

HU-Semesterprojekt

# **Strategien zur Dekodierung des 'Versuchszwecks'**

# Gesetzlicher Auftrag und Konzeption

**TierSchG § 7a (2) Unerlässlichkeit eines Tierversuchs:**

*„Es ist zu prüfen, ob der verfolgte Zweck nicht durch andere Methoden oder Verfahren erreicht werden kann.“*

**Unser Ziel:**

Entwicklung und Bereitstellung eines frei verfügbaren Online-Tools für die versuchszweckgenaue Recherche nach potentiellen Alternativmethoden zu einem vorgegebenen Tierversuch.



**Schritt 1:** Suche nach wiss. Arbeiten mit identischem oder „ähnlichem“ Versuchszweck (= wiss. Fragestellung/Problemstellung in all ihren Details)

**Schritt 2:** Suche nach potentiellen Alternativen in der Ergebnisliste von Schritt 1

**Frage: Wie lässt sich der jeweilige 'Versuchszweck' dekodieren, mit Techniken die verallgemeinert werden können?**

Versuchszweck = wissenschaftliche Fragestellung/Problemstellung

# PMID\_21494637 ... mit Vorwissen ...

Dopaminergic neuronal loss, [REDACTED] in  
*transgenic mice expressing G2019S mutant LRRK2.*

Mutations in the leucine-rich repeat kinase 2 (LRRK2) gene cause **late-onset, autosomal dominant familial Parkinson's disease (PD)** [REDACTED]

[REDACTED] Currently, transgenic mice expressing [REDACTED] disease-causing mutants of LRRK2 have failed to produce overt neurodegeneration, [REDACTED]

[REDACTED] Here, we describe the development and characterization of *transgenic mice expressing human LRRK2 bearing the familial PD mutation [REDACTED] G2019S.* Our study demonstrates that expression of G2019S mutant LRRK2 induces the degeneration of *nigrostriatal pathway* dopaminergic neurons in an *age-dependent* manner. [REDACTED]

[REDACTED] These new LRRK2 *transgenic mice* will provide important tools for understanding the mechanism(s) through which familial mutations precipitate neuronal degeneration and PD. [REDACTED]

**Versuchszweck:** Entwicklung eines experimentellen Modells für Parkinson; Wichtig! → „neuronal loss“

## **PMID\_21494637 ... ohne Vorwissen ...**

Dopaminergic neuronal loss, reduced neurite complexity and autophagic abnormalities in transgenic mice expressing G2019S mutant LRRK2.

Mutations in the leucine-rich repeat kinase 2 (LRRK2) gene cause late-onset, autosomal dominant familial Parkinson's disease (PD) and also contribute to idiopathic PD. LRRK2 mutations represent the most common cause of PD with clinical and neurochemical features that are largely indistinguishable from idiopathic disease. Currently, transgenic mice expressing wild-type or disease-causing mutants of LRRK2 have failed to produce overt neurodegeneration, although abnormalities in nigrostriatal dopaminergic neurotransmission have been observed. Here, we describe the development and characterization of transgenic mice expressing human LRRK2 bearing the familial PD mutations, R1441C and G2019S. Our study demonstrates that expression of G2019S mutant LRRK2 induces the degeneration of nigrostriatal pathway dopaminergic neurons in an age-dependent manner. In addition, we observe autophagic and mitochondrial abnormalities in the brains of aged G2019S LRRK2 mice and markedly reduced neurite complexity of cultured dopaminergic neurons. These new LRRK2 transgenic mice will provide important tools for understanding the mechanism(s) through which familial mutations precipitate neuronal degeneration and PD.

**Frage: Wie kann man Übereinstimmungen im Versuchszweck feststellen, wenn man diesen nicht versteht?**

→ Suche nach sprachlichen und strukturellen Mustern, die man vergleichen kann

## Hypothese:

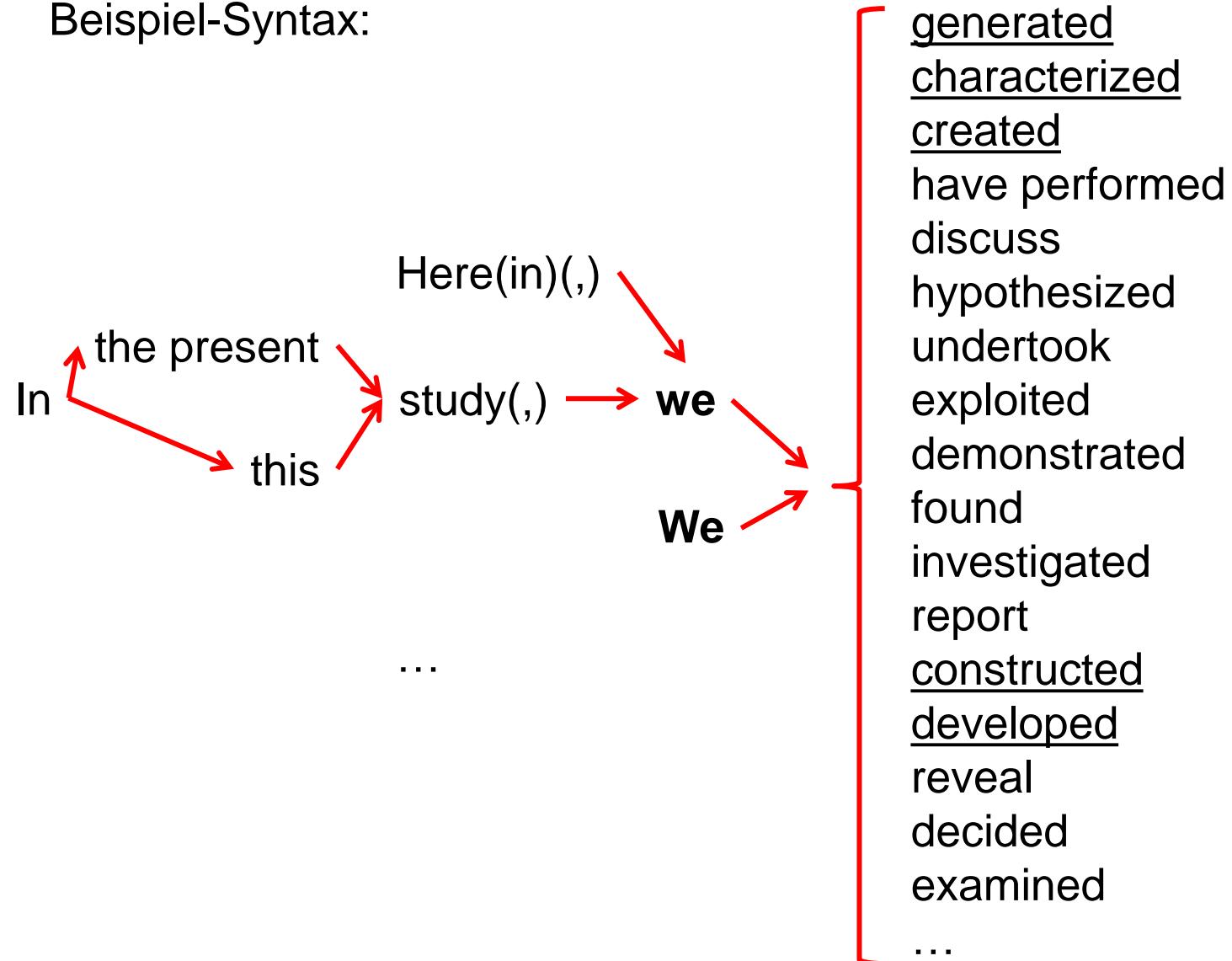
„Es gibt semantische ‘Clues’, die Sätze einleiten, welche den Versuchszweck beschreiben!“ („Here we ...“)

## Dopaminergic neuronal loss, reduced neurite complexity and autophagic abnormalities in *transgenic mice expressing G2019S mutant LRRK2*.

Mutations in the leucine-rich repeat kinase 2 (LRRK2) gene cause **late-onset, autosomal dominant familial Parkinson's disease (PD)** and also contribute to idiopathic PD. LRRK2 mutations represent the most common cause of PD with clinical and neurochemical features that are largely indistinguishable from idiopathic disease. Currently, transgenic mice expressing wild-type or disease-causing mutants of LRRK2 have failed to produce overt neurodegeneration, although abnormalities in nigrostriatal dopaminergic neurotransmission have been observed. **Here, we describe the development and characterization of transgenic mice expressing human LRRK2 bearing the familial PD mutations, R1441C and G2019S. Our study demonstrates that expression of G2019S mutant LRRK2 induces the degeneration of *nigrostriatal pathway* dopaminergic neurons in an *age-dependent* manner.** In addition, we observe autophagic and mitochondrial abnormalities in the brains of *aged* G2019S LRRK2 *mice* and markedly reduced neurite complexity of cultured dopaminergic neurons. These new LRRK2 *transgenic mice* will provide important tools for understanding the mechanism(s) through which familial mutations precipitate neuronal degeneration and PD.

# „Here we“-Sätze sind in den ersten beiden neu-generierten Testsets (2 x n=100) meist vorhanden (~95%)

Beispiel-Syntax:



# „Here we“-Sätze lassen sich für „Zoning“ einsetzen

**Dopaminergic neuronal loss, reduced neurite complexity and autophagic abnormalities in transgenic mice expressing G2019S mutant LRRK2.**

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= Einleitung, Stand der Forschung, Problemstellung

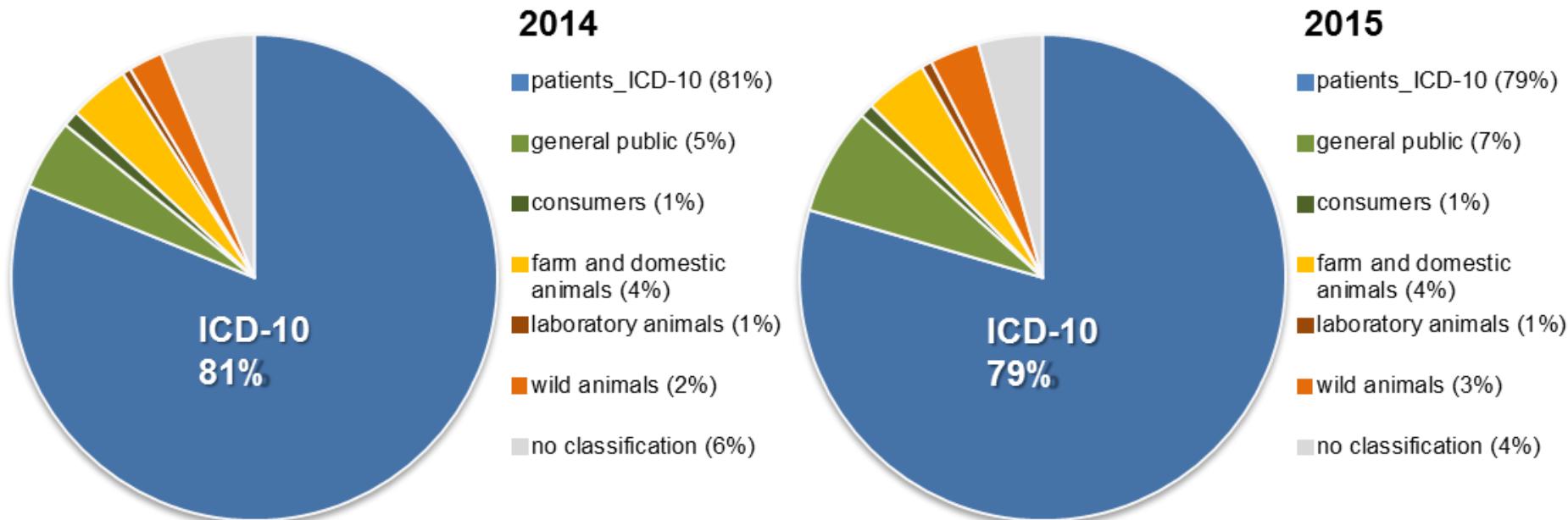
= Ausblick

## Hypothese:

„Es gibt in großen Bereichen der tierexperimentellen biomedizinischen Forschung überhaupt nur eine begrenzte Zahl von ‘Muster-Versuchszwecken’!“ ( $n \leq 10$ )

# Für welchen Bereich der Forschung gilt die Hypothese?

- Hypothese soll für den Bereich der tierexperimentellen biomedizinischen Forschung gelten, die auf Therapien für Krankheiten abzielt!



Quelle: AnimalTestInfo;  
„Zu erwartender Nutzen des Versuchsvorhabens“

- Auswertung der NTPs : ~ 80% der genehmigten TV-Vorhaben lassen einen Nutzen im humanmedizinischen Bereich erwarten

# Bisherige Ergebnisse: 4 unterscheidbare `Baupläne'

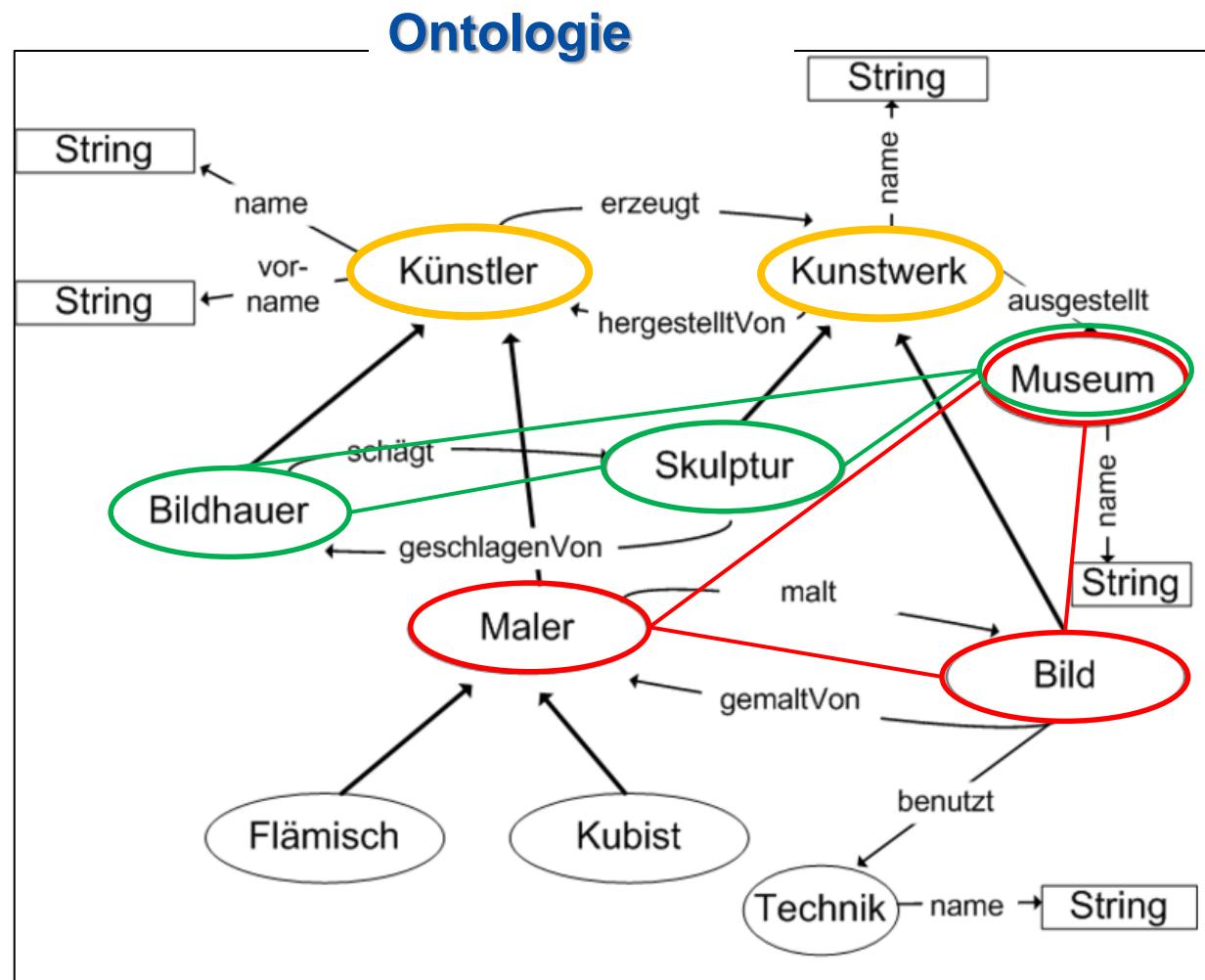
- `Model development'
- `Pathomechanism' (incl. Targetidentification/-characterisation)
- `Efficacy-MoA' ( incl. Targetvalidation, Targetinhibition/-knockout)
- `Adverse Effects-MoA'

MoA = `Mechanism of Action', `Mode of Action'

## Hypothese:

„Die betrachteten Versuchszwecke sind in einer biomedizinischen Ontologie `repräsentiert'. Durch Abstraktion lassen sich allgemeingültige sprachliche Muster finden.“

# Ontologie: ein Netzwerk von semantischen 'Konzepten' und 'Typen'



Auguste Rodin [Bildhauer]  
Das Hölletal [Skulptur]  
Musée Rodin [Museum]

Vincent van Gogh [Maler]  
Sternennacht [Bild]  
Musée d'Orsay [Museum]

Ein Bildhauer 'aktiviert' das grüne Netzwerk, ein Maler 'aktiviert' das rote Netzwerk.  
Es gibt **allgemeine Oberbegriffe**, die für beide stehen.

## **PMID\_21494637**

### **Dopaminergic neuronal loss, reduced neurite complexity and autophagic abnormalities in transgenic mice expressing G2019S mutant LRRK2.**

Mutations in the leucine-rich repeat kinase 2 (LRRK2) gene cause **late-onset, autosomal dominant familial Parkinson's disease (PD)** and also contribute to idiopathic PD. LRRK2 mutations represent the most common cause of PD with clinical and neurochemical features that are largely indistinguishable from idiopathic disease. Currently, transgenic mice expressing wild-type or disease-causing mutants of LRRK2 have failed to produce overt neurodegeneration, although abnormalities in nigrostriatal dopaminergic neurotransmission have been observed. Here, we describe the development and characterization of transgenic mice expressing human LRRK2 bearing the familial PD mutations, R1441C and G2019S. Our study demonstrates that expression of G2019S mutant LRRK2 induces the degeneration of *nigrostriatal pathway* dopaminergic neurons in an *age-dependent* manner. In addition, we observe autophagic and mitochondrial abnormalities in the brains of aged G2019S LRRK2 mice and markedly reduced neurite complexity of cultured dopaminergic neurons. These new LRRK2 transgenic mice will provide important tools for understanding the mechanism(s) through which familial mutations precipitate neuronal degeneration and PD.

# Vom `Abstrakt-Wording` zu den `Konzepten` und `Typen`

NIH NATIONAL CANCER INSTITUTE [www.cancer.gov](http://www.cancer.gov)

EVS Enterprise Vocabulary Services

## NCI metathesaurus

NCIm Version: 201706 (Browser Version 2.7.1, using LexEVS 6.4.1.2)

heuronal degeneration

Contains  Exact Match  Begins With  
 Name  Code  Property  Relationship

Source ALL

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### Welcome

NCI Metathesaurus (NCIm) is a wide-ranging biomedical terminology database that covers most terminologies used by NCI for clinical care, translational and basic research, and public information and administrative activities.

NCIm features:

- Maps 6,400,000 terms from more than 75 sources into 2,700,000 biomedical concepts that represent their meaning.
- Displays preferred terms, synonyms, definitions, and other information from each source.
- Links to [NCI Thesaurus](#) and other related information sources.
- More than 30,000,000 cross-links between content elements.
- Updated frequently by a team of biomedical terminology and subject matter experts.

NCIm contains most public domain terminologies from the National Library of Medicine's [UMLS Metathesaurus](#), as well as many other biomedical terminologies created by or of interest to NCI and its partners. Some propriety terminologies are included, with permission, and have restrictions on their use (see [details](#)). The current version of the NCI Metathesaurus, based on the UMLS build [2016AB](#), covers up to National Cancer Institute Thesaurus, 17.06d. A viewer for the UMLS changes document can be downloaded from [here](#).

**EVS** [NCI Enterprise Vocabulary Services](#): Terminology resources and services for NCI and the biomedical community.

**NCIt** [NCI Thesaurus](#): Reference terminology for NCI, NCI Metathesaurus and NCI informatics infrastructure.

**NCI Term Browser** [NCI Term Browser](#): NCI and other terminologies in an integrated environment.

**cancer.gov** [NCI Terminology Resources](#): More information on NCI dictionaries and resources.

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neuronal degeneration

Contains  Exact Match  Begins With  
 Name  Code  Property  Relationship  
Source ALL

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**Neuropathology shows neuronal degeneration (CUI C3281303)** [Suggest changes to this concept](#) [Add to Cart](#)

Terms & Properties

### Terms & Properties

Concept Unique Identifier (CUI): C3281303

Semantic Type: Finding

Synonyms & Abbreviations: [\(see Synonym Details\)](#)  
Neuropathology shows neuronal degeneration

External Source Codes: (none)

Other Properties: [?](#) (none)

Additional Concept Data: (none)

URL to Bookmark: <https://ncim.nci.nih.gov/ncimbrowser/ConceptReport.jsp?dictionary=NCI Metathesaurus&code=C3281303>

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U.S. Department of Health and Human Services | National Institutes of Health | National Cancer Institute | USA.gov

# Vom 'Abstrakt-Wording' zu den 'Konzepten' und 'Typen'

Dopaminergic neuronal loss, reduced neurite complexity and autophagic abnormalities in transgenic mice expressing G2019S mutant LRRK2.

Mutations in the leucine-rich repeat kinase 2 (LRRK2) gene cause late-onset, autosomal dominant familial Parkinson's disease (PD) and also contribute to idiopathic PD. LRRK2 mutations represent the most common cause of PD with clinical and neurochemical features that are largely indistinguishable from idiopathic disease. Currently, transgenic mice expressing wild-type or disease-causing mutants of LRRK2 have failed to produce overt neurodegeneration, although abnormalities in nigrostriatal dopaminergic neurotransmission have been observed. Here, we describe the development and characterization of transgenic mice expressing human LRRK2 bearing the familial PD mutations, R1441C and G2019S. Our study demonstrates that expression of G2019S mutant LRRK2 induces the degeneration of nigrostriatal pathway dopaminergic neurons in an age-dependent manner. In addition, we observe autophagic and mitochondrial abnormalities in the brains of aged G2019S LRRK2 mice and markedly reduced neurite complexity of cultured dopaminergic neurons. These new LRRK2 transgenic mice will provide important tools for understanding the mechanism(s) through which familial mutations precipitate neuronal degeneration and PD.

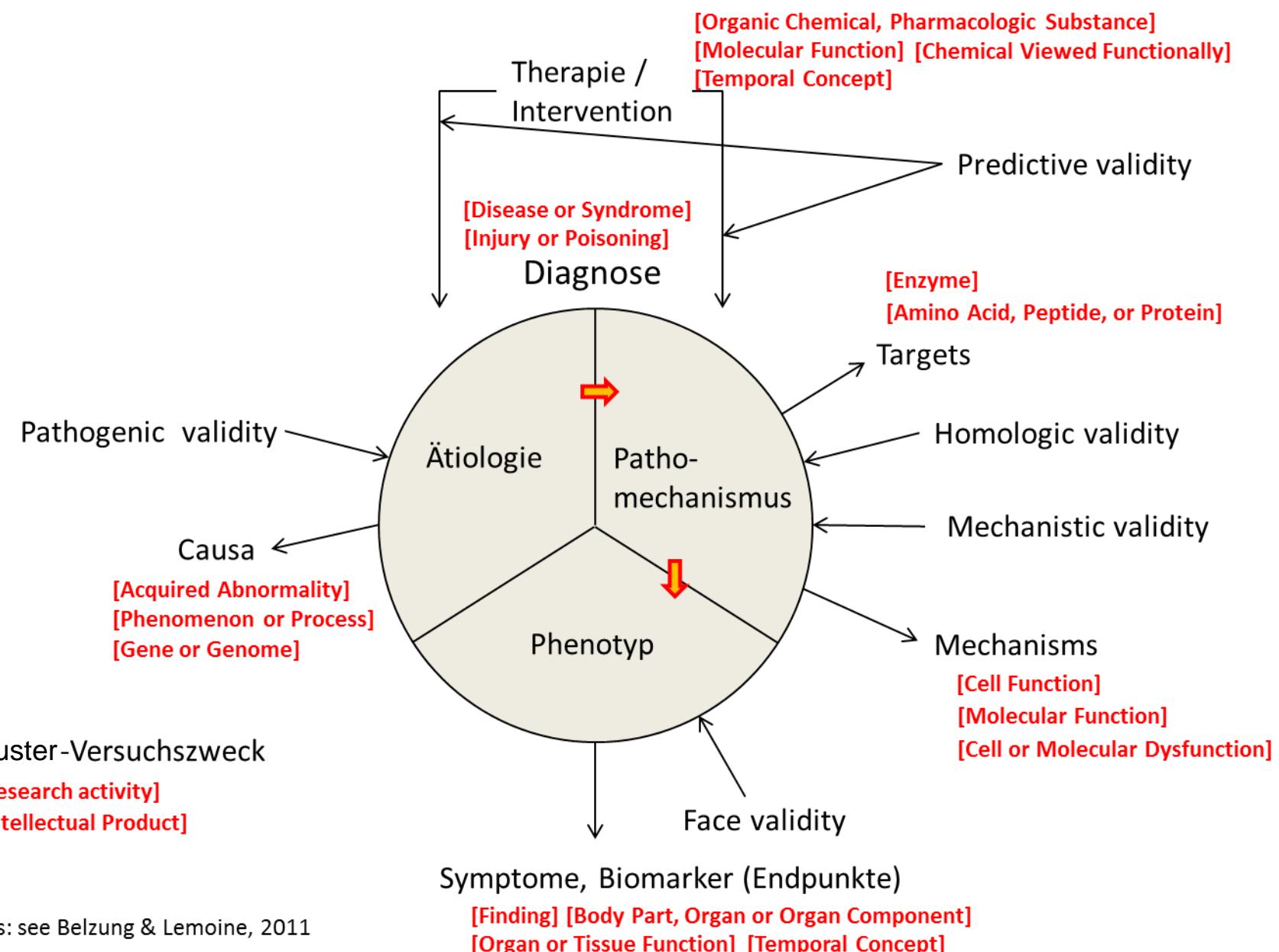
1. Model development [Intellectual product]
2. Parkinson's Disease [Disease or Syndrome]
3. PARKINSON DISEASE 8, AUTOSOMAL DOMINANT [Disease or Syndrome]
- > 4. LRRK2, GLY2019SER [Gene or Genome]
5. LRRK2, ARG1441CYS [Gene or Genome]
6. Neuropathology shows neuronal degeneration [Finding]
7. Neuronal loss in the substantia nigra [Finding]
8. Loss of dopaminergic neurons in the substantia nigra [Finding]
9. Age-dependent penetrance [Finding]

UMLS: Unified Medical Language System



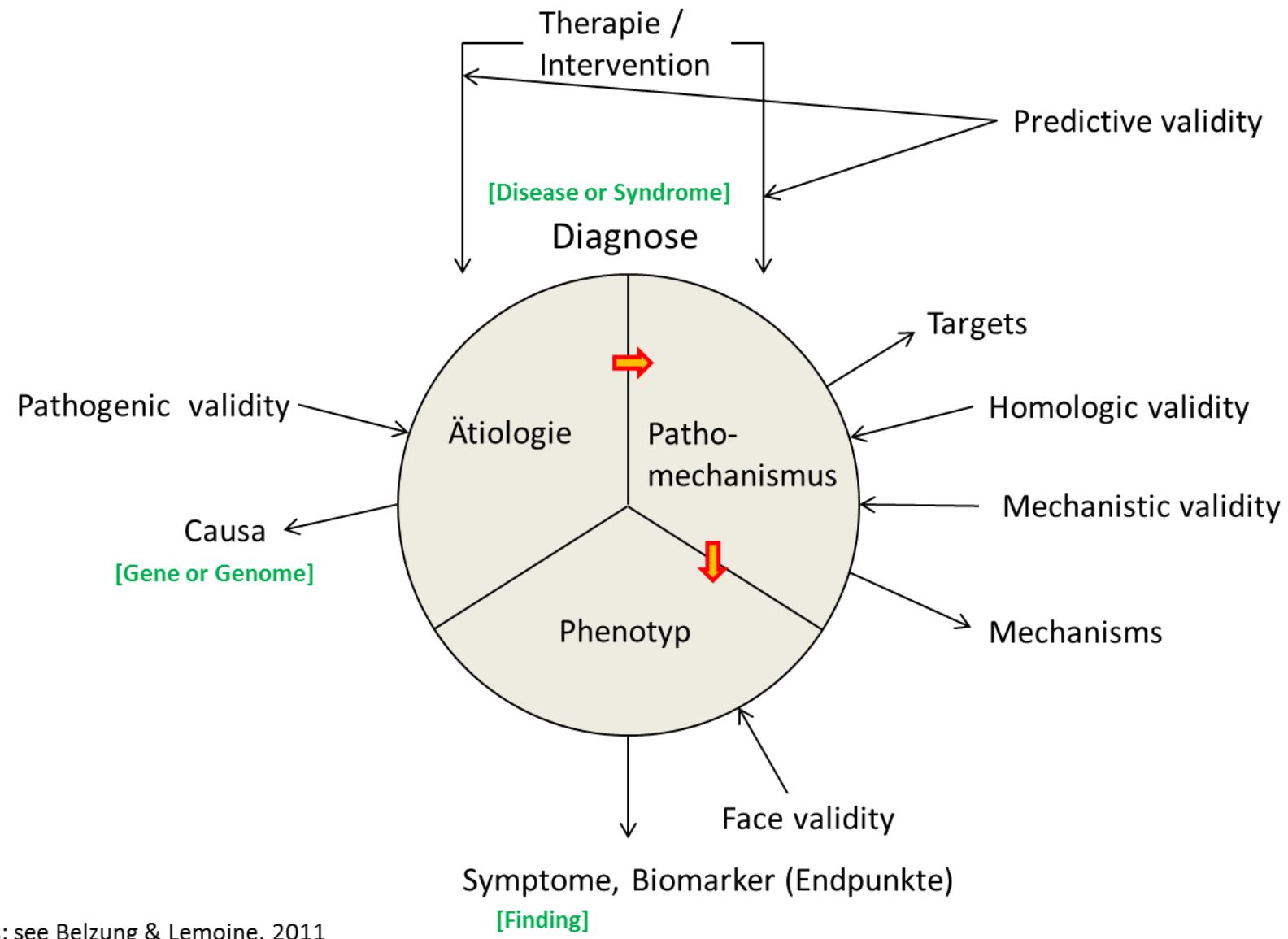
# Modell der Kodierung des 'Versuchszwecks'

[NCI Metathesaurus Semantic Types]



Validities: see Belzung & Lemoine, 2011

# Kodierung von PMID\_21494637



# Vom 'Abstrakt-Wording' zu den 'Konzepten' und 'Typen'

Dopaminergic neuronal loss, reduced neurite complexity and autophagic abnormalities in transgenic mice expressing G2019S mutant LRRK2. → ...autophagic ... [cell function]

Mutations in the leucine-rich repeat kinase 2 (LRRK2) gene cause late-onset, autosomal dominant familial Parkinson's disease (PD) and also contribute to idiopathic PD. LRRK2 mutations represent the most common cause of PD with clinical and neurochemical features that are largely indistinguishable from idiopathic disease. Currently, transgenic mice expressing wild-type or disease-causing mutants of LRRK2 have failed to produce overt neurodegeneration, although abnormalities in nigrostriatal dopaminergic neurotransmission have been observed. Here, we describe the development and characterization of transgenic mice expressing human LRRK2 bearing the familial PD mutations, R1441C and G2019S. Our study demonstrates that expression of G2019S mutant LRRK2 induces the degeneration of nigrostriatal pathway dopaminergic neurons in an age-dependent manner. In addition, we observe autophagic and mitochondrial abnormalities in the brains of aged G2019S LRRK2 mice and markedly reduced neurite complexity of cultured dopaminergic neurons. These new LRRK2 transgenic mice will provide important tools for understanding the mechanism(s) through which familial mutations precipitate neuronal degeneration and PD.

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UMLS: Unified Medical Language System



## Hypothese:

„In den Literatur-Zitaten, die einem individuellen AnimAltZEBET-Methodenportrait zugeordnet sind, wird ein gleicher (oder ähnlicher) Versuchszweck beschrieben. Dieser Versuchszweck wird durch ein sprachliches Muster repräsentiert, welches häufig in diesen Zitaten vorkommt.“

Ziel: Automatische Extraktion sprachlicher Muster des Versuchszwecks durch „Unsupervised Learning“

# AnimAlt-ZEBET Datenbank (~150 Berichte):

Methoden    Drucken    Fenster schließen

Method No. 16  
Last Revision 18.06.2012  
Section Heading Physiology

**Title** fMRI with multivariate pattern classification as non-invasive in vivo technique to test cognitive models of visual attention

**Terms** BOLD; Macaca mulatta; ROI; ZEBET; animal experiments; animal testing alternatives; animal use alternatives; animal welfare; blood oxygenation-level dependent contrast; cognitive neurosciences; cortical orientation columns; fMRI; feature-based attention; feature-similarity gain; functional magnetic resonance imaging; non-human primates; object-based attention; pattern classification; receptive field; region-of-interest; resolution; spatial attention; visual attention

**Evaluation** Replacement  
**Status** Development  
**Regulation** Not used for regulatory purposes  
**Abstract** 3R RELEVANCE

Functional magnetic resonance imaging (fMRI) is a non-invasive technique for recording high-resolution images of the brain activity. It has been used in the basic cognitive neuroscience research since the early 1990ies and since then has undergone a spectacular progress in scanner technology, acquisition protocols, experimental designs and analysis methods. Since fMRI cannot easily differentiate between "bottom-up" neuronal information processing and "top-down" modulatory effects (e.g., due to attention), a priori functional knowledge about the cortical region under consideration may be essential. The temporal resolution is in the range of a couple of seconds. The spatial resolution in human fMRI experiments typically is in the range of a few cubic millimeters, but can be increased considerably below this value. By combining fMRI with elaborate experimental designs and data analysis techniques (e.g. multivariate pattern classification), possibly even the activities of distributed functional cortical modules with spatial dimensions below the specified fMRI-resolution limit may be resolved. Thus, fMRI might be used instead of invasive microelectrode-techniques to address compatible questions in cognitive neuroscience research.

**BACKGROUND**

Most complex life-forms, primates and others, are confronted with a vast amount of visual information from their environment. Visual attention is a neuronal mechanism that enables perception to focus on a momentous subset of information picked up by the eyes (Maunsell & Treue, 2006). It enhances the neuronal representations of behaviorally relevant aspects of the visual input in the cortex at the expense of less relevant portions. As result, we are "active participants in the construction of our own perceptual experience" (Downing et al. 2001). The advent of a scientific interest in the characteristics and mechanisms of attention dates back to the 19th century (see Engel et al. 2006), or even earlier (see Anderson 2011). Since then, scientists of several closely related disciplines like ethology, psychology, psychophysics and neurobiology have compiled an extensive body of empirical data documenting the "modus operandi" of attention. According to Downing et al. (2001) there are four classic questions in the psychology of visual attention: 1.) Are some 'special' classes of stimuli (e.g. faces) immune to attentional modulation?; 2.) What are the information units on which attention operates?; 3.) How early in stimulus processing are attentional effects observed?; and 4.) Are common mechanisms involved in different modes of attentional selection (e.g. spatial and non-spatial selection)?

Regarding the second question, concerning the information units of attention, several seemingly competing models have been proposed. Thus, visual attention might work - like a spotlight - via selection of spatial location (spatial attention), or via selection of highly relevant visual features such as motion or color (feature-based attention) or whole objects (object-based attention) (e.g. Posner et al. 1980, Duncan 1984, Luck et al. 1997, Roelfsema et al. 1998, Treue & Martinez Trujillo 1999, O'Craven et al. 1999; Saenz et al. 2002). While some of the earlier work regarded these models as mutually exclusive alternatives, most current theories of attention can accommodate the predictions of all three (e.g. Boynton 2009, Reynolds & Heeger 2009).

In search for the correlates of attention in the plethora of brain activities, researchers had to rely on EEG and invasive microelectrode recordings in the early days. With the rapid advancement of functional imaging techniques like PET and fMRI (Raichle, 2008; Smith 2012), there also has been a seminal enhancement in the technical repertory available for addressing questions in the cognitive neurosciences area (Bandettini 2009). However, "perhaps stemming from the fact that important early studies of neural correlates of behavior took the mean spiking rate (of neurons) to be the gold standard for quantifying neuronal activation" (Logothetis 2008), some researchers still deny a potential role of neuroimaging techniques for their specific research project beyond a simple complementation. Others point out that fMRI currently is the best tool available for gaining insights into brain function and that the spectacular progress in technology, acquisition protocols, experimental designs and analyses is really pushing this non-invasive technique to be the mainstay in the study of brain organization. In the sections to come, two approaches (one invasive, the other non-invasive) are compared, which actually have been used to dissect and characterise different modes of attention (especially spatial vs. feature-based).

# AnimAlt-ZEBET Datenbank:

## BACKGROUND

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## METHOD

### Principle:

Magnetic resonance imaging (MRI) was introduced in the clinics in the 1980ies and since then has been elaborated to play a fundamental role in diagnostic medicine. Besides the possibility to non-invasively produce structural images of organs, it can also be used to gain information on the physico-chemical state of tissues, their vascularisation and perfusion (Logothetis 2008). With the emergence of functional MRI (fMRI) in the early 1990ies, the technique also found widespread entrance into basic neuroscience research. This variant is capable of measuring hemodynamic changes (in particular BOLD, blood oxygenation-level dependent contrast changes) after enhanced neural activity. Please refer to Logothetis 2008 and Boynton 2011 for a comprehensive review of advantages and limitations of fMRI in cognitive research and its relatedness to neuronal electrophysiology.

In the experiment described below, fMRI/BOLD was used to predict the attentional state of human observers as they monitored a visual feature. Visual features are grouped in superordinate categories like motion, color, etc. and can be further divided into subordinate categories like specific directions of motion (e.g. 45°) or specific colors (e.g. red). In feature selective cortical areas (e.g. "motion-selective" areas V3A and hMT+) subordinate categories are represented by corresponding columns of neurons that show a well-arranged distribution (see Hubel & Wiesel 1968; Albright et al. 1984). Traditionally, fMRI studies have been thought to be restricted to the superordinate level of analysis (cortical areas on a whole) because the size of the orientation selective columns is well below the size of an ordinary fMRI voxel. As result, one voxel contains various columns selective for many different directions. Averaging across opposed columns, however, would theoretically nullify any directional selectivity in the BOLD response signal.

Practically, this limitation has recently been challenged by using multivariate pattern classification methods (Kamitani & Tong 2005, 2006; Haynes & Rees 2005). Thus, by chance, a preponderance of neurons preferring a particular subordinate category might be sampled within a single fMRI voxel, giving rise to a small but detectable feature-selective response bias. By considering the pattern of activity across many such weakly selective voxels, the features of a stimulus (e.g. orientation or direction of motion) an observer is actually attending to may be predicted. Furthermore, the gain of activity (BOLD response) through mechanisms of feature-based attention may be quantified for selective voxels.

# AnimAlt-ZEBET Datenbank:

## Literature 31

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[http://ac.els-cdn.com/S0960982206014643/1-s2.0-S0960982206014643-main.pdf?\\_tid=60d10c669acd3bdb1c66f18eb1adca35&acdnat=1342001763\\_f2f960f38c5c51b984adab615e892faa](http://ac.els-cdn.com/S0960982206014643/1-s2.0-S0960982206014643-main.pdf?_tid=60d10c669acd3bdb1c66f18eb1adca35&acdnat=1342001763_f2f960f38c5c51b984adab615e892faa) (11.07.2012)
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<http://jn.physiology.org/content/77/1/24.full.pdf+html> (23.07.2012)

# Beispiel für „Muster“, die häufig in vielen Zitaten vorkommen:

## Literature 18

- |    |                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|----|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1  | Adams MD, Celinker SE, Holt RA, Evans CA, Gocayne JD, Amanatides PG, Scherer SE, Li PW, Hoskins RA, Galle RF, George RA, Lewis SE, Richards S, Ashburner M, Henderson SN, Sutton GG, Wortman JR, Yandell MD, Zhang Q: The Genome Sequence of <i>Drosophila melanogaster</i> .; <i>Science</i> 287(5461); 2185-2195 (2000)                                                                                                                   |
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| 12 | Friggi-Grelin F, Coulom H, Meller M, Gomez D, Hirsh J, Birman S: Targeted gene expression in <i>Drosophila</i> dopaminergic cells using regulatory sequences from tyrosine hydroxylase.; <i>Developmental Neurobiology</i> 54; 618-627 (2003)                                                                                                                                                                                               |
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| 16 | Masliah E, Rockenstein E, Veinbergs I, Mallory M, Hashimoto M, Takeda A, Sagara Y, Sisk A, Mucke L: Dopaminergic Loss and Inclusion Body Formation in alpha-Synuclein Mice: Implications for Neurodegenerative Disorders.; <i>Science</i> 287(5456); 1265-1269 (2000)                                                                                                                                                                       |
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3R 

TV 

# Beispiel für „Muster“, die häufig in vielen Publikationen vorkommen:

[Nature](#). 2000 Mar 23;404(6776):394-8.

## A Drosophila model of Parkinson's disease.

Feany MB<sup>1</sup>, Bender WW.

[⊕ Author information](#)

### Abstract

Parkinson's disease is a common neurodegenerative syndrome characterized by loss of dopaminergic neurons in the substantia nigra, formation of filamentous intraneuronal inclusions (Lewy bodies) and an extrapyramidal movement disorder. Mutations in the alpha-synuclein gene are linked to familial Parkinson's disease and alpha-synuclein accumulates in Lewy bodies and Lewy neurites. Here we express normal and mutant forms of alpha-synuclein in Drosophila and produce adult-onset loss of dopaminergic neurons, filamentous intraneuronal inclusions containing alpha-synuclein and locomotor dysfunction. Our Drosophila model thus recapitulates the essential features of the human disorder, and makes possible a powerful genetic approach to Parkinson's disease.

### Comment in

Parkinson's pathology in a fly. [Nature. 2000]

PMID: 10746727 DOI: [10.1038/35006074](https://doi.org/10.1038/35006074)

[Science](#). 2000 Feb 18;287(5456):1265-9.

## Dopaminergic loss and inclusion body formation in alpha-synuclein mice: implications for neurodegenerative disorders.

Masliah E<sup>1</sup>, Rockenstein E, Veinbergs I, Mallory M, Hashimoto M, Takeda A, Saqara Y, Sisk A, Mucke L.

[⊕ Author information](#)

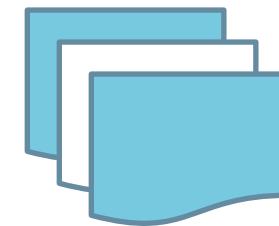
### Abstract

To elucidate the role of the synaptic protein alpha-synuclein in neurodegenerative disorders, transgenic mice expressing wild-type human alpha-synuclein were generated. Neuronal expression of human alpha-synuclein resulted in progressive accumulation of alpha-synuclein-and ubiquitin-immunoreactive inclusions in neurons in the neocortex, hippocampus, and substantia nigra. Ultrastructural analysis revealed both electron-dense intranuclear deposits and cytoplasmic inclusions. These alterations were associated with loss of dopaminergic terminals in the basal ganglia and with motor impairments. These results suggest that accumulation of wild-type alpha-synuclein may play a causal role in Parkinson's disease and related conditions.

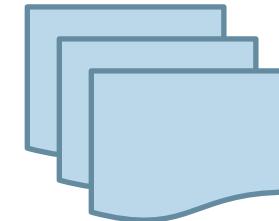
PMID: 10678833

# Machine learning:

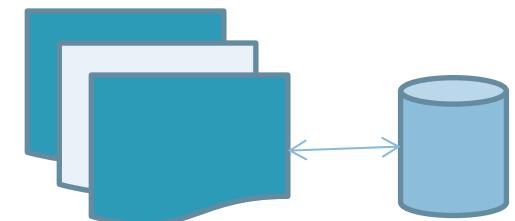
„**Supervised approaches** use manually labelled training and test data.“



„**Unsupervised approaches** do not need any annotated data for training.“



„[...] **distant supervision or self-supervised learning** approaches. The idea is to exploit large knowledge bases [...] to **automatically label** [...] text and use the annotated text to extract features and train a classifier.“



Definitionen von Augenstein et al. (<http://www.semantic-web-journal.net/system/files/swj742.pdf>)

# Der „Frequent Pattern Mining“ Algorithmus für Data Mining:

Seq 1: [C, A, A, B, C]

Seq 2: [A, B, C, B]

Seq 3: [C, A, B, C]

Seq 4: [A, B, B, C, A]



4:[A, B, C]

3:[C, B]

2:[A, A]

2:[A, B, B]

2:[C, A, B, C]

3:[C, A]

# „Frequent Pattern Mining“ für biomedizinisches Textmining:

The screenshot shows the homepage of the **Journal of Biomedical Semantics**. At the top, there's a logo for **BioMed Central** featuring a green stylized 'C' icon. Below the logo is a small graphic of a DNA double helix with binary code (0101110011100) overlaid. The main title "Journal of Biomedical Semantics" is displayed prominently. A navigation bar below the title includes links for **HOME**, **ABOUT**, **ARTICLES** (which is underlined), and **SUBMISSION GUIDELINES**. The **ARTICLES** section has a decorative banner with red and grey diagonal stripes. Below the navigation bar, there are two categories: **RESEARCH ARTICLE** and **OPEN ACCESS**. The main content area features a large, bold title: **Sequential pattern mining for discovering gene interactions and their contextual information from biomedical texts**. Below the title, the authors are listed: **Peggy Cellier**, **Thierry Charnois**, **Marc Plantevit**, **Christophe Rigotti**, **Bruno Crémilleux**, **Olivier Gadrillon**, **Jiří Kléma**, and **Jean-Luc Mangin**. At the bottom of the page, there's a note about the journal: **Journal of Biomedical Semantics** 2015 6:27 | <https://doi.org/10.1186/s13326-015-0023-3> | © Cellier et al.; licensee BioMed Central. 2015. The publication dates are also provided: **Received: 25 July 2013**, **Accepted: 22 April 2015**, and **Published: 18 May 2015**.

(Source: <https://biomedsem.biomedcentral.com/articles/10.1186/s13326-015-0023-3>)

# Der „Frequent Pattern Mining“ Algorithmus für Textmining:

Seq 1: [Neural, mechanisms, spatial, selective, attention, in, areas, V2, V4, macaque, visual cortex]

Seq 2: [the, very, weak, inconsistent, areas, only, one, two, stimuli, receptive field]

Seq 3: [size, effect, attention, reduced, the, ignored, stimuli, presented, simultaneously]

Seq 4: [Spontaneous, firing rates, according to, within the, attended]

....



3:[PI, P2, actomyosin]

3:[loss, of, neurons]

(Muster von Wörter)

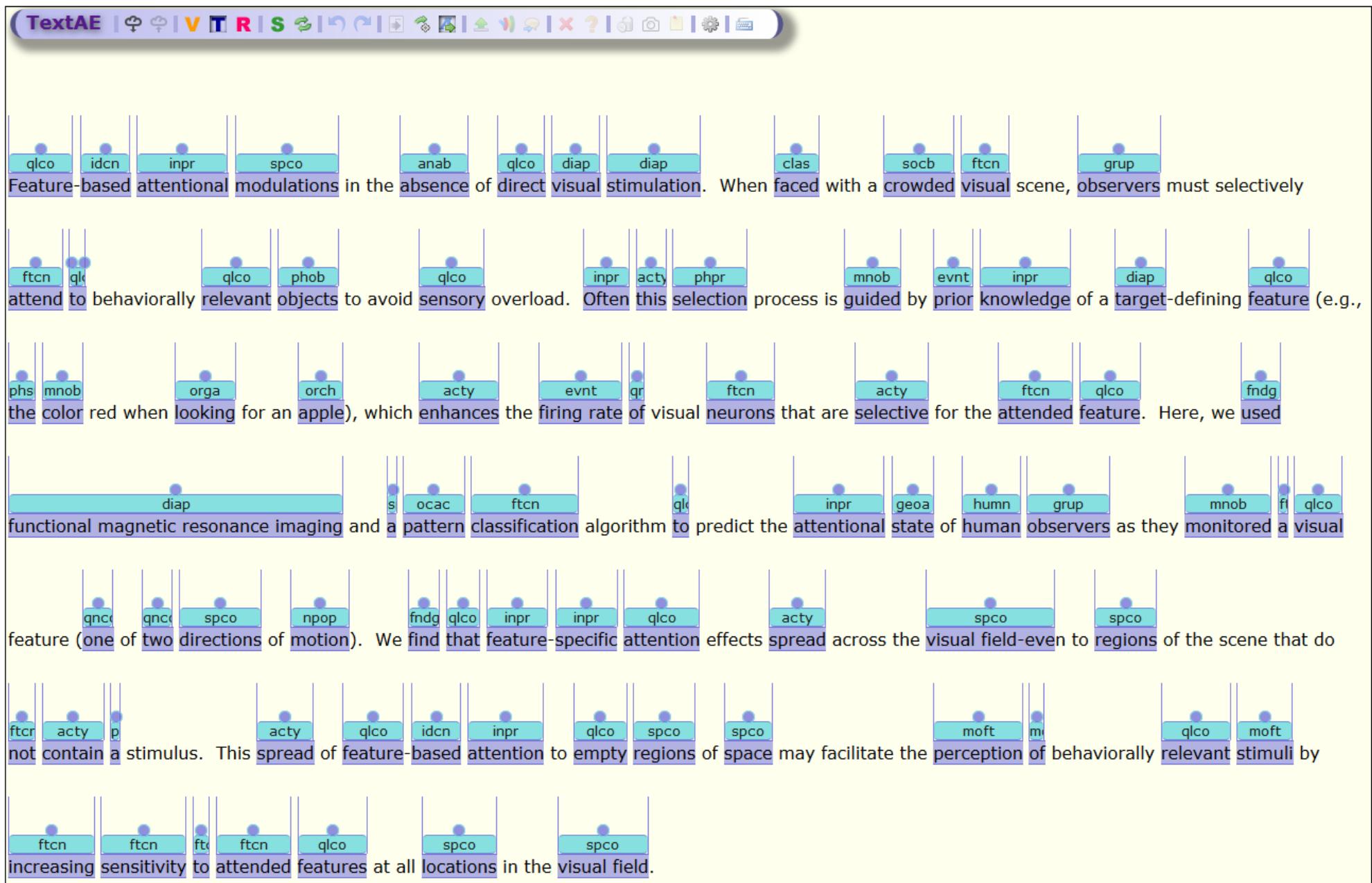


3:[fndg, fndg, fndg]

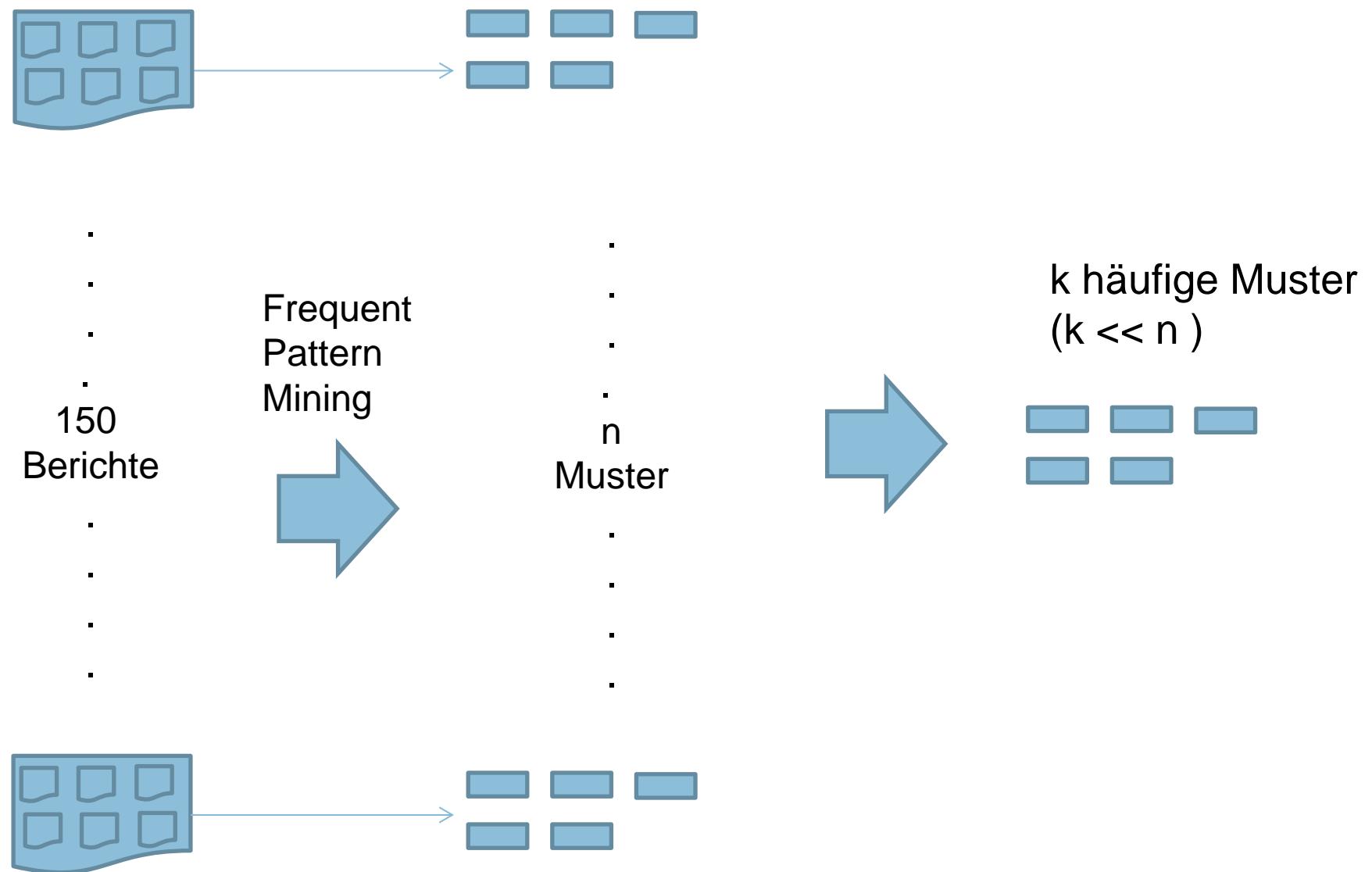
3:[inpr, bpoc, celc]

(Muster von Typen)

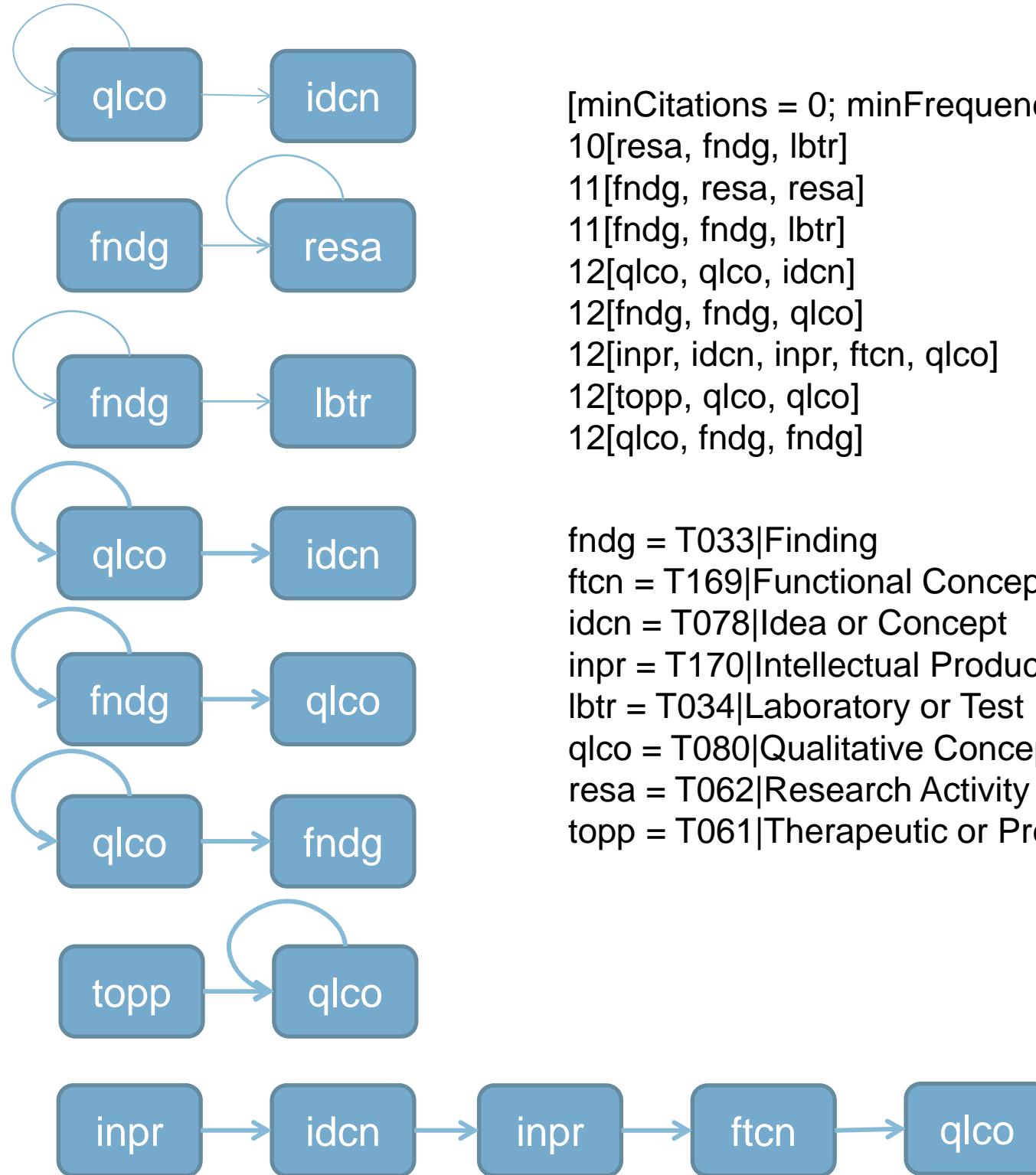
# „Named-entity recognition“ mit MetaMap:



# Welches sind die häufigen Muster in AnimAlt-ZEBET?



# Ergebnisse (Muster):



[minCitations = 0; minFrequency = 10]

10[resa, fndg, lbtr]

11[fndg, resa, resa]

11[fndg, fndg, lbtr]

12[qlco, qlco, idcn]

12[fndg, fndg, qlco]

12[inpr, idcn, inpr, ftcn, qlco]

12[topp, qlco, qlco]

12[qlco, fndg, fndg]

fndg = T033|Finding

ftcn = T169|Functional Concept

idcn = T078|Idea or Concept

inpr = T170|Intellectual Product

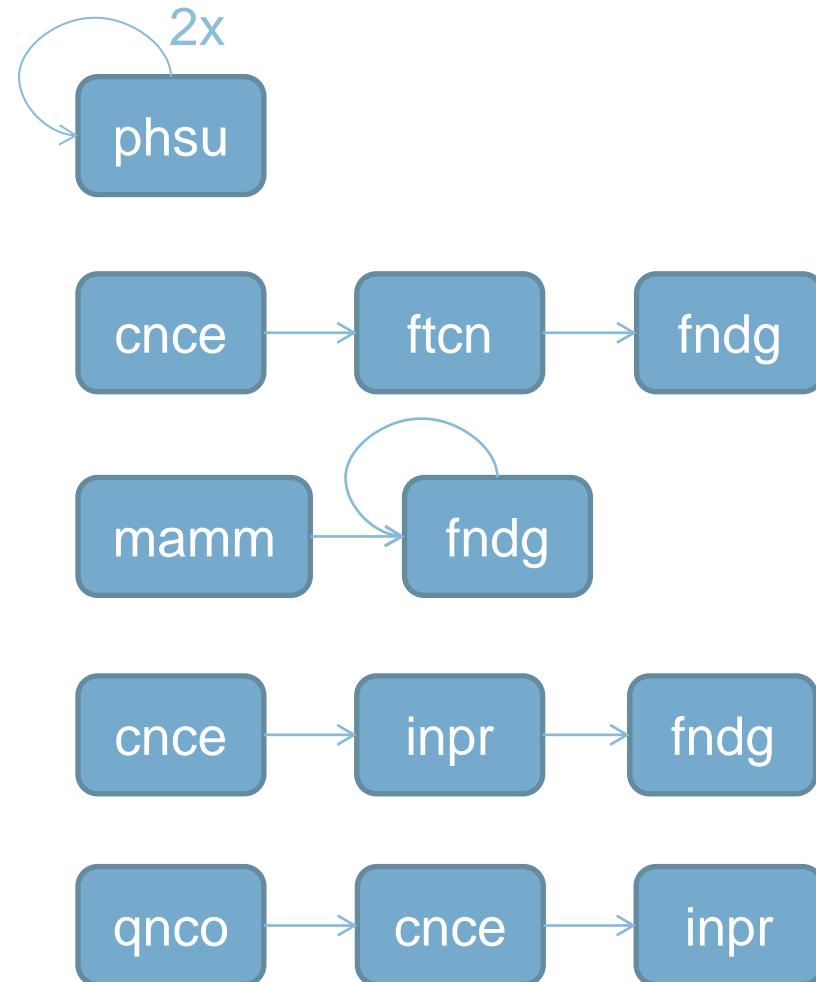
lbtr = T034|Laboratory or Test Result

qlco = T080|Qualitative Concept

resa = T062|Research Activity

topp = T061|Therapeutic or Preventive Procedure

# Ergebnisse (Muster):



[minCitations = 0; minFrequency = 6]  
6[phsu, phsu, phsu]  
9[cnce, ftcn, fndg]  
9[mamm, fndg, fndg]  
9[cnce, inpr, fndg]  
9[qnco, cnce, inpr]

cnce = T077|Conceptual Entity  
fndg = T033|Finding  
ftcn = T169|Functional Concept  
inpr = T170|Intellectual Product  
mamm = T015|Mammal  
phsu = T121|Pharmacologic Substance  
qnco = T081|Quantitative Concept

# Evaluation des Muster (to-do):

- Durch Dokument Ähnlichkeit: Helfen die Muster ähnliche Dokumenten zu finden?
- Durch Informationsextraktion: Vergleich mit manuellen Annotationen (von Daniel).

Recent studies showed that the low-frequency component of local field potentials (LFPs) in monkey motor cortex carries information about parameters of voluntary arm movements. Here, we studied how different signal components of the LFP in the time and frequency domains are modulated during center-out arm movements. Analysis of LFPs in the time domain showed that the amplitude of a slow complex waveform beginning shortly before the onset of arm movement is modulated with the direction of the movement. Examining LFPs in the frequency domain, we found that direction-dependent modulations occur in three frequency ranges, which typically increased their amplitudes before and during movement execution: < or =4, 6-13, and 63-200 Hz. Cosine-like tuning was prominent in all signal components analyzed. In contrast, activity in a frequency band approximately 30 Hz was not modulated with the direction of movement and typically decreased its amplitude during the task. This suggests that high-frequency oscillations have to be divided into at least two functionally different regimes: one approximately 30 Hz and one >60 Hz. Furthermore, using multiple LFPs, we could show that LFP amplitude spectra can be used to decode movement direction, with the best performance achieved by the combination of different frequency ranges. These results suggest that using the different frequency components in the LFP is useful in improving inference of movement parameters from local field potentials.

## Hypothese:

„Es gibt bereits Modelle und Trainings-Daten aus anderen Bereichen (z.B. Informatik-Publikationen). Wir könnten diese für unser Projekt adaptieren.“

Ziel: Automatische Extraktion eines Modells des Versuchszwecks durch „Supervised Learning + Domain Adaptation“

# Schemas für Elemente in wissenschaftliche Publikationen:

1. **USAGE** is an asymmetrical relation. It holds between two entities X and Y, where, for example:

X is used for Y

X is a method used to perform a task Y

2. **RESULT** is an asymmetrical relation. It holds between two entities X and Y, where, for example:

X gives as a result Y (where Y is typically a measure of evaluation)

X yields Y (where Y is an improvement or decrease)

3. **MODEL-FEATURE** is an asymmetrical relation. It holds between two entities X and Y, where, for example:

X is a feature/an observed characteristic of Y

X is a model of Y

(Source: [https://competitions.codalab.org/competitions/17422#learn\\_the\\_details-semantic-relations](https://competitions.codalab.org/competitions/17422#learn_the_details-semantic-relations))

# Schemas für Elemente in wissenschaftliche Publikationen:

4. **PART\_WHOLE** is an asymmetrical relation. It holds between two entities X and Y, where, for example:

X is a part, a component of Y

X is found in Y

Y is built from/composed of X

5. **TOPIC** is an asymmetrical relation. It holds between two entities X and Y, where, for example:

X deals with topic Y

X (author, paper) puts forward Y (an idea, an approach)

6. **COMPARE** is a symmetrical relation. It holds between two entities X and Y, where:

X is compared to Y (e.g. two systems, two feature sets or two results)

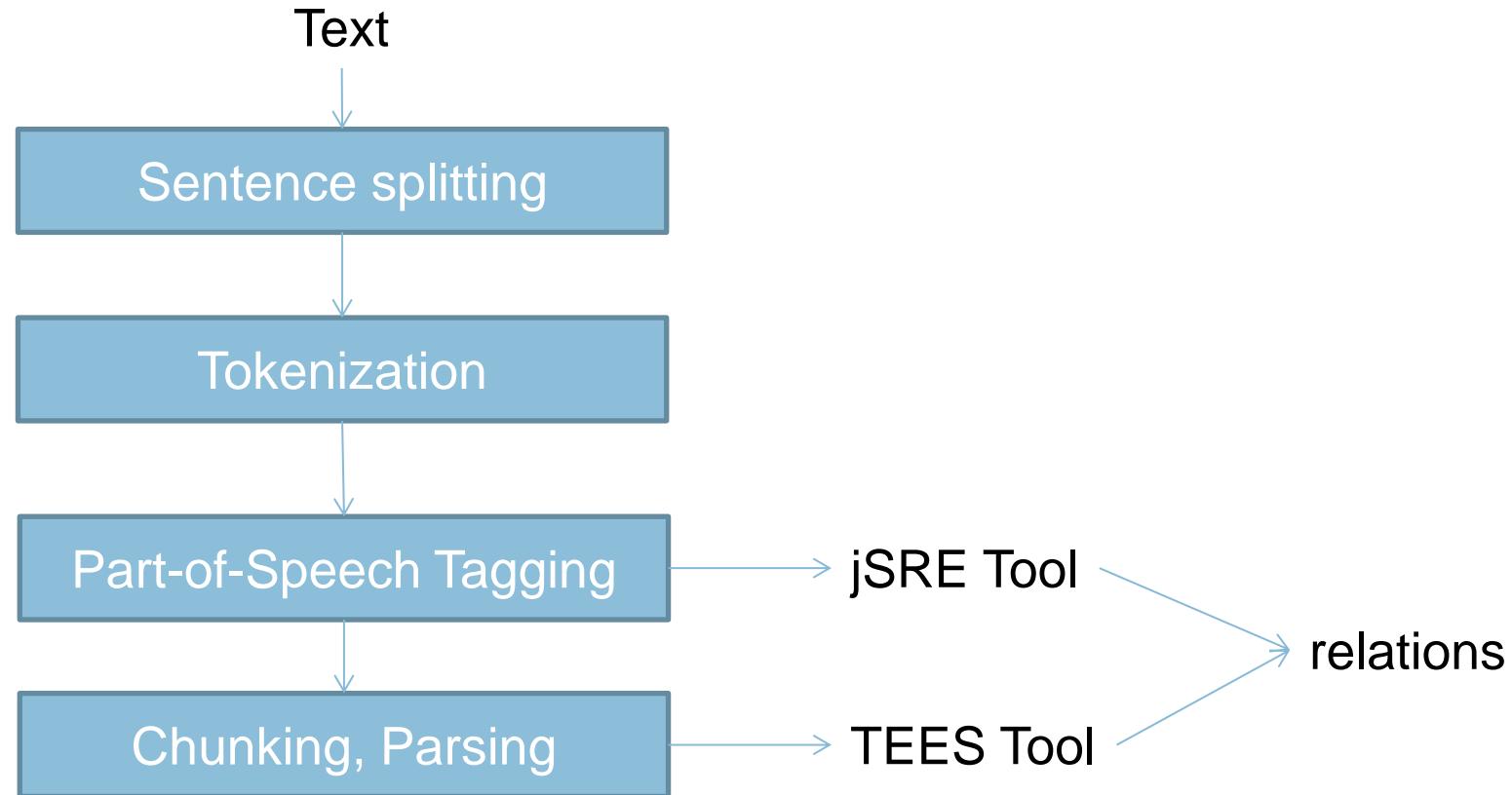
(Source: [https://competitions.codalab.org/competitions/17422#learn\\_the\\_details-semantic-relations](https://competitions.codalab.org/competitions/17422#learn_the_details-semantic-relations))

# Training Daten:

```
<text id="H01-1017">
<title>Dialogue Interaction with the DARPA Communicator Infrastructure: The Development of Useful Software</title>
<abstract> To support engaging human users in robust, <entity id="H01-1017.1">mixed-initiative speech dialogue interactions</entity> which reach beyond current capabilities in <entity id="H01-1017.2">dialogue systems</entity> , the <entity id="H01-1017.3">DARPA Communicator program</entity> [1] is funding the development of a <entity id="H01-1017.4">distributed message-passing infrastructure</entity> for <entity id="H01-1017.5">dialogue systems</entity> which all <entity id="H01-1017.6">Communicator</entity> participants are using. In this presentation, we describe the features of and <entity id="H01-1017.7">requirements</entity> for a genuinely useful <entity id="H01-1017.8">software infrastructure</entity> for this purpose. </abstract>
```

MODEL-FEATURE(H01-1017.4,H01-1017.5)

# Experimenten mit „Relationextraktion“ Tools:



(Source: <https://hlt-nlp.fbk.eu/technologies/jsre>  
<http://bjorne.github.io/TEES/>)

# DANKE FÜR IHRE AUFMERKSAMKEIT

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