

Varieties of Process Tracing and Methodological Issues

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Introduction

- ❖ Over the last years, a recent theme of discussion in the philosophy of science literature deals with the role that mechanistic evidence can (or should) play in establishing causal claims
- ❖ Several authors have proposed process tracing (PT) as a strategy to discover causal mechanisms in the health science as well as in the social sciences
- ❖ Recently, Beach and Pedersen (2013) advanced the debate on PT by identifying three variants of this methodology: theory-testing, theory-building and explaining-outcome
- ❖ Is this taxonomy sufficient and, if not, how can we improve it?

Plan

I examine a case study in which PT is performed in medicine: the study of chronic traumatic encephalopathy in professional football players

I show:

- ❖ how the three variants of PT can be connected to each other
- ❖ that mechanistic evidence has been collected by using different methods: case studies, experimental studies and large-scale studies

I suggest that these three methodological variants can be considered different forms of PT and that, in order to understand complex causal mechanisms, scientists are likely to require evidence from more than one methodological variants of PT

Beach and Pedersen's variants of PT

1. Theory-testing PT: evaluating whether evidence shows that a hypothesized causal mechanism is present in a particular case and that it operates as theorized.

To test the hypothesis, scientists have to translate a theoretical expectation into a specific prediction of what observable manifestations of the mechanism should be present if the hypothesized mechanism worked. Then, empirical evidence can be collected and, according to what is observed, scientists should be able to infer whether their confidence in the hypothesis should be updated and whether the mechanism functioned as predicted.

2. Theory-building PT: building a theory about a causal mechanism between X and Y that can be generalized to a population of a given phenomenon.

To build a theory, scientists investigate the empirical material available to infer whether it reflects an underlying causal mechanism at work. Once the theory is built, it has to be tested.

3. Explaining-outcome PT: crafting a sufficient mechanistic explanation of a particular outcome.

Sufficiency can be confirmed when it can be validated that there are no important aspects of the outcome for which the explanation does not account.

Chronic traumatic encephalopathy



- ❖ Starting point: explaining-outcome PT
- ❖ Autopsy meant to conclusively determine the principal cause of death of a professional football player (Omalu et al. 2005)
- ❖ The principal cause of death was claimed to be a chronic traumatic encephalopathy (CTE)
- ❖ From explaining-outcome PT, scientists moved to theory-building PT: they wanted to develop a general hypothesis of the mechanism producing CTE

Chronic traumatic encephalopathy



Justification of theory-building PT:

- ❖ In 1969 Roberts published a book providing detailed clinical information on a random sample of 224 retired professional boxers
- ❖ Some years later, Corsellis et al. (1973) described CTE in 15 boxers
- ❖ CTE was thought to be found almost entirely in boxers prior to 2005
- ❖ In 2005, the autopsy led scientists to think that different kinds of brain injury could cause CTE

Chronic traumatic encephalopathy



Justification of theory-building PT:

- ❖ Surveys shew that many professional football players manifested symptoms like a) alteration of awareness or consciousness and b) persistent headaches, vertigo, loss of balance, memory disturbance, hearing and visual loss...
- ❖ The autopsy enabled scientists to some pieces of evidence for a generalizable mechanistic hypothesis
- ❖ Further pieces of evidence were collected through the autopsies of other 4 professional football players (Omalu et al. 2010, Bailes et al. 2013)

Chronic traumatic encephalopathy



A mechanistic hypothesis was developed:

- ❖ The pathological mechanism was thought to be a complex combination of biochemical cascades induced by cumulative effects of repeated low-grade concussive brain injury and rapid acceleration-deceleration of the body when the brain was free to move within the cranium
- ❖ Several potential mechanisms were thought to be of potential interest: mechanisms related to cell survival/death, regulation of tau phosphorylation/dephosphorylation (kinases/phosphatases), bioenergetics, and propagation of tau-based changes (Turner et al. 2015a)

Chronic traumatic encephalopathy



- ❖ This mechanistic hypothesis included a broad target population of boxers, football players, soccer players, hockey players and soldiers
- ❖ By developing their hypotheses, scientists started to consider many questions such as the role of impact severity, the time interval between impacts, the total number of impacts sustained and the age at which impacts occur
- ❖ These particular characteristics of the causal mechanisms are very important to provide public health advices
- ❖ In order to develop a more complete mechanistic hypothesis, scientists are searching for further pieces of evidence

Chronic traumatic encephalopathy



- ❖ McKee was able to study samples from 85 brains and examine them for evidence of CTE. The clinical history was established through interviews with the families of the deceased. The neuropathology examination was conducted using tissue samples from the brain bank.
- ❖ The results linked CTE to a history of repeated head trauma in 63% of the cases
- ❖ He collected evidence supporting the role of hyperphosphorylated tau protein deposition in CTE development (McKee 2012)

Chronic traumatic encephalopathy



- ❖ Experiments were conducted with rodents to study hyperphosphorylated tau protein accumulation: groups of mice and rats were subjected to exposure to single or repetitive brain injury and subsequently their behaviour and their brains were analysed and compared to those of the control groups (Petraglia et al. 2014, Turner et al. 2015b)
- ❖ Given the potential role that age plays in this mechanism, animals from both groups had to be of the same age
- ❖ Control animals had to be anesthetized for the same duration as injured animals
- ❖ Special helmets were designed to allow for accurate delivery of injury and diffuse spread of the force of the impacts

Chronic traumatic encephalopathy



- ❖ Data recorder through accelerometers and recording systems have been used to find the thresholds of head impact and to understand the influence of linear and rotational impacts (Ban et al. 2016)
- ❖ New projects based on accelerometers aim to gather new mechanistic evidence concerning the role played by peak accelerations, impact duration, location of the impact, linear and rotational impacts...

Chronic traumatic encephalopathy



Summary

- ❖ Starting point: explaining-outcome PT
- ❖ Development of a general mechanistic hypothesis (theory-building PT)
- ❖ Case studies (autopsies), experimental studies and large-scale studies used together to advance the hypothesis and to corroborate mechanistic evidence

Conclusion

Theory-building PT, theory-testing PT and explaining-outcome PT are often very interconnected

When the aim is to build a hypothesis about a complex mechanism, it seems that before testing the complete hypothesis, hypotheses about smaller parts of the mechanism are tested

Such tests are particularly important when the quality of mechanistic evidence used to build the hypothesis appears not very high

In such cases, mechanistic evidence collected via different methods can be used to develop/test parts of the mechanism

Conclusion

Three methodological variants of PT, with different methodological implications

❖ **Case studies PT:** observational studies based on autopsies

- Representative case and idiosyncratic features (genetic predisposition)

❖ **Large-scale PT:** accelerometers and recording systems

- Aggregation of datasets and origin of data

❖ **Experimental PT:** intervention on a (model) population of rodents

- Problem of extrapolation, experiment design

	Theory-building	Theory-testing	Explaining-outcome
Case-study PT	Find evidence of a causal mechanism generalizable outside of the individual case to a bounded context	Test a causal mechanism by searching for supporting evidence in a representative case	Develop a sufficient explanation of a particular puzzling event by observing the event itself
Large-scale PT	Use the analysis of a large sampled cohort to discover evidence of a causal mechanism generalizable outside of the cohort itself	Test a causal mechanism by analysing data concerning a large cohort related to the target population	Develop a sufficient explanation of a particular puzzling event by examining a great amount of data on a related large cohort
Experimental PT	Find evidence of a causal mechanism generalizable outside of the model population to a target population	Test a causal mechanism by searching for supporting evidence in a model population	Develop a sufficient explanation of a particular puzzling event through experiments on a model population

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Thank you for your attention!

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NFL

NFL official acknowledges link between head trauma and brain disease CTE

Jeff Miller, the league's senior vice-president of health and safety, admits link to degenerative brain disease during congressional committee roundtable