipants were awake and sitting up. Furthermore, the EEG study took place in the quiet research facilities at the university. Not in the messy clinical setting. There is also a less visible but equally relevant uncertainty in using the EEG paradigm, which is that even this particular stimuli and paradigm has not been tested on healthy subjects in the fMRI-scanner (apart from one pilot scan at the hospital). That is, there is no statistical evidence of activation patterns as measured by an fMRI scan for this particular paradigm. Transferring a paradigm and stimuli from one imaging modality to another is not straight forward and introduces uncertainty (Warbrick, Reske, and Shah 2013). This uncertainty has to be weighed up against the uncertainties of developing an entirely new paradigm with new stimuli.

It is remarkable to observe that the salient scientific uncertainties for the researchers are methodological uncertainties linked to the implementation of the method and acquisition of data. In contrast, conceptual uncertainties, which have been central to the philosophical debate, such as inadequacy in models of consciousness and how brain activity relates to levels of consciousness and fundamental methodological uncertainties about reverse inference from brain activity to consciousness (Klein 2010; Owen 2013), were not at the forefront of the uncertainties of the research informants in this project.

The Clinical Perspective

Scientific Uncertainty in the Clinic

As mentioned previously, the fMRI researchers were able to detect a response in a patient otherwise believed to be in a vegetative state, despite poor image quality. When learning about the response the physician was surprised, as this was not the expected outcome for the patient who in all behavioral tests in the clinic had presented to be vegetative (see also opening vignette of the paper). Yet, confronted with this finding the physician interpreted this in concordance with a previous observation of eye movement in the patient, seemingly responding to the noise of a stirring of a teaspoon in a coffee cup. In the end, however, the prognosis of the patient was not changed, as the physician decided to leave the information out of the prognosis and inform the relatives that the test was inconclusive. The physician considered the data material that served as the basis for the result as too uncertain due to the methodological uncertainty caused by the movements of the patient mentioned earlier. Thus, while the fMRI researchers, in the end, were

certain of their findings, the initial methodological uncertainty was considered by the physician as a reason for not integrating the result.

At the same time, the fMRI result was interpreted as conflicting with the knowledge otherwise gained in the clinic. This highlights an experience of scientific uncertainty especially salient for the clinicians due to the complexity of prognostics. In order to develop a prognosis, the fMRI measurements are to be integrated with results from other prognostic tools. An uncertainty arising from this complexity is how one should weigh evidence acquired through neuroscientific methods against other kinds of evidence when dealing with questions about the mind (Andersen 2017). An uncertainty is how to rate a detected brain response to the stimuli in the fMRI paradigms to responses to the stimuli observed in the course of recording a behavioral test (CRS-R). In the particular case of the previously mentioned scan of an OCHA-patient, the methodological uncertainty due to ambiguity explains the apparent lack of influence of the fMRI result on the prognosis. However, the observation makes one question come to the forefront: whether the result, had it been more certain, would have made any difference for the prognosis of the individual patient after all? How does a response to music, detectable only in the fMRI scanner, rate in comparison to a response detectable by behavior? The CRS-R relies on multimodal stimuli and in this sense, the auditory stimuli of the fMRI only cover a narrow part of the spectrum. Should these tests count as equal? In the philosophical literature, this issue has been approached in different ways. Bayne, Hohwy and Owen (2017) have argued that the recent results of neuroimaging highlight taxonomical uncertainties about the adequacy of the current diagnostic categories. They suggest to reform the taxonomy based on additional brain-based criteria. In contrast, Fisher and Truog (2017) argue that the uncertainties in diagnostics distinguishing between VS and MCS by detecting consciousness are so severe that the taxonomical distinction is not tenable. On this ground, they advocate for deemphasizing the role of consciousness in decisions surrounding unresponsive patients. Instead, they suggest to make decisions in collaboration with the relatives based on presumed values of the patient. However, as we shall see in the following, the values of the patient are themselves the source of considerable uncertainty.

Personal Uncertainty Due to Ambiguity

Based on our work, the framing of personal uncertainty by Han et al. (2011 and 2017) is too narrowly focused on the patient. The clinicians also experience uncertainty about issues relating to existential questions concerning the experienced value of life of a patient and the potential influence on the patient's social relations. Thus, the issue of personal uncertainty is not exclusively experienced by the patient as is indirectly suggested by Han et al. (2011 and 2017). The uncertainty is enhanced in situations where patients are unable to express preferences or participate in medical decisions (Kaufman 2003). It has come up in conversations with clinicians during this study how they worry about the kind of life they are able to preserve for the patient, and how this life may be experienced differently by different patients. Despite suffering similar damage, patients may have existentially very different experiences. The clinicians have experienced this difference in recovered patients. Some patients experience a renewed appreciation of life while others may not be able to cope with the new conditions and may form a wish to take their own life. In this way, the clinicians, despite having done their very best in terms of medical efforts, cannot be certain that this provides a life and an experience of life worth in accordance with the values of the patient.

Would the development of neuroscientific methods be able to alleviate this kind of uncertainty? By employing active paradigms (where people have to react to the stimuli by imagining things like playing tennis (Owen et al. 2006)) some researchers believe that we may be able to communicate with some of the unresponsive patients. A meta-analysis of the research shows that about 15% of patients believed to be in a vegetative state are able to follow orders when asked to imagine certain scenarios (Kondziella et al. 2016). This has been suggested as a method for assessing the quality of life of patients with DOC (Tung et al. 2019). However, this kind of assessment would require a substantial amount of time in the scanner and would not be feasible in the clinic within the near future. Given that people attach different values to their experiences, it must be based on the values of each individual. Thus, general estimates will not be sufficient. Further, it still leaves a large group of patients who are unable to actively react to stimuli but may nevertheless be able to have conscious experiences (Kondziella et al. 2016). Therefore, the hope of eliminating this kind of uncertainty entirely is limited.

Discussion

Evidently, the above outline represents only a subset of instances of uncertainty related to diagnostics, prognostics, treatment and care connected to this group of patients. In the forming of a prognosis, uncertainty is always involved when transferring knowledge about frequencies in populations into a prognosis for the individual. This uncertainty stems from probabilities and will persist regardless of the prognostic tools one employs. Also, behavioral as well as neuroscientific tests only reveal the degree of consciousness at the specific moment of testing, and consciousness in these patients is known to fluctuate (Zeman 2002). Therefore, the presence of consciousness cannot be ruled out entirely and the diagnosis of VS is given only on the basis of finding no evidence of consciousness (Coleman et al. 2007).

What is gained by using the three-dimensional model developed by Han, Klein and Arora (2011) is that the separate aspects of the uncertainties become visible. For example, by paying attention to the locus we may recognize that uncertainties having the same issue and source will lead to different actions of management depending on whether one has primarily clinical or research responsibilities. It also becomes visible how the context of loci and issue shapes the source. Ambiguity is the source of both the methodological uncertainty experienced by the researchers and the personal uncertainty experienced by the clinicians, however, the distinct features, as well as the possibilities of working towards a reduction of such uncertainty, is different in the two instances. We may also observe that while the new technology may remedy some of the methodological and conceptual uncertainties of the behavioral test (CRS-R), such as not equating behavior and consciousness and (potentially) leading to less misdiagnosis, it does introduce new methodological and conceptual uncertainties.

A conceptual limitation of the three-dimensional framework is the insistence on the subjective nature of uncertainty. Han, Klein and Arora (2011) take it as their point of departure that uncertainty is »*the subjective perception of ignorance*« (p. 830) and a »*state of mind rather than a feature of the objective world*« (p. 829). However, they provide no reason for assuming that this definition is correct. It seems that this definition could conflict with their understanding of uncertainty arising from probability (aleatory), which is assumed to be intrinsic to the phenomenon and thereby a feature of the objective world. A philosophical discussion of the subjective nature of the three-dimensional framework is outside the scope of this article, however, we wish to highlight that this assumption constitutes a conceptual li-

mitation of the framework. Recognizing non-subjective variants of uncertainties would lead the way for recognizing other possible loci as carriers of uncertainties, such as for example documents (i.e. patient records and research protocols).

One of the advances of the three-dimensional framework, according to Han, Klein and Arora (2011), is that it seeks to encompass all manifestations of uncertainty in health care, whereas others, e.g. Mishel (1981) or Kasper et al. (2008), focus exclusively on uncertainty experienced by patients. However, utility does not in itself come with the possibility of capturing the full range. Utility depends on purpose. Compare it to the case where you have a map of a city. This map details roads etc. and is practical for locating an address. However, it is of no use if you want to find the highest point in the city or see where the city is located relative to other cities in the country. In contrast, a full map of the country provides a good overview but is useless when it comes to locating an address. Capturing the full range comes with a price, namely the price of abstraction. One challenge that we experienced in our work was that categorizing the individual instances of uncertainty by using the theoretical framework of the dimensions directed our attention to the particular instances of uncertainty as separate from the situation. This focus creates a tendency to neglect the influence of the environment of the situation and how different uncertainties may influence each other just by being part of the same situation and not by conceptual relations or logical implications.

Our considerations have been to create an iterative process moving back and forth and creating a dialogue (Mansnerus and Wagenknecht 2015) between the categories outlined by the theoretical framework, conceptual possibilities of uncertainties and the salience of uncertainties in the empirical setting. The advantage of this combined approach is that abstraction allows for discovering uncertainties less visible in the empirical setting (an empirical exploration which is also constrained by the access one is granted as a researcher). At the same time, close attention to the empirical setting revealed uncertainties that would perhaps go unnoticed in a purely theoretical approach. This was the case when we looked into the issue of how the stimuli and paradigm were changed for the fMRI study. At first, it seemed that employing a new and not previously tested paradigm and stimuli were incompatible with standards of good research practice. However, through our observations and interviews a second time, we became aware that this too was an attempt of managing uncertainties; uncertainties that arose in the clinical setting and in the circumstances of this particular kind of patients.

The approach of analytic philosophy of science is to work with conceptual distinctions to form a theory of uncertainty that will be able to model all types of

uncertainty at all times. It explores the possible logical spaces for abstract types of uncertainty rather than focusing on which uncertainties are in fact implemented. A scientifically informed analytic philosophy of science will, of course, seek to find examples of uncertainties. However, it is also assumed that knowledge about types of uncertainties, which may never occur, will enlighten us in our knowledge about the ones that do in fact occur. In contrast, in anthropology the goal is rarely a complete theory or model but rather, through descriptions of the emergent object in the situated practice of fieldwork, producing different ways of knowledge-making that analytically transcend the obvious. That is, analytic philosophy generally works by abstracting away from the specificities of the situation. In contrast, the object of study in anthropology is always specifically situated. In this article, we have sought to apply both approaches.

Conclusion

In this article, we have employed and critically discussed a three-dimensional taxonomy of uncertainty combined with empirical material to trace key uncertainties in the development of new prognostic tools for OHCA patients with ambiguous consciousness, as well as showed how these uncertainties relate to the uncertainties identified in the clinical settings. We argued that strictly speaking on Han, Klein and Arora (2011)'s framework, uncertainties cannot really be shared. Rather, what may be shared is the source and issue. In our analysis, we identified the salient uncertainties from the perspective of the researchers as that of methodological uncertainties and showed how these lead to different uncertainties experienced by the clinicians. At the same time, we showed how ambiguity may be the source of both personal and scientific uncertainty. However, the context of issues and loci determines the nature of the source significantly. We further argued that Han, Klein and Arora (2011)'s framework must be extended to include personal uncertainties experienced by clinicians in relation to the patients and that these are especially salient when patients are unresponsive.

As our knowledge builds and transforms, so will the uncertainties tied to it. It is not possible to predict the uncertainties of the future, however, providing a language for categorization may be of practical use to clinicians and researchers to support their practice and enable discussions of management of uncertainties related to the novel nature of these technologies. A central part of managing uncertainties is being able to identify uncertainties and their characteristics, as well as

being aware of which kinds of uncertainties, in both research and clinical practices surrounding these severely injured patients, are to be accepted and which are to be sought reduced in the future. Our focus has been the researchers and clinicians involved in research. However, this knowledge of uncertainties may also in the future prove helpful in selecting strategies for communication with surrogates of unresponsive OHCA-patients.

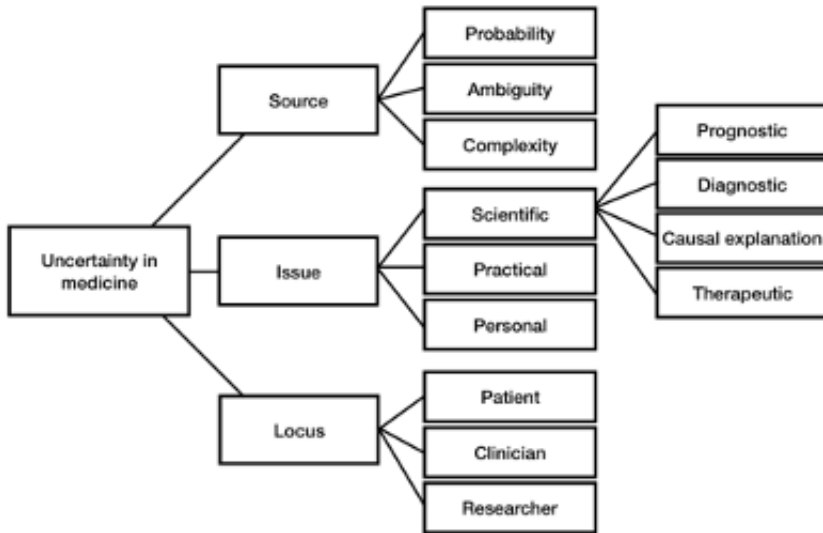


Figure 1:

Figure 1: Dimensions of Uncertainty

The figure depicts the dimensions of uncertainty in the Han, Klein and Arora (2011) framework. Note that each individual experience of uncertainty will always be a mix of all three major dimensions. The figure does not include methodological and conceptual uncertainty. Both these subspecies of uncertainty have ambiguity as their source and are tied to the issue of scientific uncertainty. These subcategories thus cut across the framework and would need to be depicted separately. (Han et al. 2017 developed a similar figure of their findings in the area of genetics. However, as they include such mixed subcategories the figure is imprecise)

Notes

1. We use the term 'vegetative state' as this is the term used by our informants. However, increasingly the term unresponsive wakefulness syndrome (UWS) is adopted in its place in order to avoid the negative connotations of the word 'vegetative' as well as a way to recognize the uncertainties regarding the degree of consciousness (Laureys et al. 2010; Machado et al. 2012).

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