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Conference paper

ON THE USE OF BAYESIAN ARTIFICIAL INTELLIGENCE FOR HYPOTHESIS GENERATION IN PSYCHIATRY

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SUMMARY

In this study, I introduce the use of Bayesian Artificial Intelligence, namely through the probabilistic and structure learning of Bayesian Network models, for hypothesis generation in psychiatry. Bayesian Networks are directed acyclic graphical models that allow researchers to account for complexity in multivariate data sets, as well as identify what is the likely causal direction in detected associations. This in turns leads to more effective designs for confirmatory studies in clinical settings, that go beyond association studies and can provide meaningful impact in clinical practice. As an example, I use three different data sets to highlight several frameworks for hypothesis generation.

Bayesian Networks are useful models since the early stages of knowledge generation in psychiatry, and they can be easily adopted by most applied and clinical researchers for use in quantitative studies.

Key words: *clinical research - data mining - machine learning - psychiatry*

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INTRODUCTION

Research designs in the medical sciences, and particularly so in the field of psychiatry, have often been distinguished as exploratory or confirmatory. Exploratory research is understood as the process of investigating a problem that has not been (thoroughly) studied in the past, and often leads to a better understanding of said problem. Confirmatory research is understood as the process of investigating a problem that is quite well defined based on extensive previous literature, with very specific hypotheses determined a priori for which proof is needed (Jaeger & Halliday 1998). This dichotomy makes it so that most research processes are identified as a sequence of 1) identifying a research question, 2) designing a study protocol, 3) collect the data, 4) analyze the data, and 5) interpret the analysis to get an answer to the initial question. However, this representation of the scientific process is oversimplified, as the identification of a research question is preceded by an overall idea on how nature works: formulating a research question and designing a study protocol are part of an iterative process.

Previously collected data can inform every step of the knowledge generation. For instance, data can help us determine whether a collection method reports unexpected data behavior, avoid given types of statistical analyses, and guide the design of research studies. Data can also help in generating research questions (Tukey 1980): in multivariate data sets and in retrospective studies, the goal is often to identify 1) pairs of independent and dependent variables may be associated, or 2) prognostic factors associated with a given variable. Cross-sectional studies are the go-to designs for such purposes. Results gathered from cross-sectional studies are often limited by the language of traditional statistics, and as such avoid talk of causal effects (Pearl & Mackenzie 2018). In fact, in both inferential statistics and basic modeling we can't infer whether two associated variables are causally connected, or which is the most likely causal direction among those. However, the more information we gather about causality, the faster we can improve clinical practice: current research practices fail to address this fundamental need, primarily because of a lack of usage of the necessary tools to do so (Etkin 2018). Another well-known limitation of traditional statistical analyses is that they limit the pace at which we may generate hypotheses, as we deal with relatively low-dimensional data sets, that is with only a few variables. As the number of variables increases, new analytical methods from the field of artificial intelligence can help us generate hypotheses faster, fully harnessing the power of collected evidence (Oquendo et al. 2012).

Finding new ways for hypothesis generation is particularly crucial in psychiatry: opposite to other medical fields, the nature of mental illness is still debated (Kendler et al. 2011), and our overall lack of understanding of the mechanisms of mental disorders has impeded progress in the past decades (Bluhm 2017). This not only applies to psychiatric illness but also to constructs, such as personality or emotions. In recent years, studying the complexity of psychiatric entities has allowed an exponential growth in knowledge generation, although such progress is limited by a lack of theory building (Fried 2020). In particular, the network framework allows for investigating psychiatric entities as complex systems of interconnected components (Borsboom 2017): this framework has gained increasing interest in recent years, thanks to tutorials and open software that renders it accessible to applied researchers (Borsboom et al. 2021, Briganti et al. 2022, Epskamp & Fried 2018). Network analysis, the statistical set of techniques that accompanies the study of complexity in psychiatric entities, is composed of many techniques from the artificial intelligence field, such as community detection (Golino & Epskamp 2017).

Studying psychiatric entities, such as mental disorders or constructs, as networks has the advantage of scaling up the hypothesis generation process by highlighting multiple connections among components at once: however, to also gain causal insight, researchers need to refer to methods from Bayesian Artificial Intelligence (Korb & Nicholson 2010). Bayesian Networks, the building blocks of Bayesian Artificial Intelligence, allow researchers to investigate complex systems in causal fashion, to perform rigorous causal inference (in case the necessary assumptions are met) or to generate hypotheses for future studies (in case assumptions are not met). In a previous work (Briganti et al. 2022), I outlined the basis for causal inference with Bayesian Networks. In the current study, I will outline how Bayesian Networks can be used for hypothesis generation in psychiatric data sets.

The present study is structured as follows. First, I will introduce Bayesian Networks. Second, using three example data sets, I will demonstrate how Bayesian Networks can be used for hypothesis generation. Thirdly, I will discuss the potential as well as the limitations of such methods in clinical and fundamental psychiatric research.

BAYESIAN NETWORKS

The network theory conceives mental disorders and other psychiatric entities (such as constructs – e.g., personality and emotions) as complex systems, or “networks” of components, such as symptoms (Borsboom 2017). Network components (“nodes”) causally influence each other, and their connections (“edges”) show the magnitude of such influence. As the edges in psychiatric network are not observed, the set of connections has to be estimated. Network theory uses graphs, which belong to field of mathematics that deals with the study of structures are meant to represent relationships between entities, like symptoms, signs or biological markers in the medical sciences.

Pairwise Markov Random Fields are the mostly used family of models for network estimation in the psychopathological literature (Borsboom et al. 2021): they encompass, for instance, the Ising Model and the Gaussian Graphical Model; they all have in common that they are undirected models. Therefore, researchers can’t retrieve a direction from one symptom to another.

Bayesian Networks (Briganti et al. 2022) are based on directed acyclic graphs and a probability distribution. A directed acyclic graph contains only directed edges. Such arcs are often interpreted as causal relationships in which the tail node is the cause and the head of the arrow is the effect. Bayesian networks cannot contain loops (the effect of a node on itself) or cycles (for instance, A goes to B, B goes to C, and C goes to A). The primary goal of a Bayesian Network is to express the conditional independence set of relationships among variables (that is, variables that do not predict each other). In addition to a directed acyclic graph, Bayesian networks are defined by the global probability distribution of the variables in the network: for instance, conditional probability tables for discrete and ordinal variables and the multivariate normal distribution for continuous variables. The directed acyclic graph and the probability distribution are linked in a Bayesian Network, as the graph is an “independence map” of the probability distribution: if two nodes are not connected by an edge in the network, then they are either independent, or conditionally independent: this is called the Markov Property (Korb & Nicholson 2010). That is, graphical separation implies probabilistic independence, which in turn makes it possible to decompose the larger model into a set of smaller models, one for each variable in the network, conditional on its parents (nodes that cause it). Two nodes A and B are said to be “d-separated” by a conditioning set of nodes S if conditioning on all members of S blocks all paths (sequence of nodes and edges with A as starting node and B as ending node) between A and B. *d-separation* is a useful instrument to algorithmically determine whether two nodes in a network are (in)dependent or conditionally (in)dependent.

Learning the structure of a Bayesian Network is achieved with specific algorithms. There are three kind of structure learning algorithms: constraint-based algorithms (based on conditional independence tests), score-based (based on goodness-of-fit measures), and hybrid algorithms (that combine both constraint-based and score-based strategies). The relationships among variables in Bayesian Networks are easily interpreted as causal relationship, as they are directed. However, three assumptions should be made before interpreting an edge as a causal effect. First, each variable (node) must be conditionally independent of its indirect and direct non-effects given its direct causes (this is the causal translation of the Markov property). Second, there must exist a directed acyclic graph faithful to the probability distribution of X so that the only dependencies in the probability distribution are those that arise from d-separations in the directed acyclic graph. The third assumption descends from the first two: there must be no latent variables that act as confounding factors (therefore developing causal effects on one or several nodes in the network without the DAG reporting such relationships). The third assumption is particularly important in clinical settings: to safely interpret a directed connection as a causal effect, the experimental design should be set as to block any confounding factors. A common device to achieve that is randomization, which severs any incoming causal link between the randomized variables and possible exogenous effects.

USING BAYESIAN NETWORKS FOR HYPOTHESIS GENERATION IN PSYCHIATRY

In most (if not all) retrospective or cross-sectional studies however, these three assumptions fail to be met. Although in such cases, we cannot perform a rigorous causal analysis of the multivariate data, we can use Bayesian Networks to generate research hypotheses for future experiments: the retrieved set of directions among variables is in fact the most likely set of causal effects. In this study, I illustrate this potential with three examples of psychiatric data, specifically, disorders and constructs data as measured through psychometrics. The analysis of these three data sets was approved by ethical committees (Comité d'Éthique hospitalier CHU Brugmann, Ref CE2020/39, CE2021/58, and Comité d'Éthique hospitalo-facultaire Erasme-ULB; Ref. P2017/379). The analyses presented in this study were performed in the R (version 4.2.0), with the package bnlearn (Scutari 2010).

Example 1: Manic symptoms

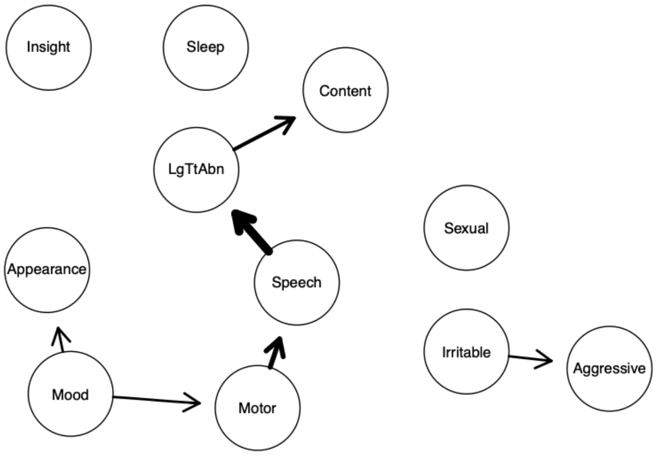
In a first data set, manic symptoms of 201 inpatients in a mood disorder unit were scored using the Young Mania Rating Scale (Briganti et al. 2021). Patients were 18–75 years old (M = 44, SD=:14.5); 51% of them were female, and 49% of them were male. The variables included are elevated mood, increased motor activity-energy, sexual interest, sleep, irritability, speech, language-thought disorder, content, disruptive-aggressive behavior, appearance, and insight.

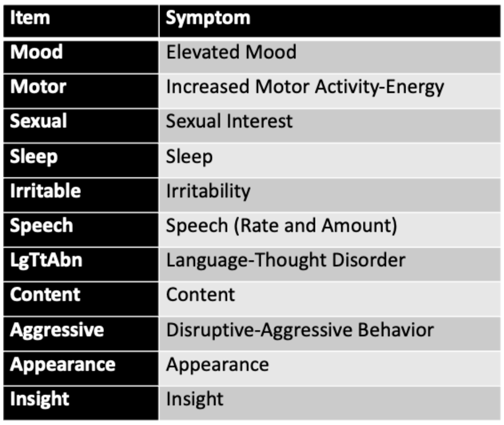
The Bayesian Network learned from the manic symptom data is shown in Figure 1. It has Mood as a root node, with Appearance and Increased Motor Activity-Energy as children. Increased Motor Activity-Energy is the parent of a chain including subsequently Speech, Language-Though Disorder, and Content. Irritable is the root node for Aggressive. The network overall supports the idea that energy is a very important symptom in bipolar disorder (McNally et al. 2021).

Example 2: Self-worth

In a second data set, 680 students scored the 35 items of the Contingencies of Self-Worth Scale (Briganti 2018, Briganti et al. 2019, Crocker et al. 2003). The subjects were 17–25 years old (M = 19 years, SD = 1.5 years), 59% of them were women and 41% men. The data set used for this analysis includes the seven domains of the self-worth emotion (Family Support, Competition, Appearance, God's Love, Academic Competence, Virtue, and Other's Approval, depicted in Figure 2). Each domain is composed of the sum score of all items meant to assess a specific domain.

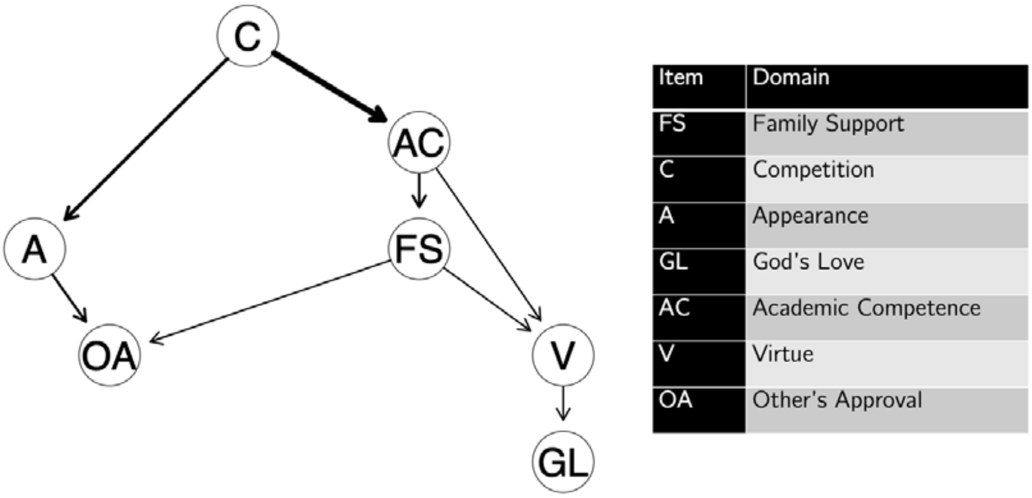
The Bayesian Network learned from the self-worth data is shown in Figure 2. It has Competition as a root node that has both Appearance and Academic Competence as children. Academic Competence is a parent node of Family Support and Virtue. Other's Approval is a child node of Appearance and Family Support. God's Love is a child node of Virtue. The self-worth Bayesian Network also empirically supports the idea that competition, grossly understood as feeling worth when self-comparing with other people, is one of the core sources of self-worth (Covington 1992, Crocker & Nuer 2003, Lamont 2019). Moreover, the three other main parent nodes for other nodes in the network, Appearance, Academic Competence, and Family Support, are all defined through an interpersonal sources of self-worth, recognized as core parts of the constructs from developmental points of view (Greno-Malsch 1998, Harter et al. 1998, Laursen et al. 2006).





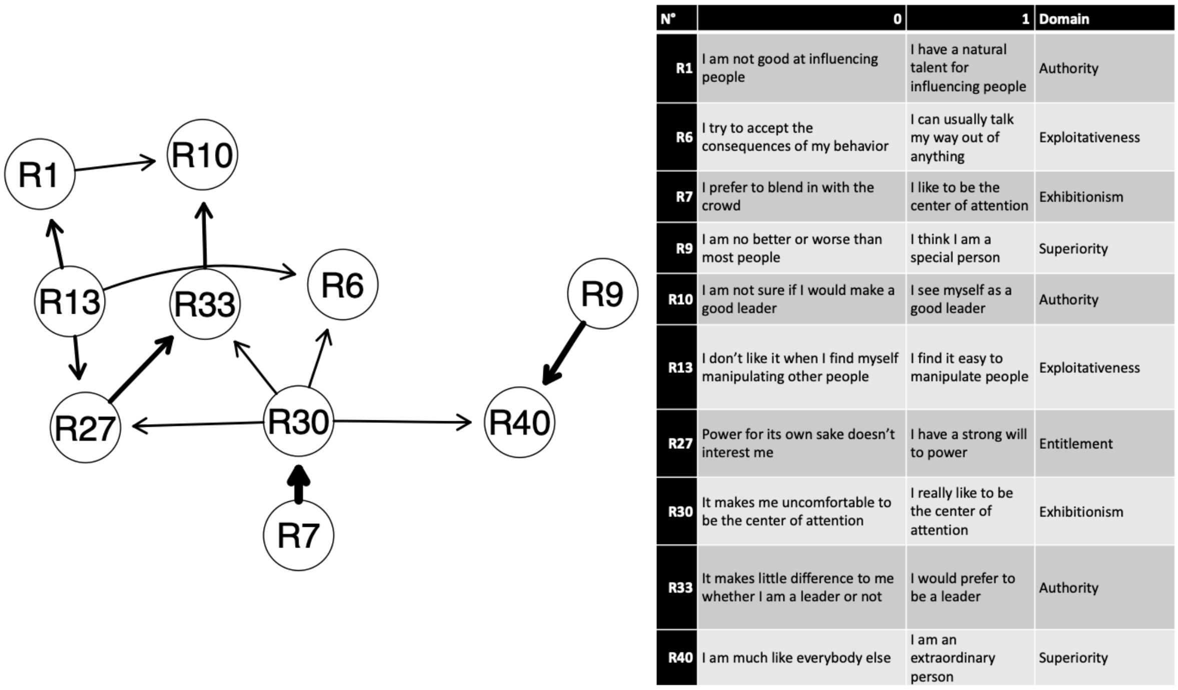
Item	Symptom
Mood	Elevated Mood
Motor	Increased Motor Activity-Energy
Sexual	Sexual Interest
Sleep	Sleep
Irritable	Irritability
Speech	Speech (Rate and Amount)
LgTtAbn	Language-Thought Disorder
Content	Content
Aggressive	Disruptive-Aggressive Behavior
Appearance	Appearance
Insight	Insight

Figure 1. Directed Acyclic Graph of manic symptoms



Item	Domain
FS	Family Support
C	Competition
A	Appearance
GL	God's Love
AC	Academic Competence
V	Virtue
OA	Other's Approval

Figure 2. Directed Acyclic Graph of Self-worth items



N°	0	1	Domain
R1	I am not good at influencing people	I have a natural talent for influencing people	Authority
R6	I try to accept the consequences of my behavior	I can usually talk my way out of anything	Exploitativeness
R7	I prefer to blend in with the crowd	I like to be the center of attention	Exhibitionism
R9	I am no better or worse than most people	I think I am a special person	Superiority
R10	I am not sure if I would make a good leader	I see myself as a good leader	Authority
R13	I don't like it when I find myself manipulating other people	I find it easy to manipulate people	Exploitativeness
R27	Power for its own sake doesn't interest me	I have a strong will to power	Entitlement
R30	It makes me uncomfortable to be the center of attention	I really like to be the center of attention	Exhibitionism
R33	It makes little difference to me whether I am a leader or not	I would prefer to be a leader	Authority
R40	I am much like everybody else	I am an extraordinary person	Superiority

Figure 3. Directed Acyclic Graph of narcissistic personality items

Example 3: Narcissistic personality

In a third data set, 942 university students scored the 40-item Narcissistic Personality Inventory (Briganti & Linkowski 2020, Raskin & Hall 1979). Participants were 17 to 25 years old (M = 20 years, SD = 1.7 years), 55% of them were female and 45% were male. For this study, I included the ten items with the highest centrality indices in the network structure (and shown in Figure 3).

The Bayesian Network of narcissistic personality items has item 7 and 30 ("I like to be the center of attention"), completely redundant with each other, as root nodes for items 6, 27, 33, and 40. Overall, the domains of exhibitionism, authority, and superiority are domains with items that are "parent nodes" more frequently than "children nodes", which is supported by current theories on narcissistic personality (Miller et al. 2016).

DISCUSSION

This study addressed the important topic of the use of Bayesian Artificial Intelligence models, namely Bayesian Networks, for generating research hypotheses in psychiatry. Modeling psychiatric entities as directed acyclic graphs can help us in three different ways for generating research hypothesis.

First, Bayesian Networks can help, as shown, in identifying a great number of sets of independent and dependent variables, as well as a great number of potential clinical prediction models: as shown in our first example, for instance, for each symptom in the network, one can identify a number of local predictors, and those predictors can in turn be predicted through other variables that are easy to identify on a graph. This is important to improve the quality of clinical prediction models (Wynants et al. 2020) that are published in the literature and that guide innovation in clinical practice. Through the identification of the best predictors, with a hint of what the potential causal direction of a relationship might be, Bayesian Networks can help in stimulating future studies.

Second, as "v-structures" (two unrelated nodes cause a third node, X → Z ← Y) the building blocks of Bayesian Networks Bayesian Networks can identify which causal structures are likely to cause bias. Collider bias, that is, a negative dependence arising among two independent variables that are unrelated is particularly difficult to identify without Bayesian Networks in multivariate data sets, and therefore such tools can help researchers avoid (or be aware of, depending on the situation) collider bias. V-structure arise for instance in the second data set of our study and can be easily identified.

Third, Bayesian Networks are a "white-box" kind of artificial intelligence: opposite to other network models, such as neural networks, the nodes in a Bayesian Network are observed variables (such as psychiatric symptoms) and not steps of a learning process. Such as in our third data set, despite the elevated number of variables, each local model (children node and parent nodes) can be easily and transparently identified by the researcher for future investigation. This helps in addressing the inherent complexity of network models and addressing many variables at once.

Using Bayesian Networks for generating research hypotheses in psychiatry comes with several limitations. We will focus on two of them. First, the assumptions for rigorous causal inference are quite difficult to verify in psychiatric data, especially for cross-sectional studies and data coming from psychometric evaluations. Psychometric tools in clinical practice, for instance, are heavily based on a common cause model of disorders, which in turn rely on hidden causes, which, if present in a data set, violate the assumptions for causal inference. However, this limitation can be overcome with the exploratory value of Bayesian Networks, especially in hypothesis generation, which is the aim of the current study. Other ways of

Second, if the sample size is too low, the results of Bayesian Network analysis are likely to be unstable (that is, fail to replicate). However, this limitation can in part be addressed using bootstrapping, that is, re-estimating the network model several times to retain only the most stable connections.

In conclusion, I recommend the use of Bayesian Network in multivariate data sets for hypothesis generation in psychiatry. Researchers may benefit from this advanced set of tools to plan more accurate future studies, as well as to uncover previously unseen relationships in data.

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