Towards Dementia Diagnosis Logic

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Abstract

Historical motivations for classification systems in health care are requirements of data collections for statistics. Aims to unify data collections eventually becomes a starting point for nomenclature and ontology developments. Diagnosis encoding plays an important role in shifting the paradigm from providing statistics to making decisions. For logic and decision support the situation is non-trivial as nomenclatures continuously change and diagnostic categories are extended. Further, management of both phenomenology and etiology in differential diagnosis requires organisation and logical structure of information modalities and disease taxonomies.

In this paper we provide a logical analysis of a diagnostic manual dividing mental disorders into disorder types. The subdivision is based on criteria (rule) sets and defining features (facts). Our focus is on dementia and we show and compare how particular underlying logic for encoding the dementia classifier can manage heterogeneity of individuals sharing a diagnosis and many-valuedness of truth regarding diagnosis of boundary cases.

Keywords: DSM-IV, dementia, diagnosis, many-valued logic.

1 Introduction

Evidence-based approaches in medicine are well rooted and provide statistical tools to establish validity of formulas by hypothesis testing. However, this typically provides confidence concerning isolated independent decisions or choices. Validity of guidelines, i.e. sets of decision or choice rules, such as appearing in differential diagnosis frameworks, however, cannot be managed by conglomerated hypothesis testing. Rules interact, are usually cascaded, and purely statistical analysis of rules become unfeasible.

Developments in medical decision support still struggle with the leap from statistically rooted evidence-based choices to logically well-founded decision making with respect to sets of rules representing guidelines. In a knowledge and reasoning scenario, sets of rules are always syntactically represented in some logic, where inference mechanisms provide tools by which conclusions are drawn. In a logical framework, language constructions and its semantics need to fulfill correctness and completeness criteria. Furthermore, a set of rules formulated in a particular logic needs additionally to be validated, in the end by motivations provided in evidence-based medicine.

Statistics and logic do indeed meet, even if meeting points and computational mechanisms therein are still rather unclear. Recent decades, however, present several candidate solutions to "statistical logic". Key issues are e.g. conditionalities, where we already know...
that purely Bayesian approaches cannot be logically formulated. However, turning probabilities to possibilities, knowledge to beliefs, certainties to many-valuedness, and so forth, opens up a wide range of candidate logic machineries subject to investigations concerning suitability for medical decision support frameworks.

In this paper we will use dementia (differential) diagnosis as a case study for such an investigation. A selection of logics are used for guideline implementation and logical frameworks are measured and validated with respect to decision correctness as well as guideline management.

The paper is organised as follows. Section 2 provides required detail on our case studies concerning differential diagnosis of cognitive diseases. In Section 3, we take Hájek’s basic many-valued logic [6] as an entrance point of logic presentation as we use propositional logics in a many-valued framework considering absolute as well as graded truth values. The latter is represented by Neural Propositional Logic. Section 4 provides some results on differential diagnosis for four selected patients.

2 Dementia differential diagnosis

Diagnosing dementing diseases, can be viewed as a three step process where the first step determine whether there is a cognitive disorder in a wide perspective, the second distinguishes between cognitive disorders and the third distinguishes between dementia types in the case of dementia. This line of reasoning follows the categorization of cognitive disorders in the clinical guideline Diagnostic and Statistical Manual of Mental Disorders - 4th edition (DSM-IV) [2]. The DSM-IV describes cognitive syndromes and disorders, but requires the International Classification of Diseases (ICD-9-CM) as a source of other medical conditions which has to be taken into account for determining the cause of the disorder. For example, the DSM-IV provides criteria for the dementia of Alzheimer type (DAT), while the cause Alzheimer’s disease (AD) is found in the ICD-9-CM. Therefore there is a diagnosis in the DSM-IV called “Dementia due to” where the causing general medical condition from ICD-9-CM is to be noted. For simplicity we use the notions as synonyms and use the notion (AD) for dementia of the Alzheimer type. The DSM-IV provides recommended diagnostic criteria for the identification of a state of dementia (De), for the dementia of Alzheimer type (AD) and vascular dementia (VaD), which we use in our case studies. However, criteria for other types of dementia are not provided, nor criteria for mild cognitive impairment (MCI), therefore we include consensus criteria for Lewy body dementia (DLB) [8] and MCI [11] into our knowledge base as examples of additional criteria needed in the diagnostic process. However, integrating different sources of knowledge requires careful analysis of the contents in order to handle contradictions and different levels of reliability assigned to diagnoses, caused by different valuations of signs and priorities among signs. DSM-IV provides one priority rule included in the criteria for dementia of Alzheimer type: to exclude all other possible causes of dementia before dementia of Alzheimer type can become a reliable diagnosis. However, studies have shown that cases of mixed aetiologies are common, often with Alzheimer’s disease in combination with another type. Therefore, the guideline NINCDS ADRDA is included in our knowledge base which uses the notion of possible Alzheimer’s disease for the cases where other diagnoses are not excluded. In the case of vascular dementia, the guideline NINCDS AIRDENS is also included, since it provides a stricter interpretation of vascular signs and requires more evidence than DSM-IV to obtain a probable diagnosis of vascular dementia. This is considered useful for a second evaluation in borderline cases. For a review of clinical guidelines in the domain see [9].

The criteria for determining whether there is a state of dementia includes memory deficit and at least one other cognitive dysfunction of aphasia, apraxia, agnosia and executive dysfunction. All present cognitive dysfunctions
need to be of the magnitude that they significantly decrease the person’s ability to perform activities of daily life, which we here denote severe (Sev) in inferences.

We use three typical patient’s cases (Brynolf (B), William (W) and Karin (K)) in our case study and one borderline case (Olof (O)) where more than one set of diagnostic criteria match the clinical findings. The following is descriptions of the cases with abbreviations used in the inference-rules shown in parentheses. In short, Brynolf has had growing difficulties since a year back (GrOn, Pr) with memory (Amn) and to perform tasks where planning and sequencing ability (ExFuncDef) is crucial. William has a history of vascular diseases with angina pectoris (AngPec), small strokes with neurological symptoms. His cognitive ability has slowly decreased (GrOn, Pr) with apraxia (Apr), memory dysfunction (Amn) and executive functioning deficits (ExFuncDef), well covered behind an aggressive behaviour. His cognitive ability tends to fluctuate (FlCo). Physical examination shows focal neurological signs (FoSi), which is confirmed with corresponding signs on Xray (VaSiX). Karin has increasing difficulties to move around as before with Parkinson-like (ExPyr) features, with fall-tendencies related to lapses of cognition, interpreted as fluctuating cognitive ability (FlCo). Memory is increasingly affected (Amn), as well as some executive functioning, and visual hallucinations (ViHa) are present. When using neuroleptic drugs for treating the hallucinations, a strong reaction (NeSens) occurred, which lead the treating physician to alter the earlier hypothetical diagnosis of Parkinson’s disease towards a dementing disease. Olof is a more complex case with gradually increased manifestations of cognitive dysfunctions involving memory (SevAmn, SevOtherCog), fluctuating cognitive ability and visual hallucinations. In addition, focal neurological signs are present and Xray shows vascular signs. At the point of our evaluation, it has already been determined that he suffers from a state of dementia (De).

3 Logics

Extension of 2-valued (propositional) logic to many-valued logic can be arranged and motivated from various viewpoints. Hájek’s basic many-valued logic [6] establishing soundness and completeness over 1-tautologies, i.e. absolute truth of formulas, involves two conjunctions, where (strong) conjunction is semantically specified by a selected t-norm. The basic many-valued logic framework nicely incorporates Łukasiewicz, Gödel as well as the product logic, simply by particular choice of a t-norm. The set of axioms for the basic many-valued logic needs for Łukasiewicz and Gödel logics be extended with one axiom, and in for the product logic with two additional axioms. As we are considering logic programming views, we are more interested in strong completeness rather than completeness. We will therefore in this paper not be concerned with axiomatic considerations.

The restriction to 1-tautologies is rather strong from application point of view. We may allow graded formulas, e.g. as in Pavelka’s logic [10]. In [5], we also use graded formulas, however, including more flexible ways to incorporate connectives. Further, and in order to enable methodology, such as parameter estimation, within evidence-based medicine, we may use only continuous logical connectives. This type of many-valued logic have been shown to be close neural network like structures. In fact, we can even transformation these neural propositional logic programs into corresponding generalized neural networks, where synaptic functions need not only be weighted sums but rather correspond to connectives of the logic. These transformation then enables us to use efficient learning algorithms involving parameters represented by certainty values of formulas [5].

Frequently, we also need to make use of conditionals for inference. Probabilistic considerations come to rescue, but purely Bayesian approaches to conditionals do not allow for suitable logic interpretations. Possibilistic logic [4], on the other hand, can handle conditional like constructions. Further, necessity mea-
sures can be used to define certainty degree of formulas, e.g. for Gödel logic, as specified within the basic many-valued logic, and its corresponding logic programming environments [1, 3].

3.1 Basic many-valued logic (BL)

BL is a propositional language, syntactically with propositional variables, a propositional constant \( \bot \) (false), and additionally with binary connectives \& (strong conjunction) and \( \to \) (implication). If \( \varphi \) and \( \psi \) are formulas then so are \( \varphi \& \psi \) and \( \varphi \to \psi \). Semantically, formulas are mapped to truth values in the unit interval \([0, 1]\). Strong conjunction is by evaluation mappings \( e \) semantically defined by a given \( t \)-norm \(*\), according to \( e(\varphi \& \psi) = e(\varphi) * e(\psi) \). Further, \( e(\bot) = 0 \) and \( e(\varphi \to \psi) = \max\{x \mid e(\varphi) * x \leq e(\psi)\} \).

A weaker conjunction is defined as \( \varphi \land \psi = \varphi \& \psi \), and negation is according to \( \neg \varphi = \varphi \to \bot \).

The deduction rule is Modus Ponens, i.e. from \( \varphi \) and \( \varphi \to \psi \) we may infer \( \psi \). Provability of a formula \( \varphi \) in a set \( T \), or a theory, of formulas, denoted \( T \vdash \varphi \), is defined in the usual way.

Łukasiewicz logic is specified using \( x * y = \max(0, x + y - 1) \), Gödel logic using \( x * y = \min(x, y) \), and product logic, respectively, using \( x * y = x \cdot y \), as corresponding \( t \)-norms.

3.2 Neural propositional logic (NPL)

Rational Pavelka Logic (RPL) [10] involves graded formulas through addition of propositional constants \( \tilde{r}, r \in [0, 1] \) with \( e(\tilde{r}) = r^1 \).

The graded formula \( \varphi : r \) denotes the formula \( \tilde{r} \to \varphi \). Deduction allows us to infer \( \psi : r \ast s \) from \( \varphi : r \) and \( \varphi : s \). Absolute provability then turns to a provability degree, i.e. of a formula \( \varphi \) with respect to a theory \( T \), which we obtain as the value \( \sup\{r \mid T \vdash \varphi : r\} \).

This extension to gradation of formulas can be further generalized to many-valued propositional logics involving a set of binary connectives rather than just one for (strong) conjunction. In the Neural Propositional Logic approach [5] the language consists of the same propositional constants as in RPL, the unary logical connective \( \neg \), the binary connective \( \to \), and a finite set \( B \) of binary connectives that are continuous, associative, and monotone increasing in both arguments. Continuity and monotonicity are required when NPL programs are transformed to neural-like networks where truth values are optimized with gradient descent techniques [5]. The semantics of negation is \( e(\neg \varphi) = 1 - e(\varphi) \) and for implication we define \( e(\varphi \to \psi) = \min\{e(\psi) - e(\varphi) + 1, 1\} \). This corresponds to the situation in BL where \( * \) is the Łukasiewicz \( t \)-norm.

Let now \( L \) denote the set of all formulas. Mappings \( \tau : L \to [0, 1] \) are called fuzzy sets of axioms. Atomic formulas are called facts, and rules are formulas of the form \( \psi \leftarrow \varphi_1 \diamond \ldots \diamond \varphi_n \), where \( n \geq 1, \psi, \varphi_1, \ldots, \varphi_n \) are facts, and \( \diamond \in B \). Facts and rules together form the program clauses.

An NPL program \( \Pi \) is a fuzzy set of axioms such that \( \Pi(\varphi) > 0 \) only for program clauses \( \varphi \), which are then also denoted as graded formulas \( \varphi : \Pi(\varphi) \).

Let \( \Pi \) and \( \Pi' \) be two fuzzy logic programs. \( \Pi' \) is directly derivable from \( \Pi \), if there is a fact \( \psi \) and a rule \( \Phi = \psi \leftarrow \varphi_1 \diamond \ldots \diamond \varphi_n \), such that for all \( \varphi \in L \setminus \{\psi\} \) we have \( \Pi'(\varphi) = \Pi(\varphi) \) and \( \Pi'(''\psi'') = \max\{\Pi(\Phi) + \circ(\Pi(\varphi_1), \ldots, \Pi(\varphi_n)) - 1, \Pi(\psi)\} \).

A fuzzy logic program \( \Pi' \) is derivable from the fuzzy logic program \( \Pi (\Pi < \Pi') \), if there exists a sequence \( \Pi_0, \ldots, \Pi_n \) of fuzzy logic programs satisfying, firstly, \( \Pi_0 = \Pi \) and \( \Pi_n = \Pi' \), and secondly, \( \Pi_{k+1} \) is directly derivable from \( \Pi_k \) for all \( k = 0, \ldots, n - 1 \).

Provability degrees are defined according to \( \Pi \vdash \psi = \sup\{\Pi(\psi) \mid \Pi < \Pi'\} \).

4 Results

Let \( \Pi = \Pi_{NPL}^{DSM-IV,cog} \cup \Pi_{NPL}^{MC1,consensus,cog} \cup \Pi_{NPL}^{DSM-IV,typ} \cup \Pi_{NPL}^{NINS-AIREN,typ} \cup \Pi_{NPL}^{NINS-ARDRA,typ} \cup \Pi_{NPL}^{NINS-PLd,typ} \cup \Pi_{NPL}^{NINS-PLd,typ} \), where respective guidelines are given.

\( ^1 \)In order to obtain a countable language, only rational constants are considered.
in the Appendix, and patient data is found in Table 1. Note that connectives $\diamond$ can be different for each rule. Differential diagnosis results as presented in Table 1 are derived using $\diamond = \min$ in all rules.

<table>
<thead>
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<th>B</th>
<th>W</th>
<th>K</th>
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<td>-</td>
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<td>0.6</td>
<td>-</td>
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<td>-</td>
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<td>-</td>
<td>0.7</td>
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<tr>
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<td>0.3</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Table 1: Patient data and differential diagnosis using NPL.

Note how a stricter interpretation of vascular signs in NINCDS-AIRDEN indicates that the connective $\diamond$ in rule $VaD \leftarrow De \diamond FoSi \diamond VaSiX : 0.9$ should not be of conjunction type.

Since the differential diagnosis process moves through several phases, the results shown in the table are a simplified summary of the process. The fact that the level of dementia affects the reliability measure of each diagnostic hypothesis in our examples indicates that the valuation whether the state of dementia is present should be separated from the dementia differential diagnosis. In the example Olof the presence of dementia was established and added as a fact at the point of investigation. However, the dementia value 0.7 for Olof is a conclusion from rules based on the presence of cognitive deficits. Entailment would indeed provide a supremum of 0.7 and the factual value 1, i.e. outcome would be 1. The level of dementia is significant in choices of treatment, but also in differential diagnosis. The criteria is under discussion, since the requirement of certain cognitive dysfunctions which have to be severe to a certain extent, prevent the detection of less common dementia cases in their early stages where the cognitive signs are not as profound. Our case Karin is an example of such case where the dementia was not detected because her cognitive deficits were not severe enough, which lead to the misstreatment with neuroleptica.

The different values for the different types of dementia for each case indicate the amount of complexity in the particular case. Brynolf and Karin represent cases of typical Alzheimer’s disease and Lewy body dementia respectively. William can be seen as a typical case of vascular dementia, although there are indications of other possible secondary diagnoses. A decision-support system should provide support in distinguishing the typical cases from cases with a mixed aetiology, but also indicate all the possible causes for the cognitive decline. It is common that vascular signs are present in Lewy body dementia, which is the case in our example Olof, where it is likely that both dementia types coexist. There are many general medical conditions which may cause cognitive dysfunctions to different extent, or represent indications of further investigations which need to be done before a diagnosis can be established. We use one such condition in the case of William who has circulation disorder in the form of angina pectoris as an example. However, this particular condition is valued low in affecting cognitive functions compared to for instance a brain tumor (see Appendix).

5 Future work

Analysis in this paper uses NPL with its flexibility to include various types of connectives. As a next step, further investigations with more patients and more precise valuations of features and criteria will be done both
for NPL and other many-valued propositional logics such as those being related to possibilistic logic. The capability of NPL to adapt parameters will also be examined and tested with respect to patient data sets. As the ambition is to provide guidelines and related decision support, guideline adherence need eventually to be measured.

References


APPENDIX

\[ \Pi_{NPL}^{DSM-{IV,cog}} = \{ \]
\[ SevAmn → Amn : 0.9 \]
\[ SevApr → Apr : 0.9 \]
\[ SevAgn → Agn : 0.6 \]
\[ SevAph → Aph : 0.3 \]
\[ SevExFuncDef → ExFuncDef : 0.9 \]
\[ SevOthCog → OthCog : 0.9 \]
\[ OthCog → Apr : 1 \]
\[ OthCog → Agn : 1 \]
\[ OthCog → Aph : 1 \]
\[ OthCog → ExFuncDef : 1 \]
\[ GenMedCon → Inf : 1 \]
\[ GenMedCon → AngPec : 0.2 \]
\[ GenMedCon → B12 : 1 \]
\[ GenMedCon → BrainTum : 1 \]
\[ De → SevAmn ∘ SevOthCog ∘ ¬GenMedCon : 1 \]
\[ AmnDis → Ann ∘ ¬OthCog : 1 \]
\[ Del → Amn ∘ OthCog ∘ FICo ∘ FastOn ∘ AttDef : 1 \]
\[ DelGenMedCon → Del ∘ GenMedCon : 0.7 \]
\[ } \]
\[ \Pi_{NPL}^{MCI\ consensus,cog} = \{ \]
\[ MCI → Ann ∘ OthCog ∘ ¬De : 1 \]
\[ } \]
\[ \Pi_{NPL}^{DSM-{IV,type}} = \{ \]
\[ AD → De ∘ GrOn ∘ Pr ∘ ¬DLB ∘ ¬VaD : 0.9 \]
\[ VaD → De ∘ FoSi : 0.8 \]
\[ VaD → De ∘ VaSiX : 0.8 \]
\[ } \]
\[ \Pi_{NPL}^{NINCDS-AIRDENS,type} = \{ \]
\[ VaD → De ∘ FoSi ∘ VaSiX : 0.9 \]
\[ } \]
\[ \Pi_{NPL}^{NINCDS-ADRDA,type} = \{ \]
\[ AD → De ∘ GrOn ∘ Pr : 0.6 \]
\[ } \]
\[ \Pi_{NPL}^{DLB\ consensus,type} = \{ \]
\[ DLB → De ∘ FICo ∘ ViHa ∘ ExPyr : 0.9 \]
\[ DLB → De ∘ FICo ∘ ViHa : 0.8 \]
\[ DLB → De ∘ FICo ∘ ExPyr : 0.8 \]
\[ DLB → De ∘ ViHa ∘ ExPyr : 0.8 \]
\[ DLB → De ∘ FICo : 0.6 \]
\[ DLB → De ∘ ViHa : 0.6 \]
\[ DLB → De ∘ ExPyr : 0.6 \]
\[ DLB → De ∘ NeSens : 0.5 \]
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\[ \Pi_{NPL}^{patient} = \{ \]
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\[ Amn : r_{Amn} \]
\[ SevAmn : r_{SevAmn} \]
\[ Apr : r_{Apr} \]
\[ ExFuncDef : r_{ExFuncDef} \]
\[ SevOthCog : r_{OthCog} \]
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\[ GrOn : r_{GrOn} \]
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\[ FoSi : r_{FoSi} \]
\[ VaSiX : r_{VaSiX} \]
\[ FICo : r_{FICo} \]
\[ ViHa : r_{ViHa} \]
\[ ExPyr : r_{ExPyr} \]
\[ NeSens : r_{NeSens} \]
\[ } \]