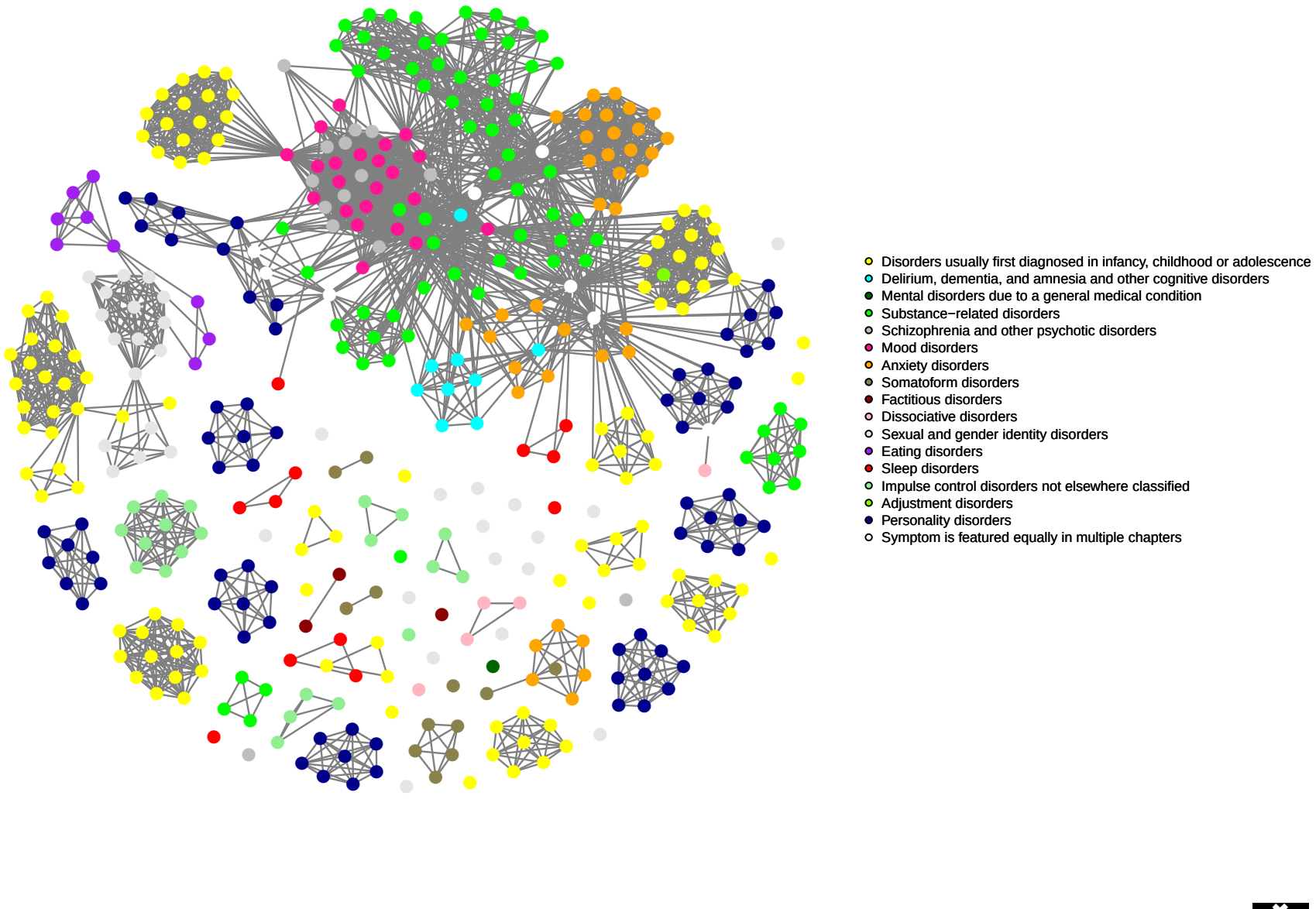
Workshop

Netwerken in de psychopathologie

Sacha Epskamp

University of Amsterdam
Department of Psychological Methods

12-12-2013
Lustrumcongres


Disorders usually first diagnosed in infancy, childhood or adolescence
Delirium, dementia, and amnesia and other cognitive disorders
Mental disorders due to a general medical condition
Substance−related disorders
Schizophrenia and other psychotic disorders
Mood disorders
Anxiety disorders
Somatoform disorders
Factitious disorders
Dissociative disorders
Sexual and gender identity disorders
Eating disorders
Sleep disorders
Impulse control disorders not elsewhere classified
Adjustment disorders
Personality disorders
Symptom is featured equally in multiple chapters

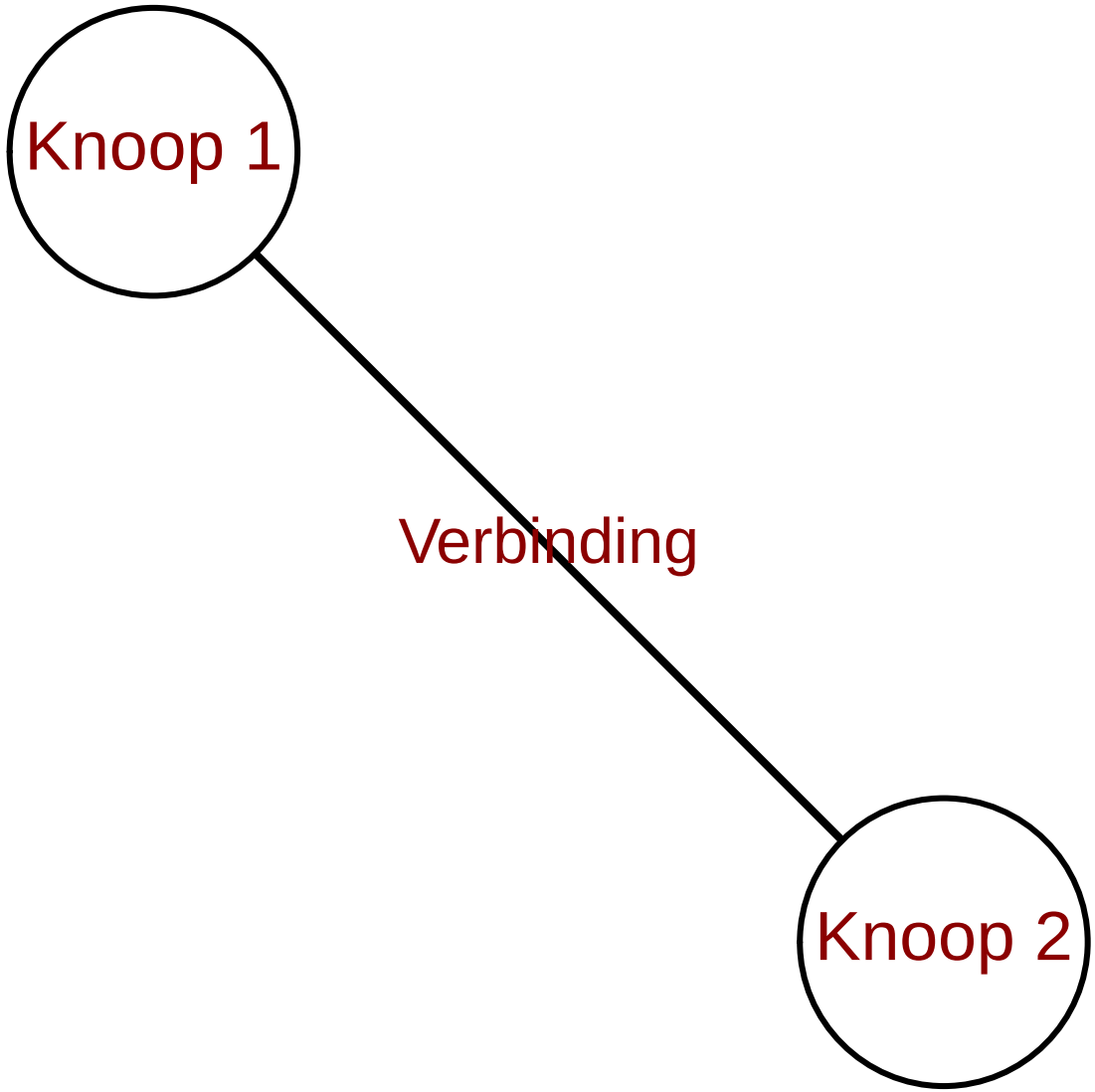
Doel

- Wat zijn netwerken?
- Wat kunnen we met netwerken?
- Hoe gebruiken wij netwerken in de psychopathologie?

Wat is een netwerk?

Wat is een netwerk?

- Een netwerk is een set *knopen* die verbonden zijn door een set van *verbindingen*


Knoop 1
Verbinding
Knoop 2

Wat is een netwerk?

- Een netwerk is een set *knopen* die verbonden zijn door een set van *verbindingen*
  - Een knoop stelt een entiteit voor. Dit kan van alles zijn:

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    - Steden

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    - Mensen
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    - Symptomen

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  - Een verbinding stelt een relatie tussen twee knopen voor. Dit kan weer van alles zijn:

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    - Vriendschap

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    - Afstand

Wat is een netwerk?

- Een netwerk is een set *knopen* die verbonden zijn door een set van *verbindingen*
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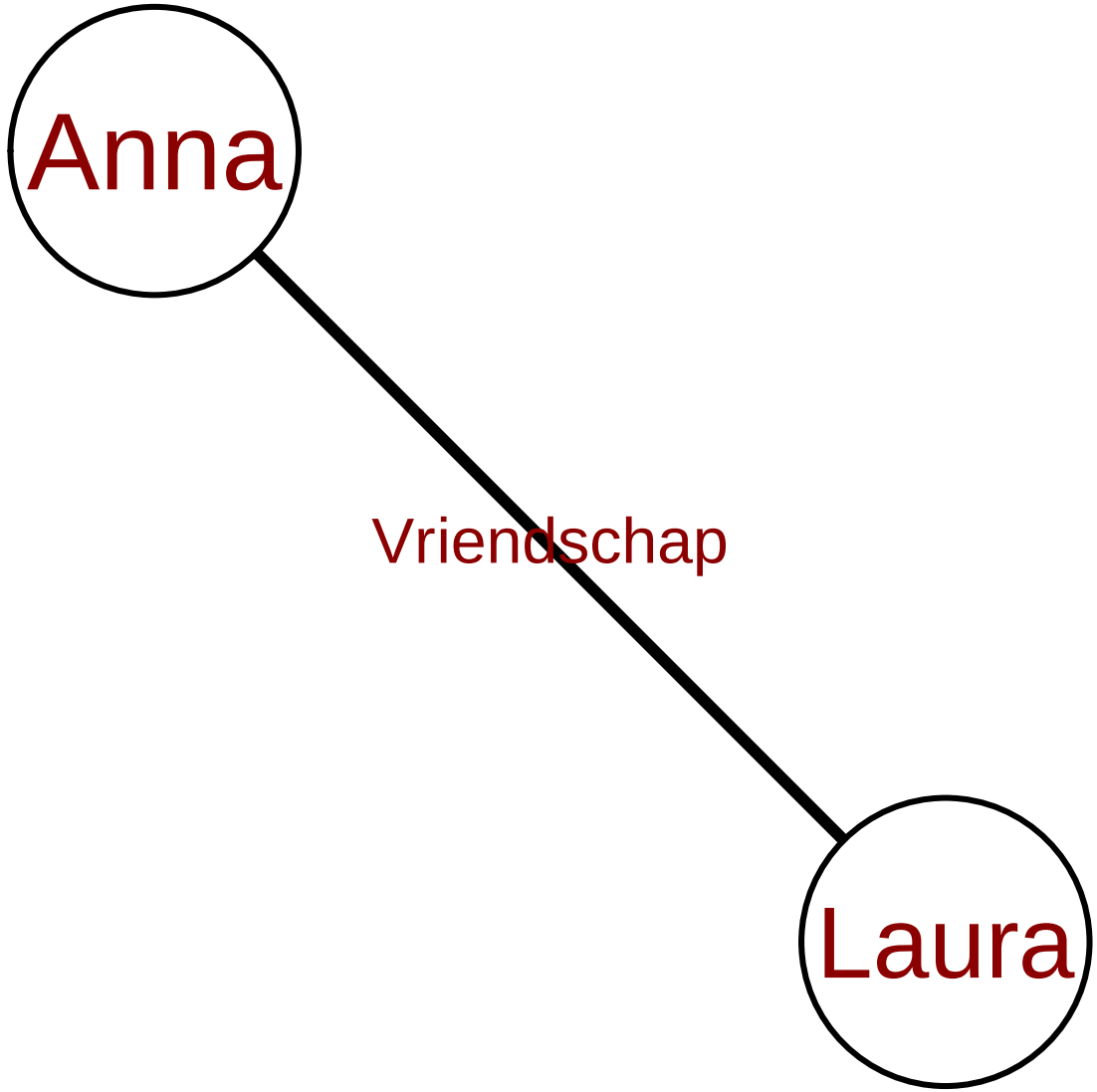
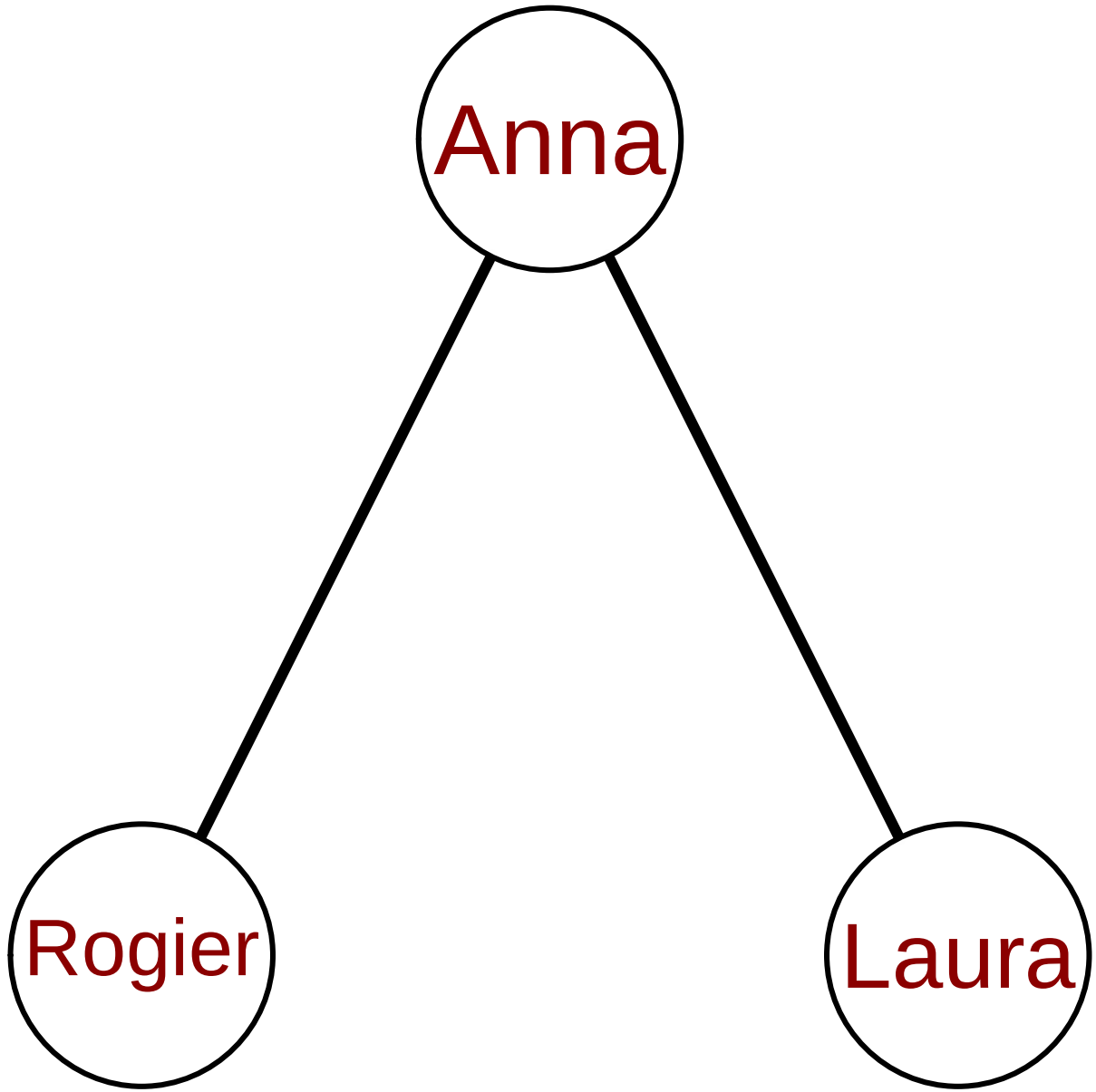
    - Mensen
    - Steden
    - Symptomen
  - Een verbinding stelt een relatie tussen twee knopen voor. Dit kan weer van alles zijn:
    - Vriendschap
    - Afstand
    - Comorbiditeit

Anna is bevriend met Laura:



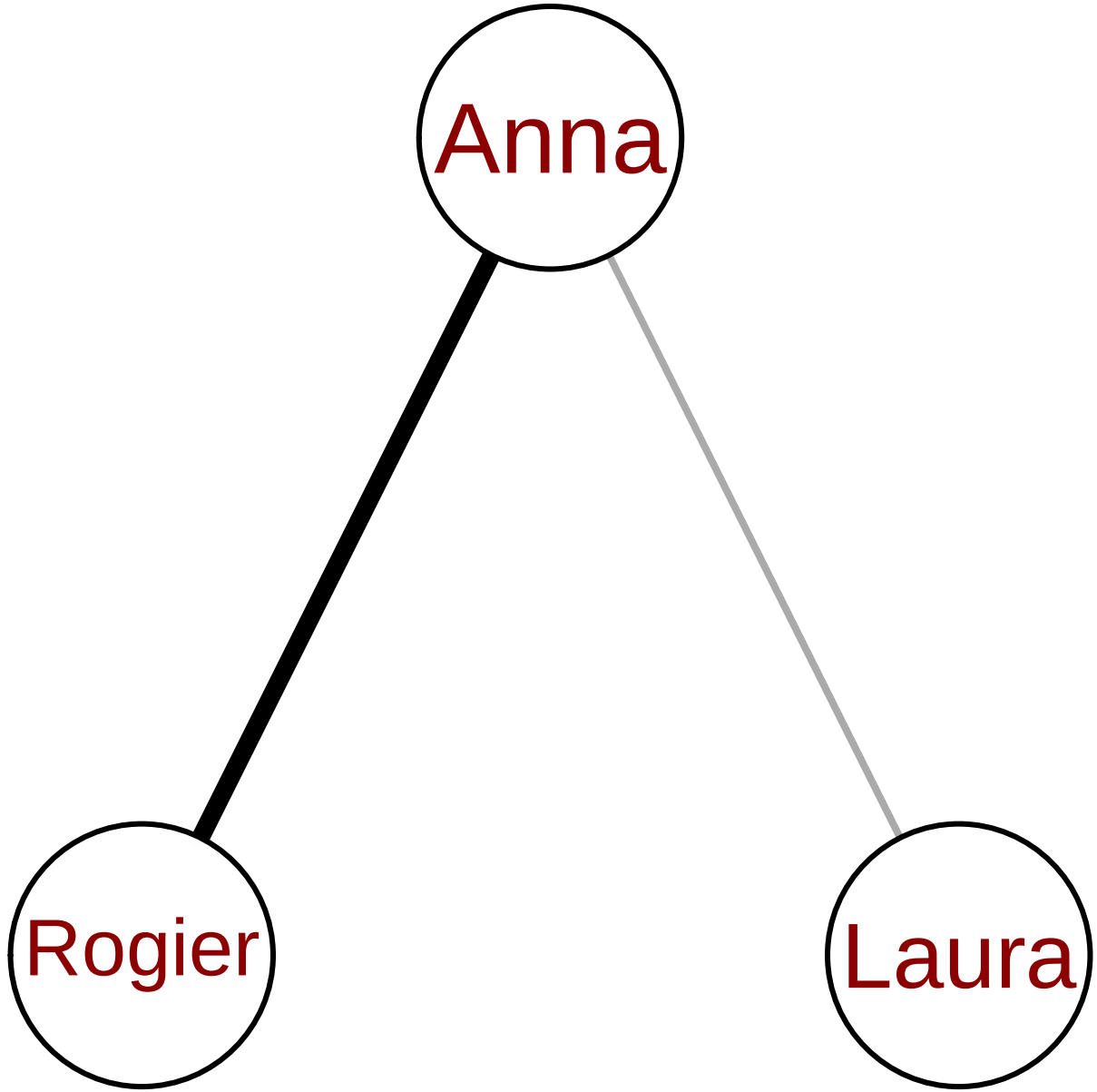
Anna is bevriend met Laura en met Rogier, maar Laura is niet bevriend met Rogier:



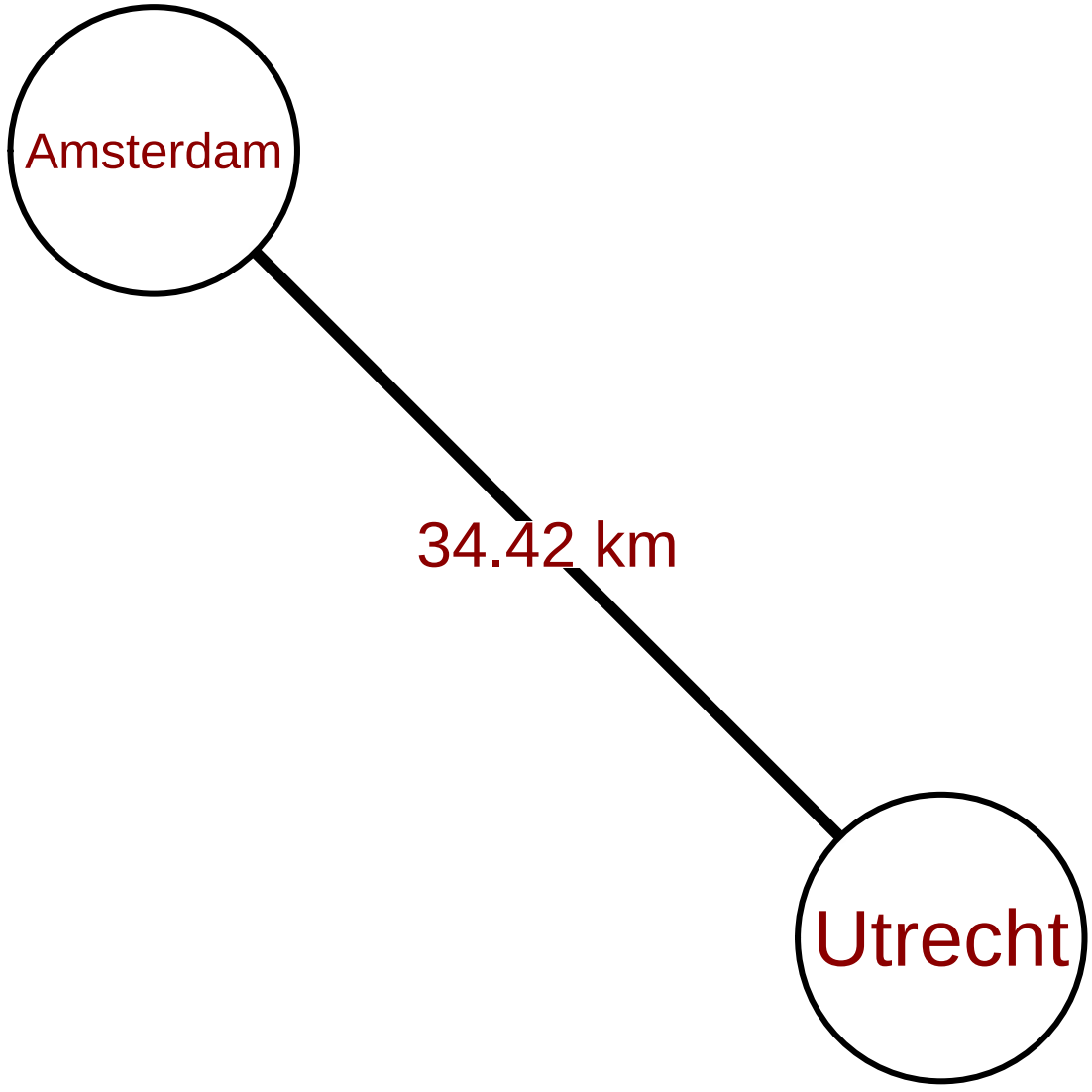
Wat is een netwerk?

- Vaak nemen we aan dat verbindingen niet allemaal even sterk zijn
- We kunnen de verbinding wegen met een *gewicht*
  - Hoe sterker het gewicht, hoe sterker de verbinding
  - Twee knopen die sterk verbonden zijn liggen “dichter bij elkaar”
    - Gewicht is daardoor het tegenovergestelde van afstand.
  - Een verbindingen met sterker gewicht geven we aan met een dikkere en meer gekleurde lijnen

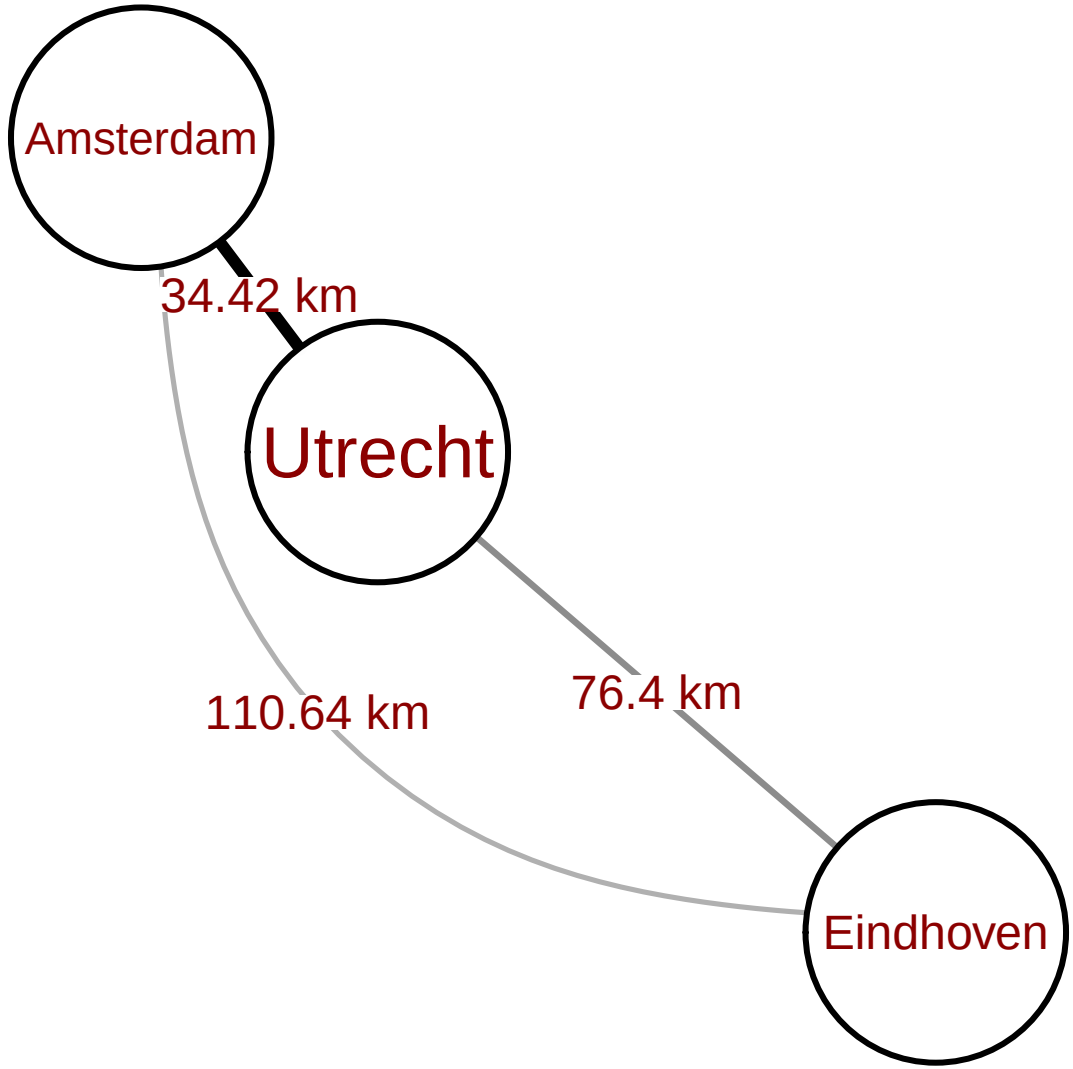
Anna is beter bevriend met Rogier dan met Laura:



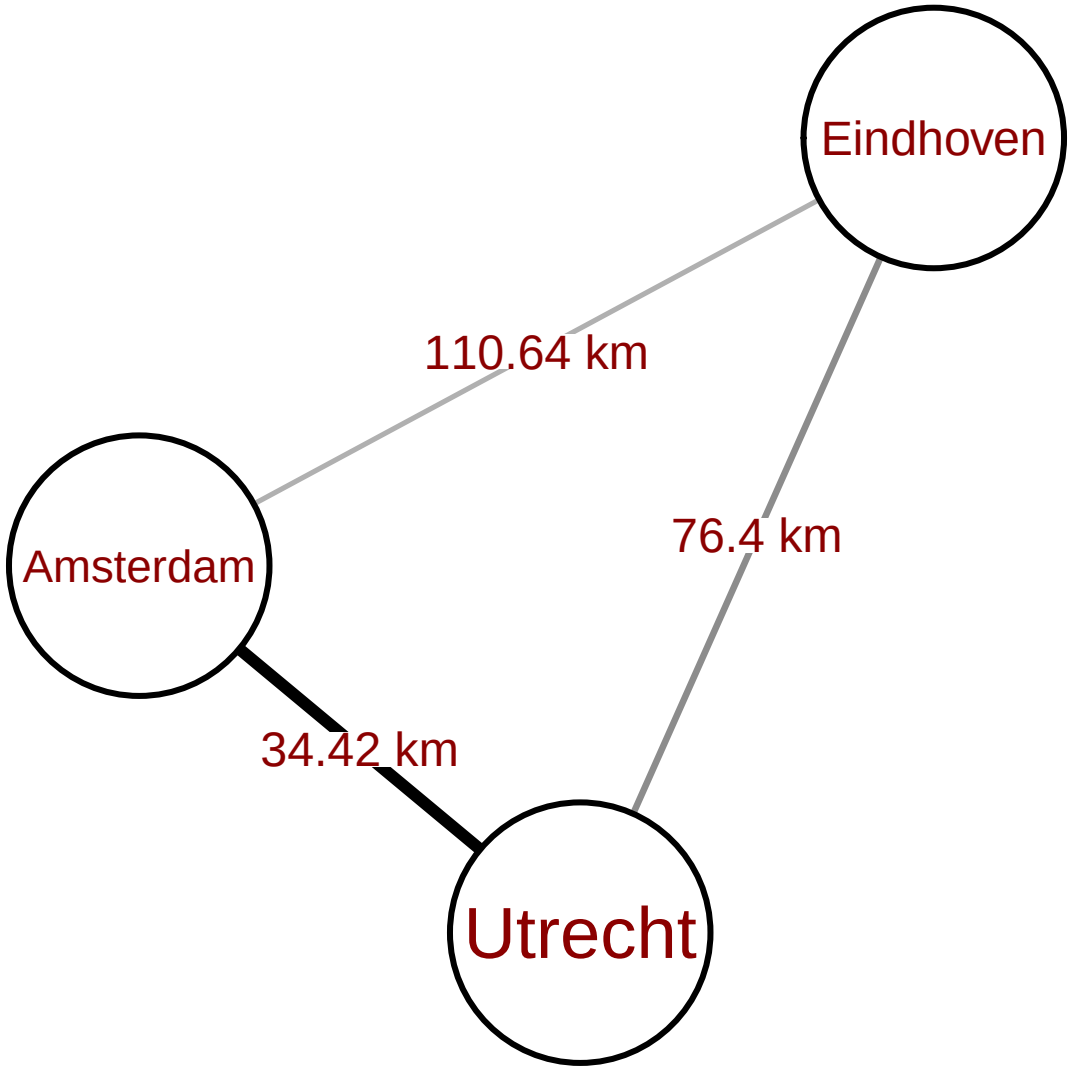
De afstand tussen Amsterdam en Utrecht is 34.42 kilometer:



De afstand tussen Amsterdam en Utrecht is kleiner dan de afstand tussen Amsterdam en Eindhoven:



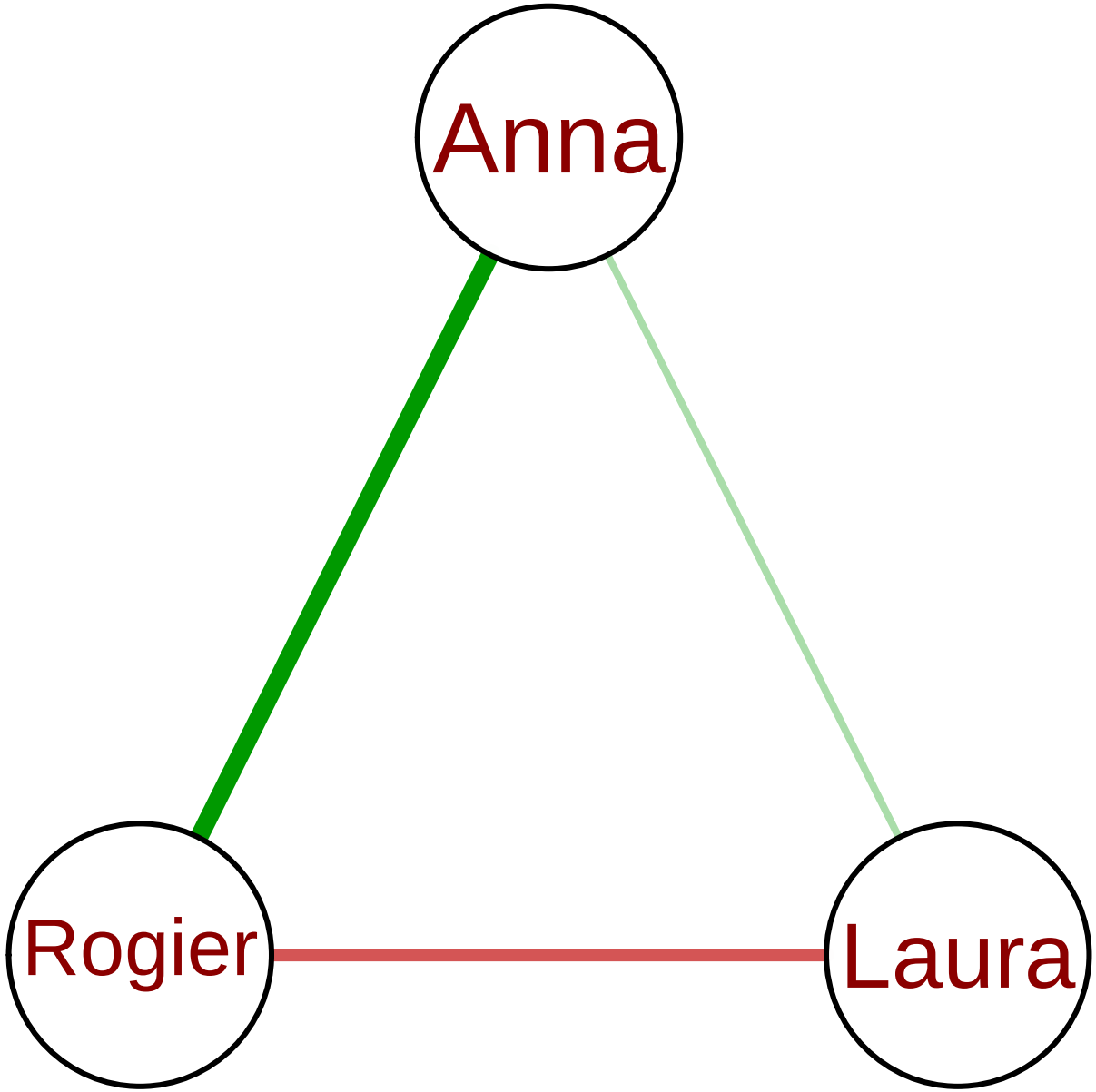
We kunnen de knopen plaatsen zoals we willen:



Wat is een netwerk?

- Deze gewichten kunnen ook negatief zijn
- Vaak kleuren we positieve gewichten *groen* en negatieve gewichten *rood*

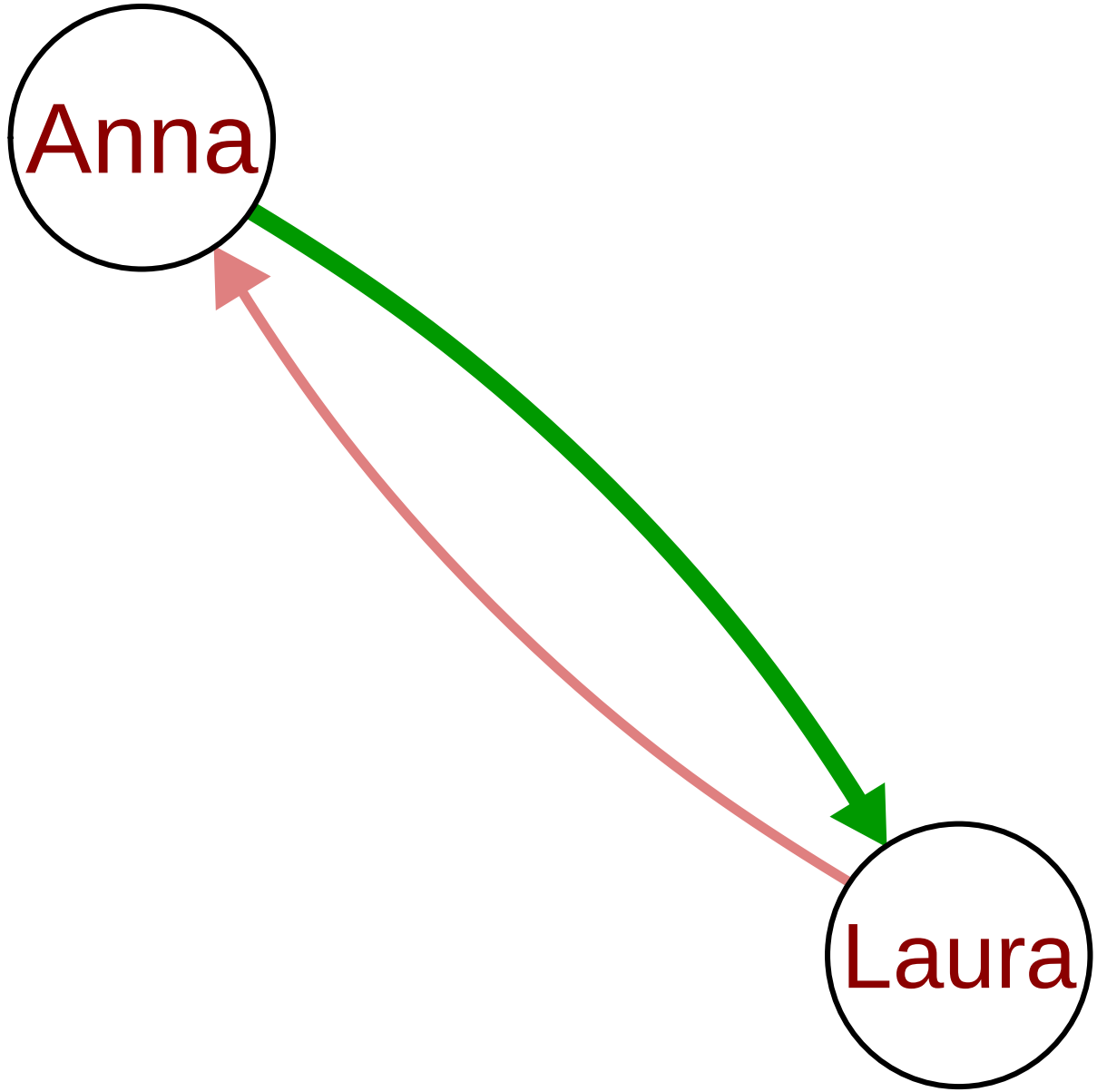
Anna is bevriend met Rogier en Laura, maar Rogier en Laura mogen elkaar totaal niet:



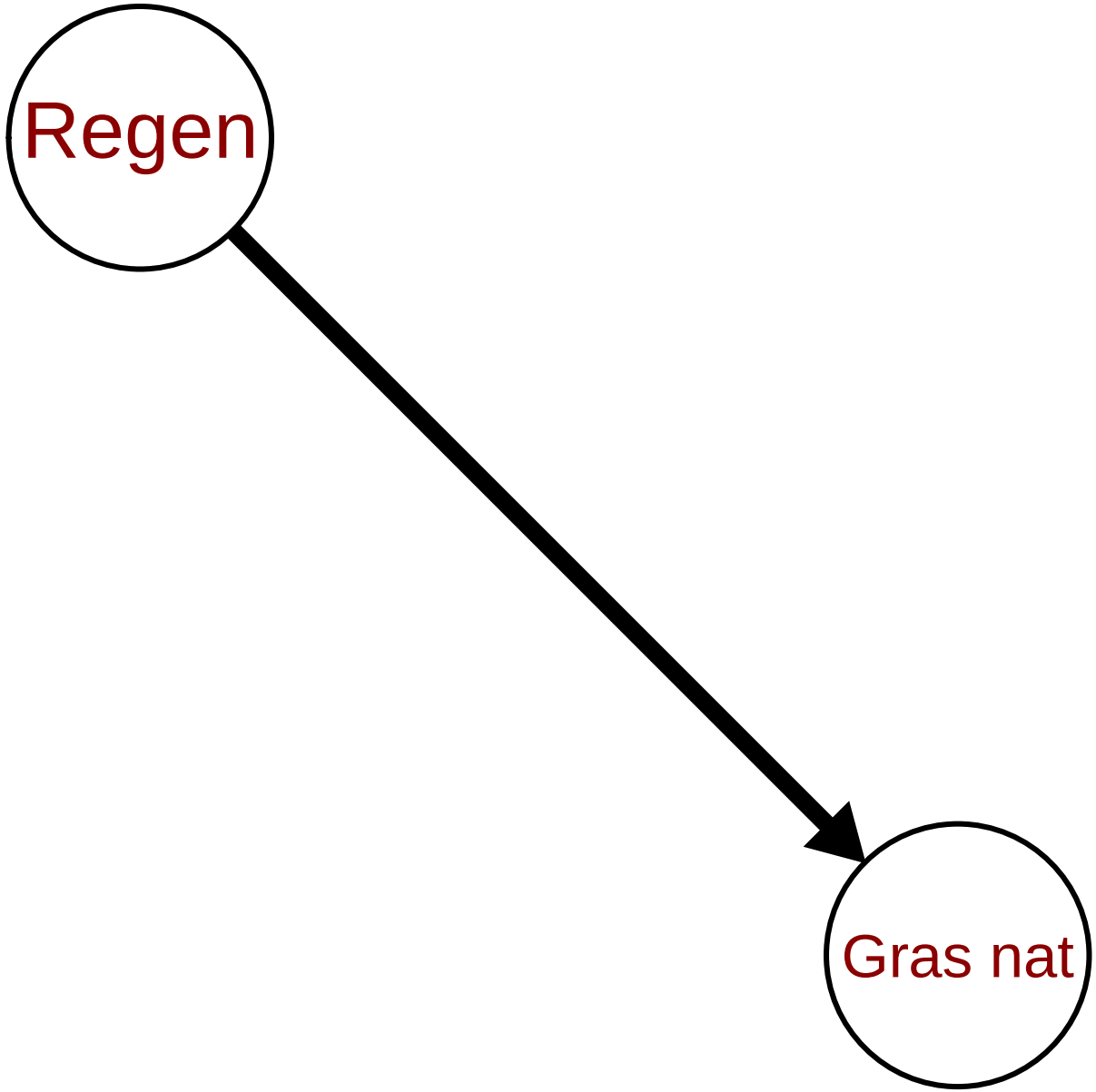
Wat is een netwerk?

- Eenzijdige verbindingen kunnen we weergeven een pijl
  - Assymetrische verhoudingen
  - Een-richtingsverkeer
  - Oorzaak - Gevolg

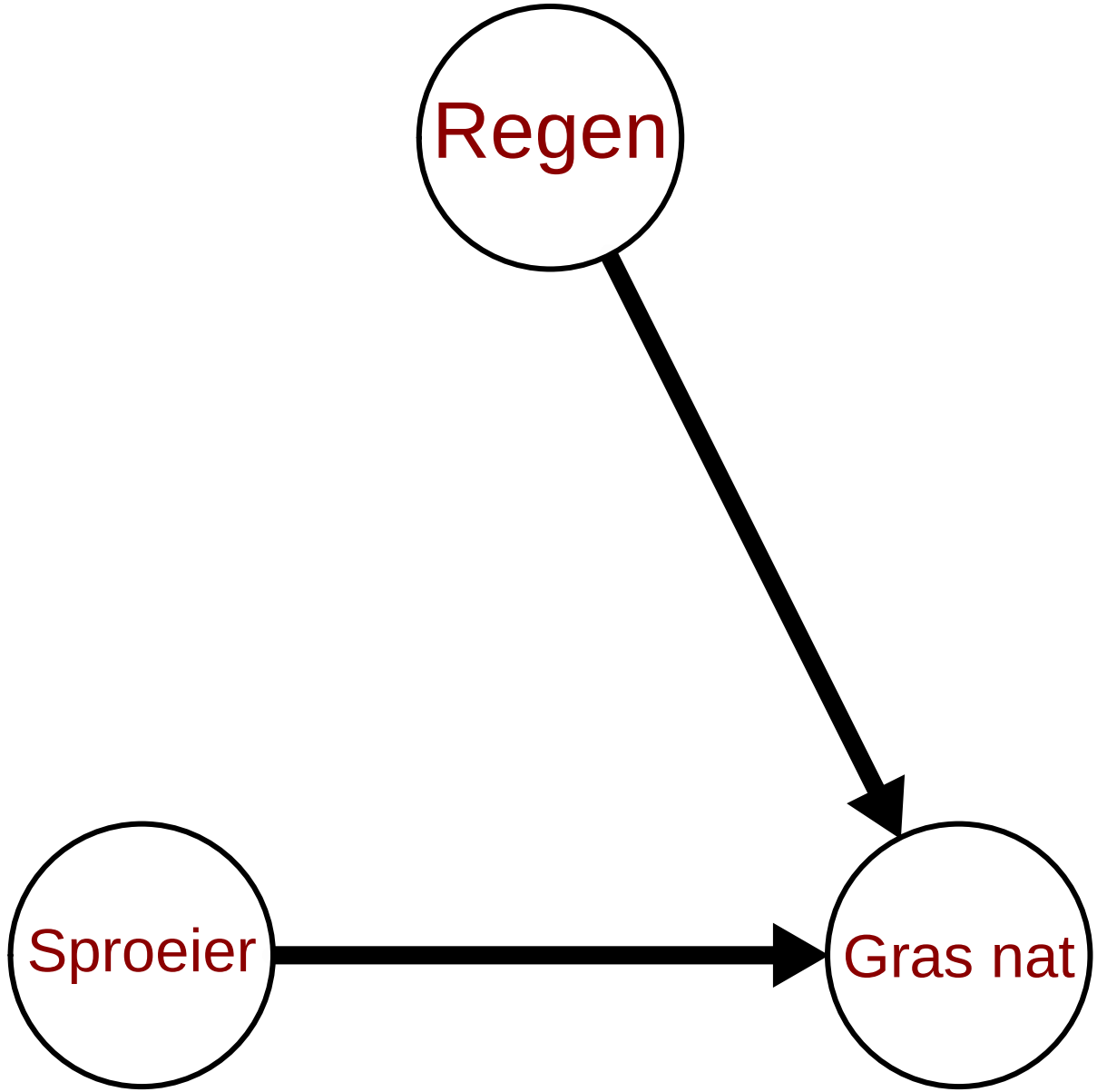
Anna mag Laura wel, maar Laura mag Anna niet:

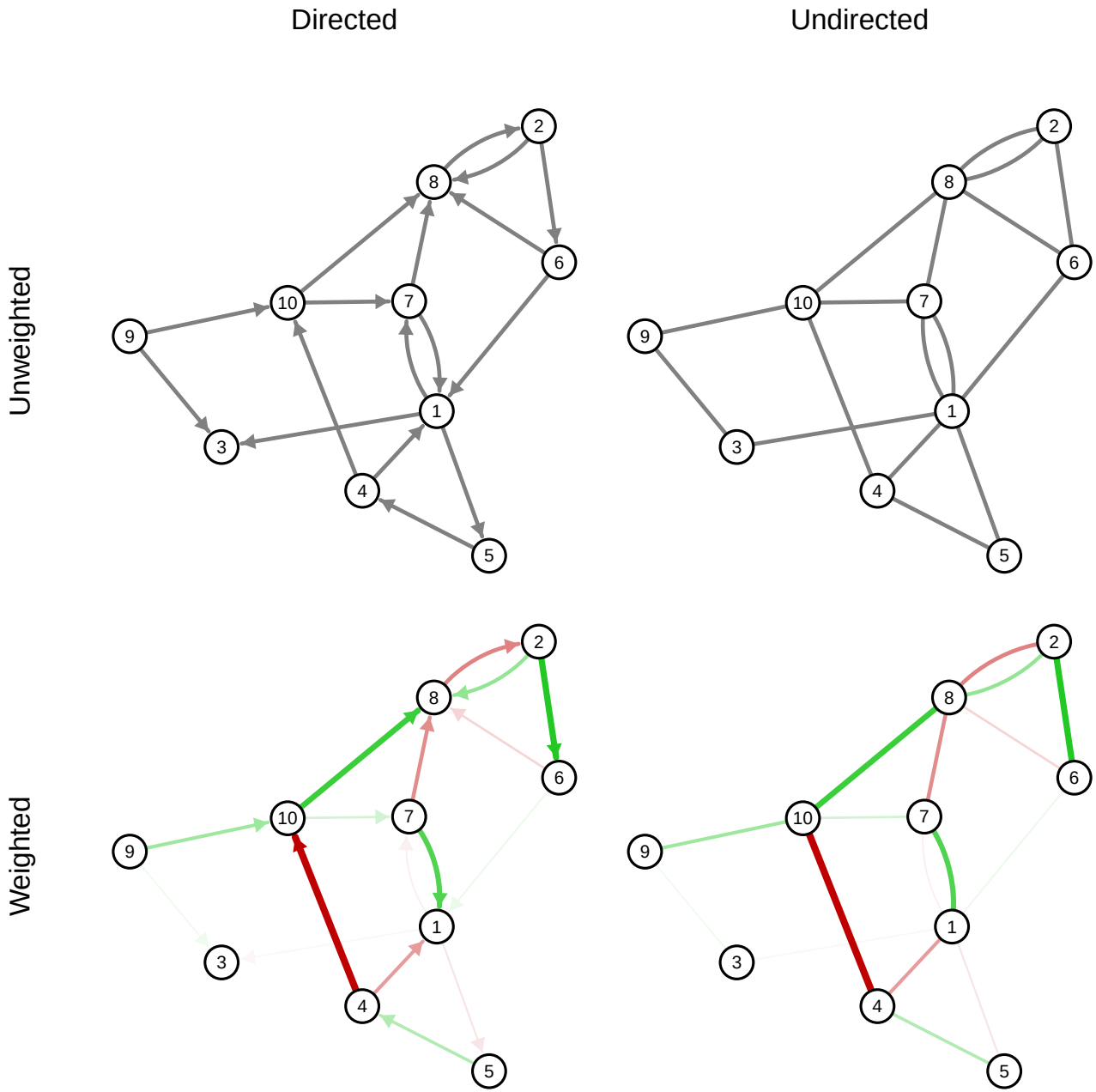


Als het regent wordt het gras nat:



Als de sproeier aan staat wordt het gras ook nat:




Directed
Undirected
Unweighted
Weighted
1
2
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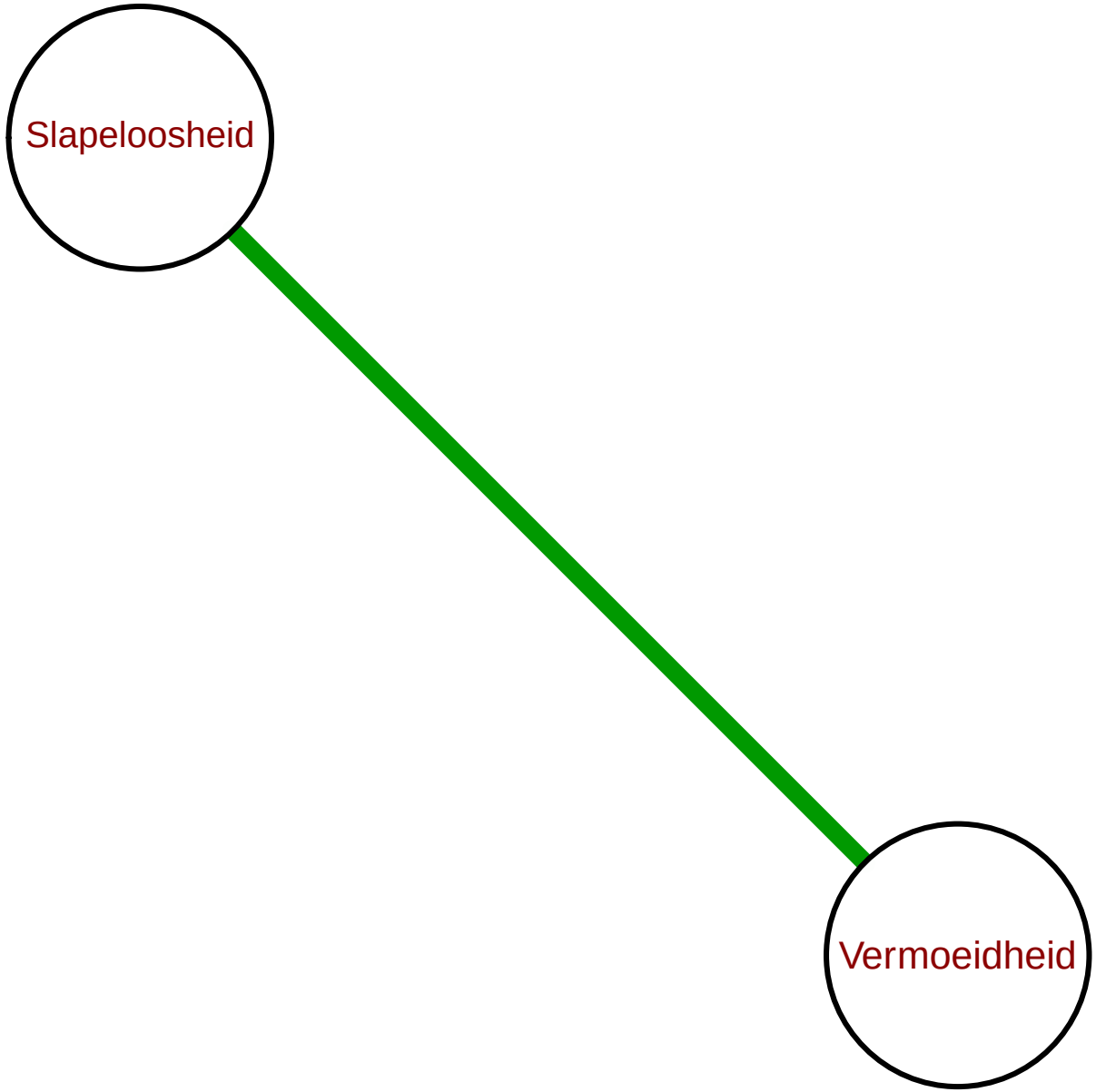
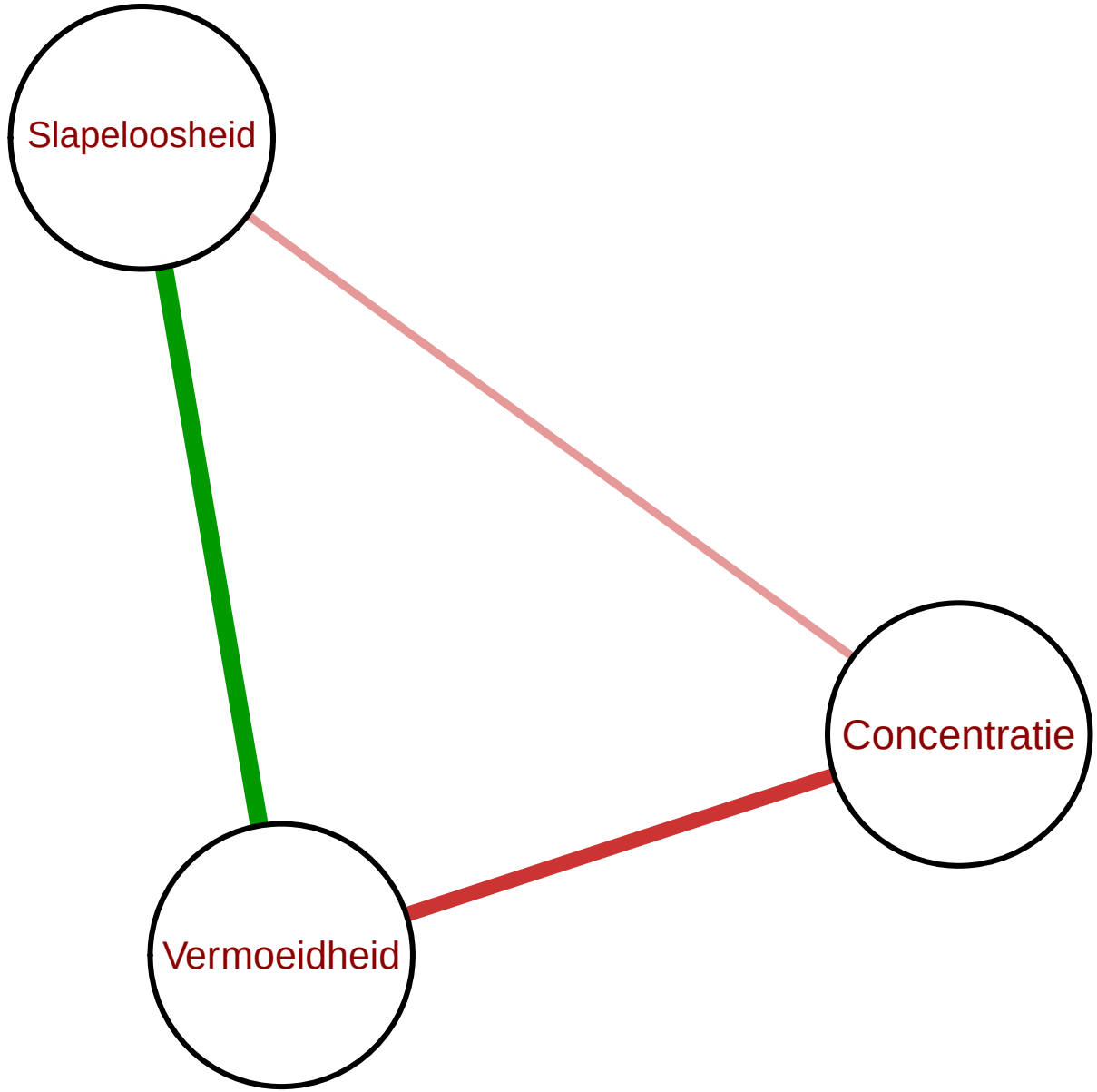
10

Wat kunnen we hiermee in de Psychologie?

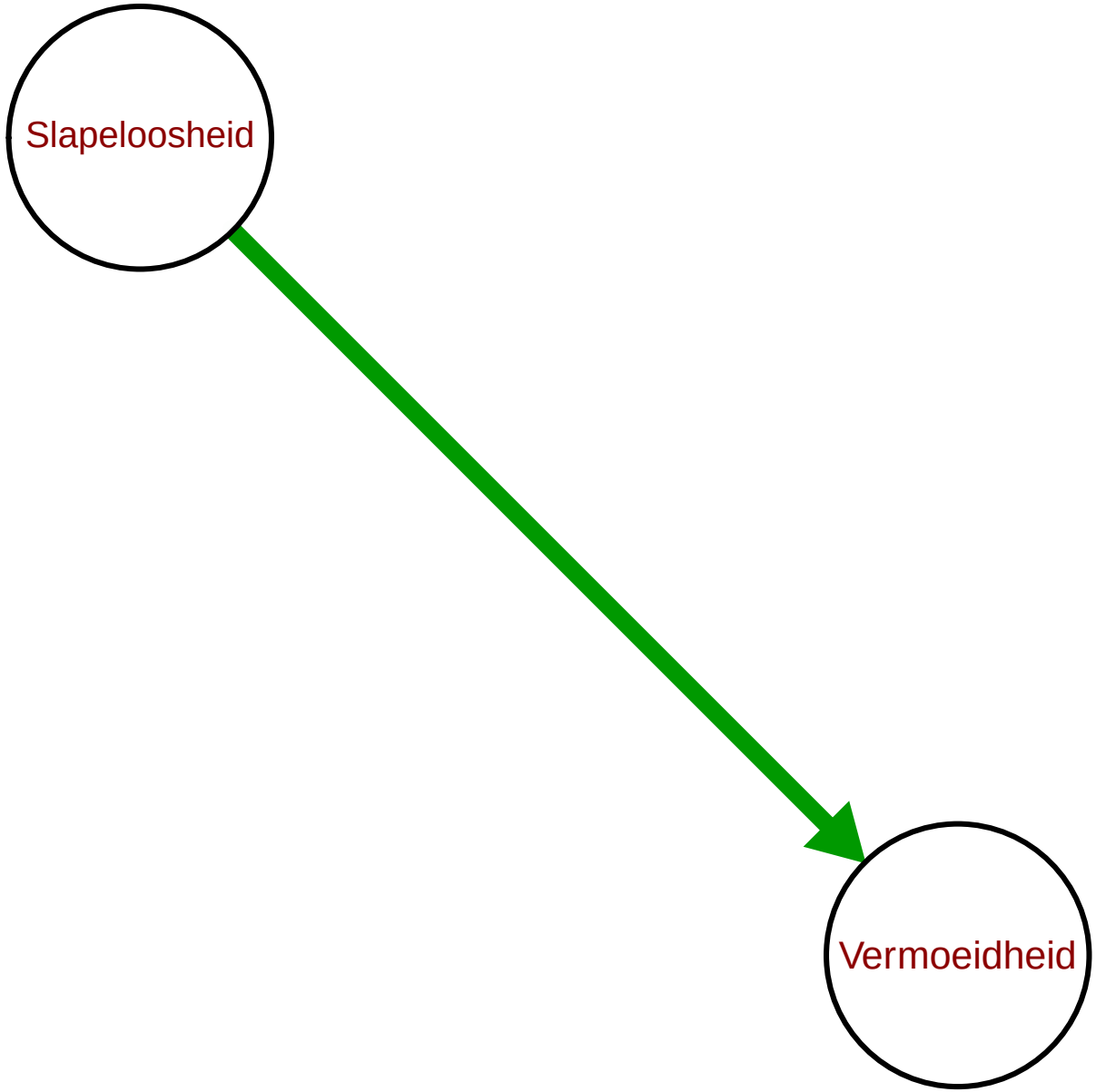
Slapeloosheid hang samen met vermoeidheid:



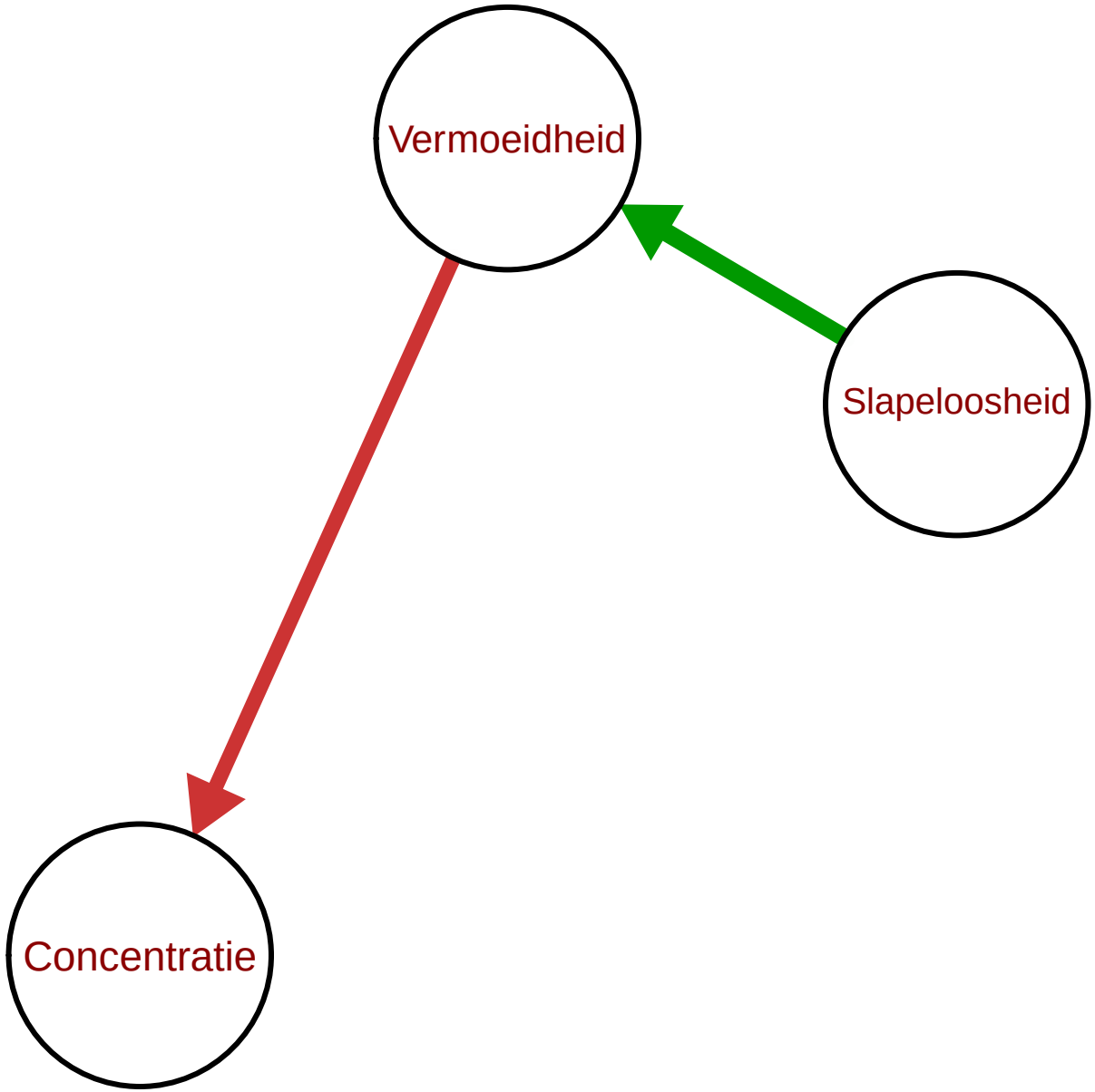
Concentratievermogen hangt negatief samen met beiden:



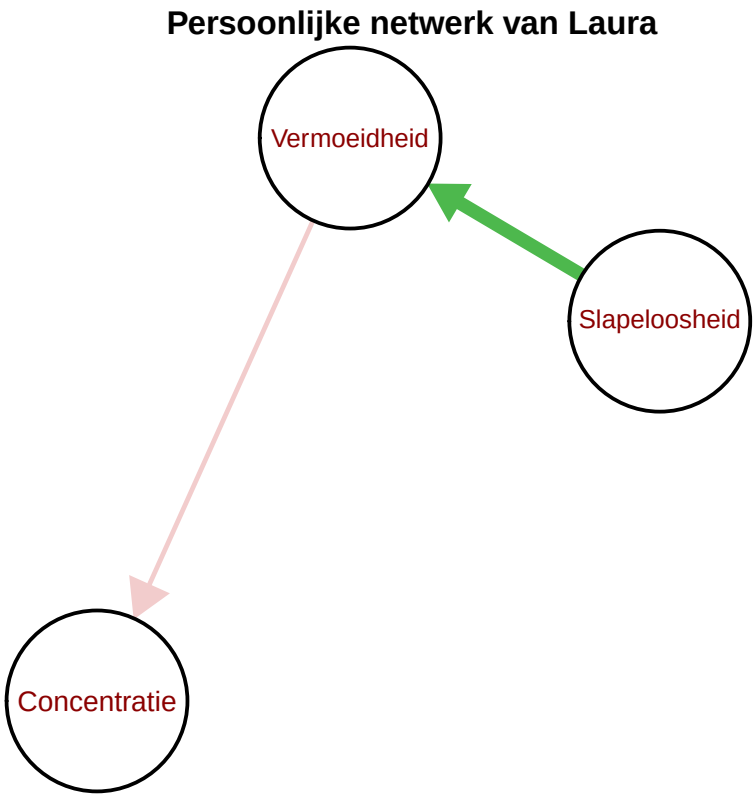
Slapeloosheid vergroot vermoeidheid:

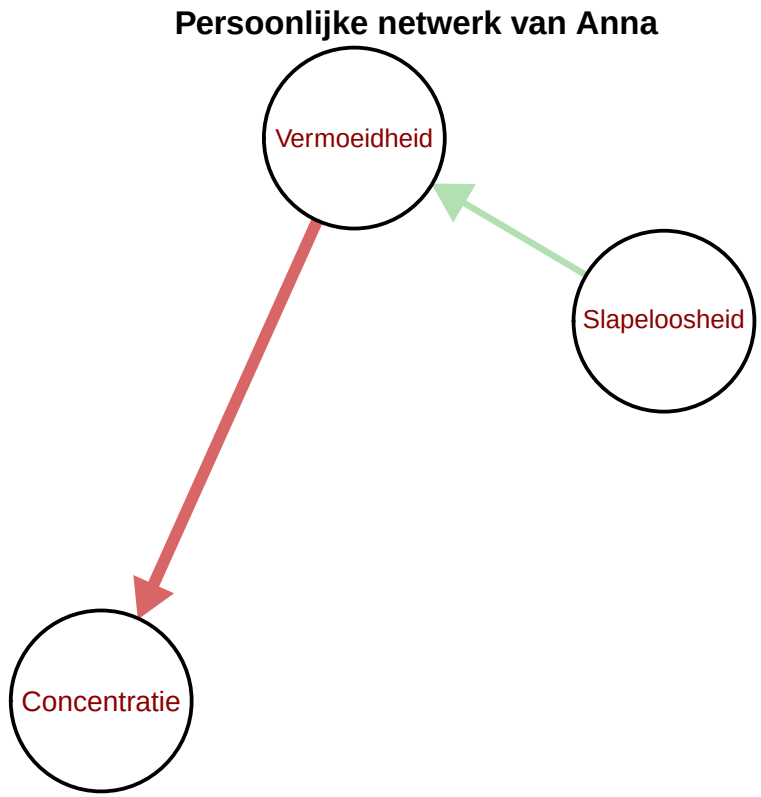


Vermoeidheid verminderd de concentratie:



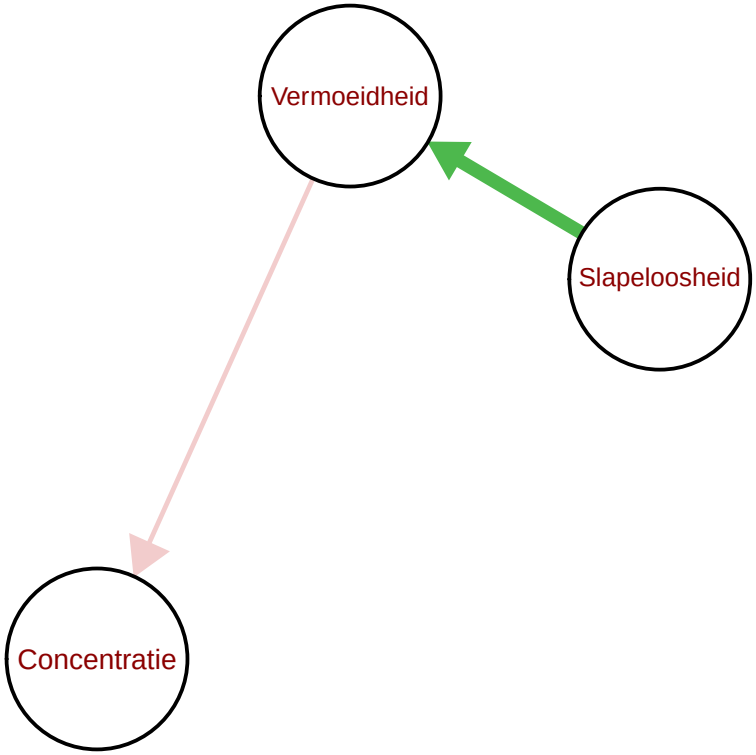
Bij Laura is de link slapeloosheid leidt tot moeheid veel sterker dan bij Anna:



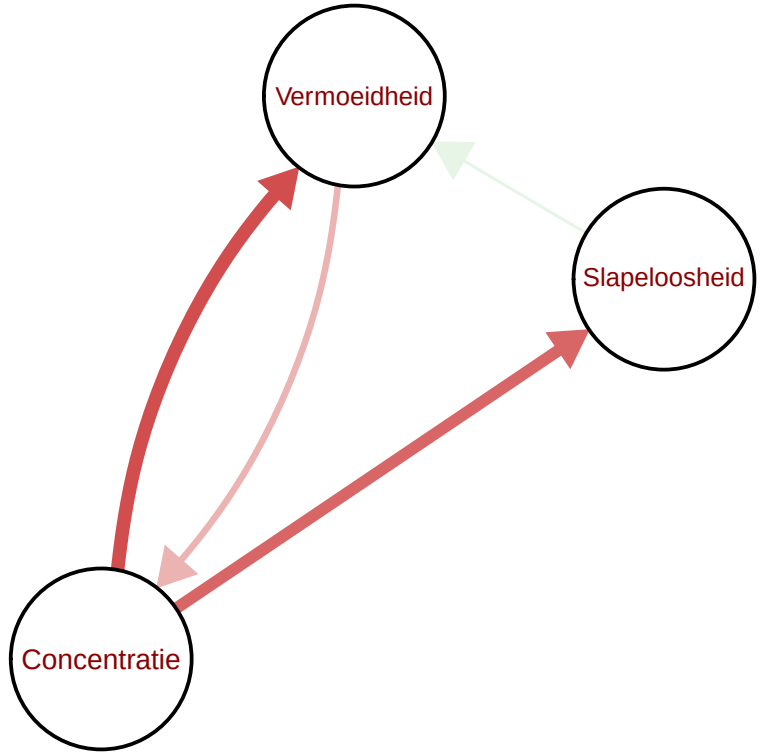


Bij Rogier spelen concentratieproblemen een veel belangrijkere rol dan bij Laura:

Persoonlijke netwerk van Laura



Persoonlijke netwerk van Rogier



Wat kunnen we met netwerken doen?

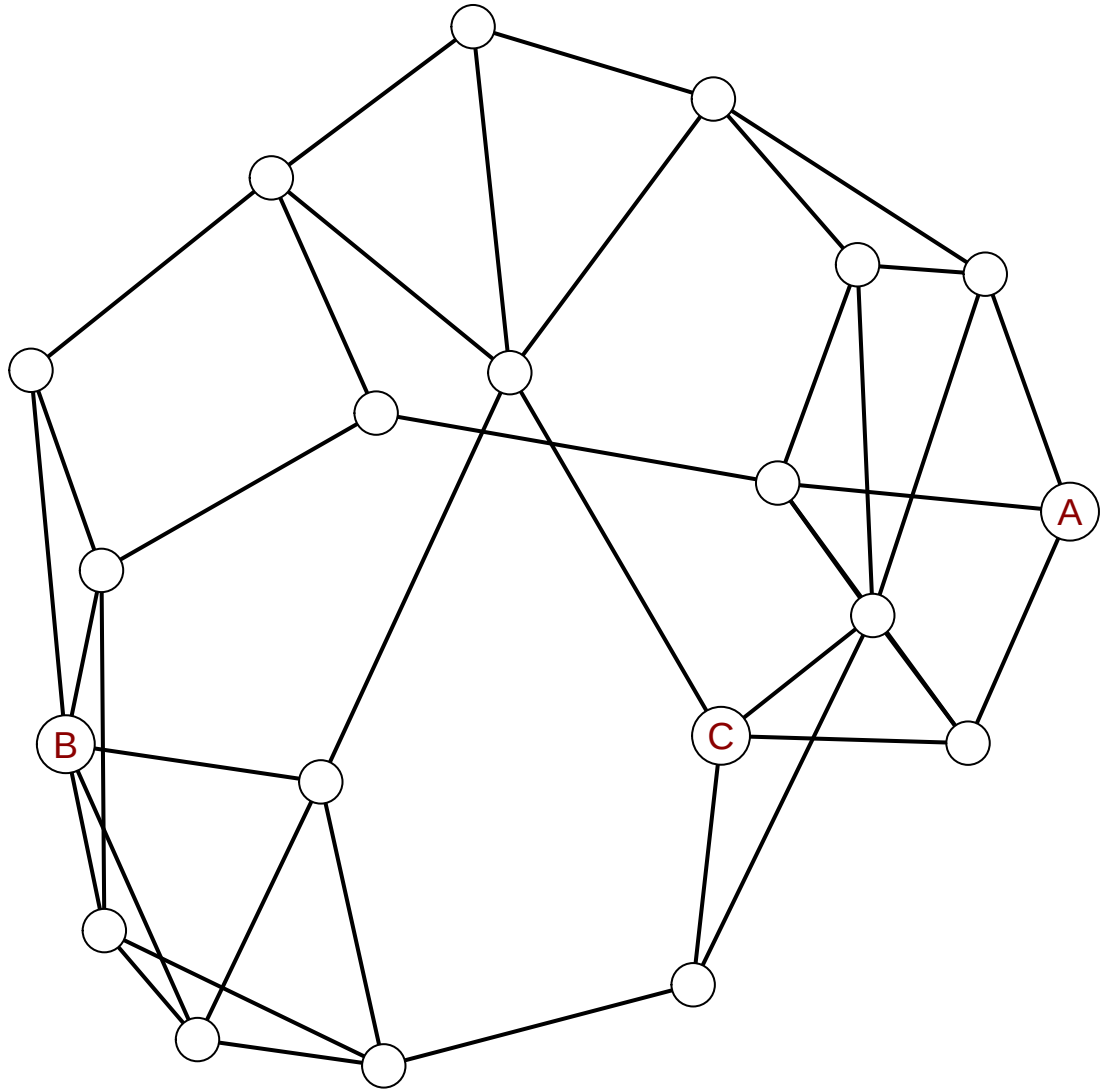
Wat kunnen we met netwerken doen?

Behalve dat netwerken een inzichtelijk beeld geven van de structuur van psychopathologie kunnen we ook met netwerken kijken naar concepten als:

- Afstand
  - Hoe snel kan één symptoom een ander symptoom beënvloeden?
- Centraliteit
  - Welke symptomen zijn het belangrijkst?
- verbondenheid
  - In hoeverre zijn symptomen met elkaar verbonden?

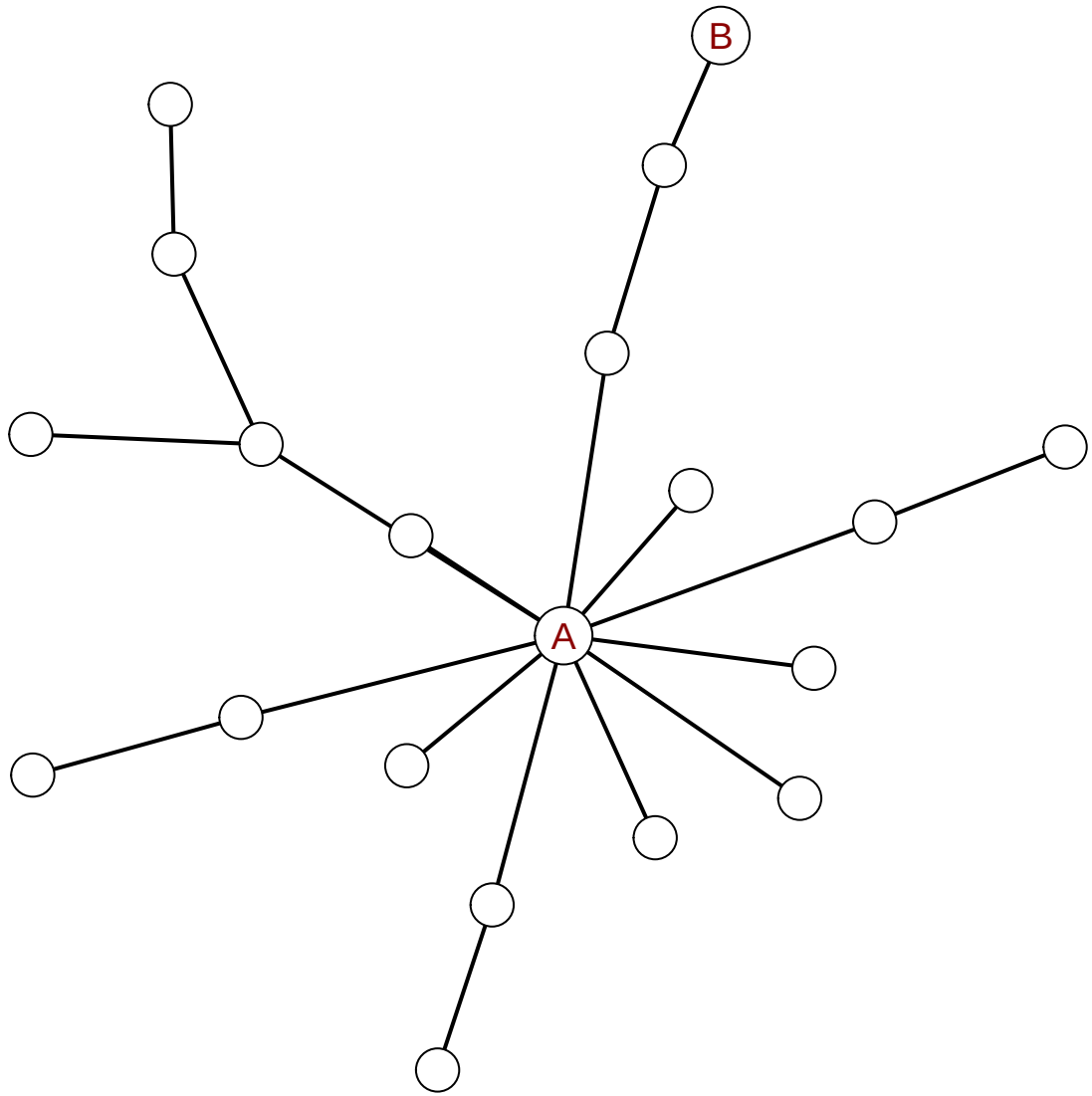
Afstand

Knoop A staat veel verder van knoop B dan van knoop C:

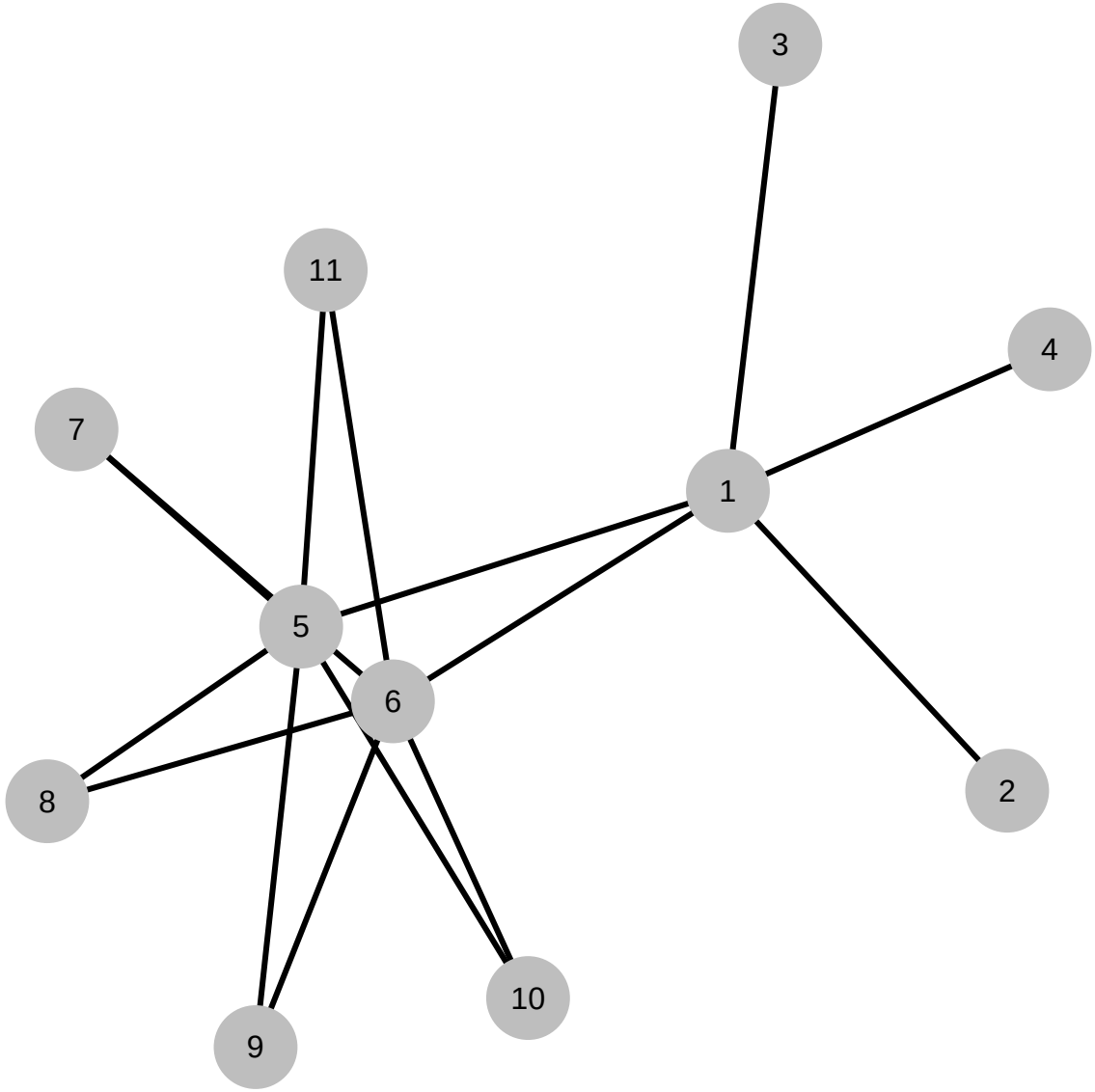


Centraliteit

Knoop A is veel invloedrijker dan knoop B



Wat is de meest centrale knoop?



Centraliteit

De vraag welke knoop het meest centraal/belangrijk/invloedrijk is kan op meerdere manieren worden beantwoord:

Centraliteit

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- Een knoop is centraal als deze *veel verbindingen heeft*

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- Een knoop is centraal als deze *veel verbindingen heeft*
  - Degree

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  - Closeness

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  - Closeness
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  - Betweenness

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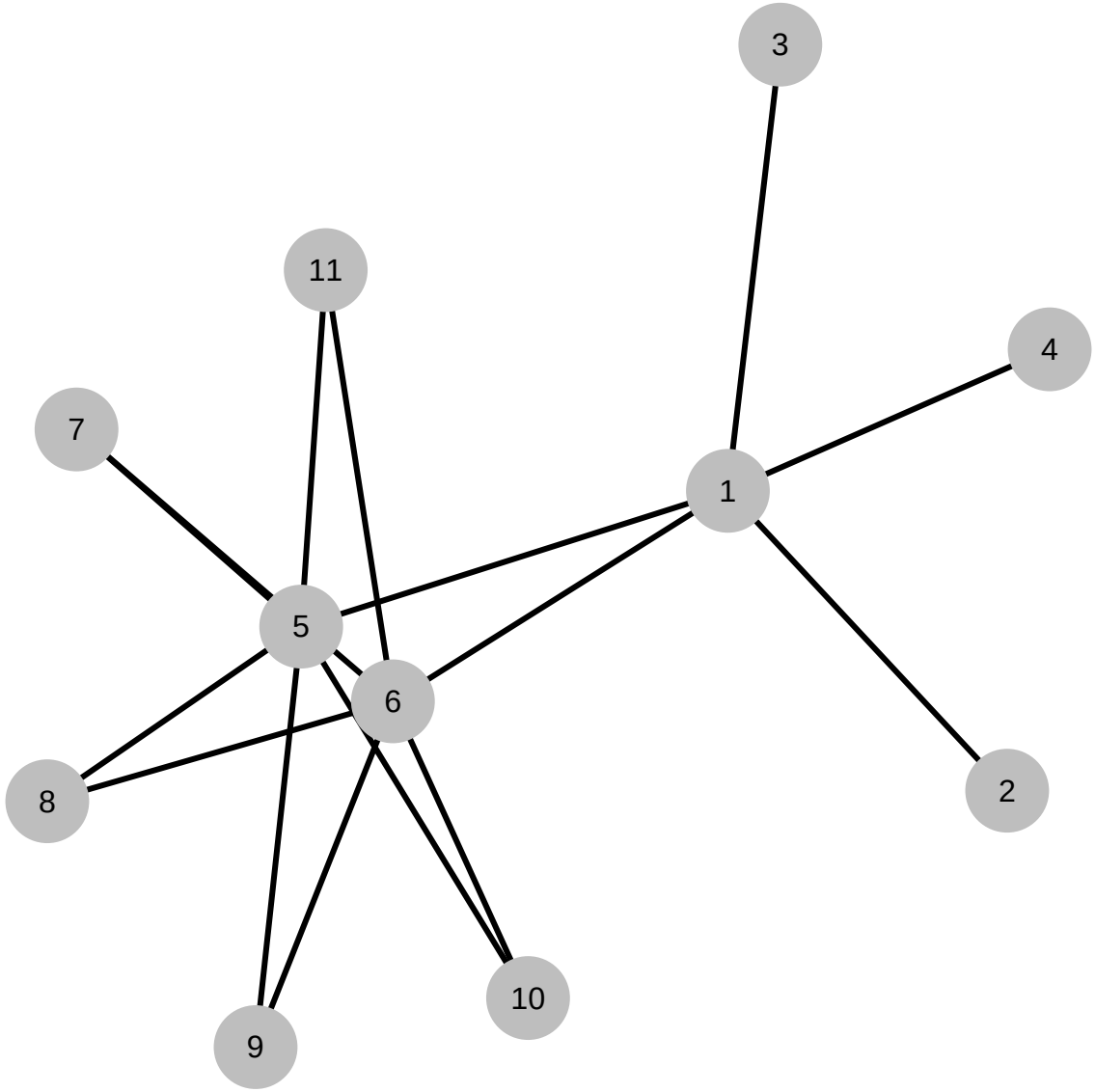

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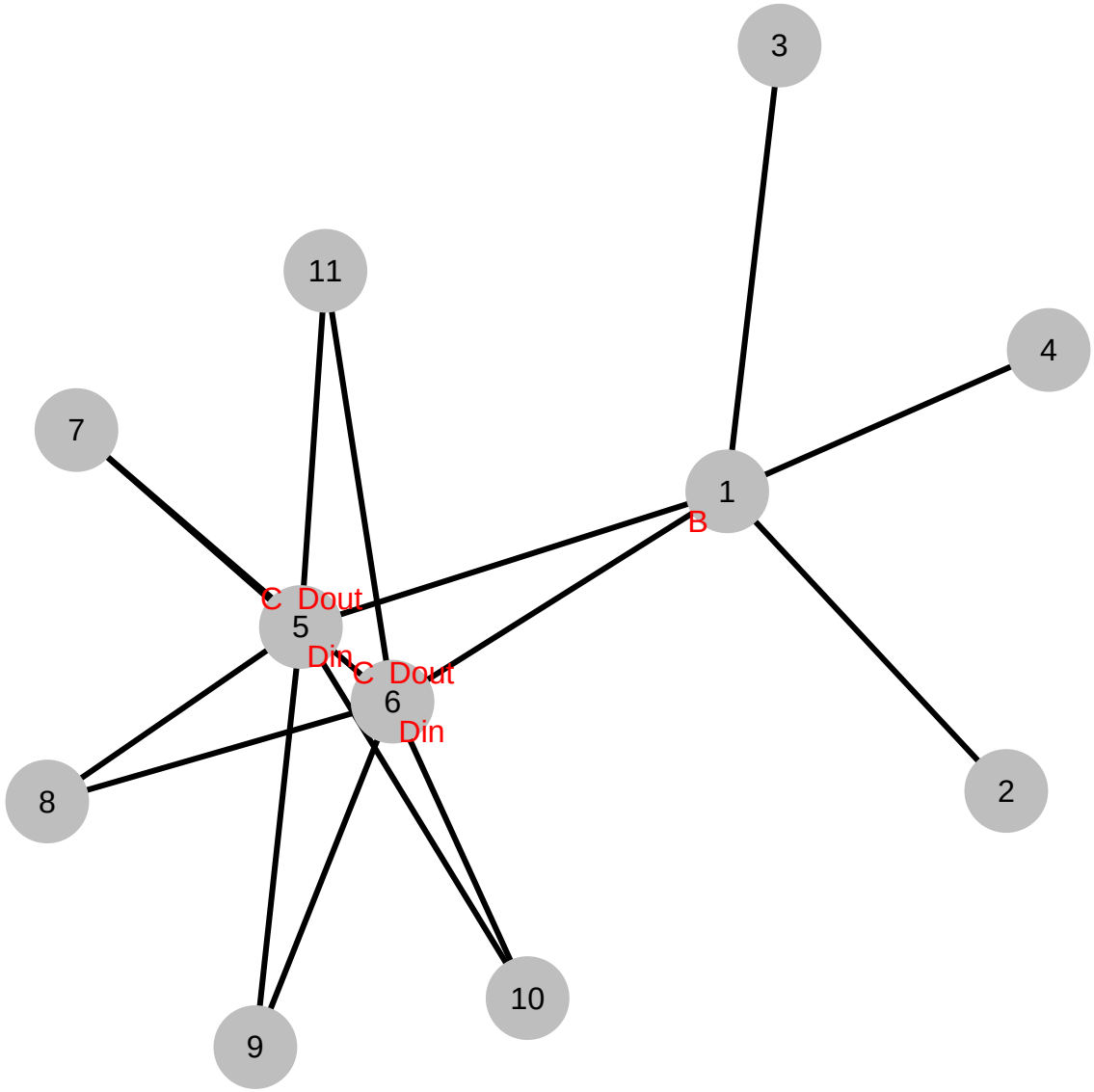
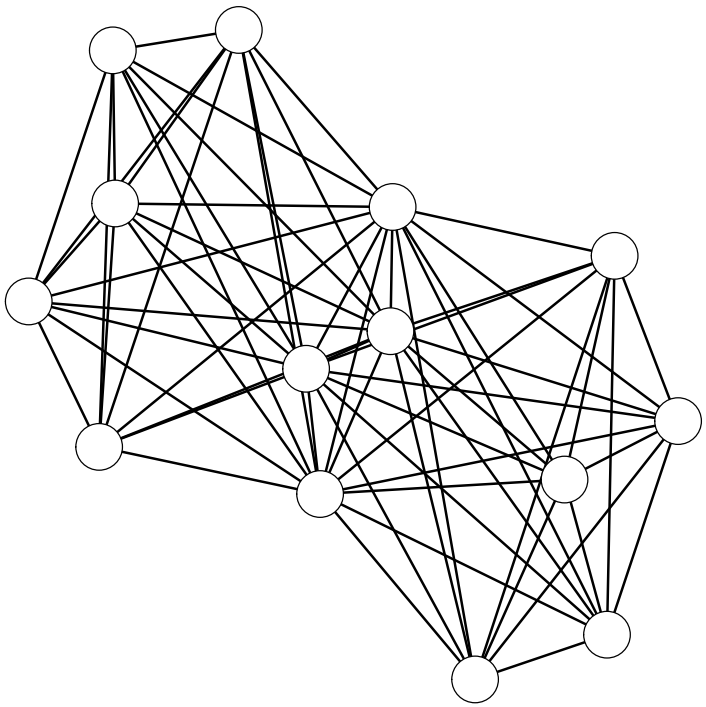
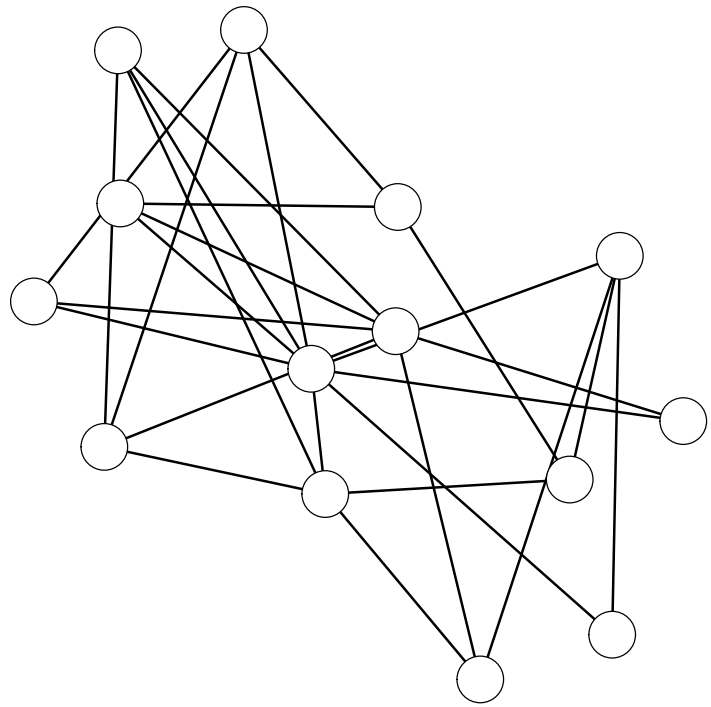


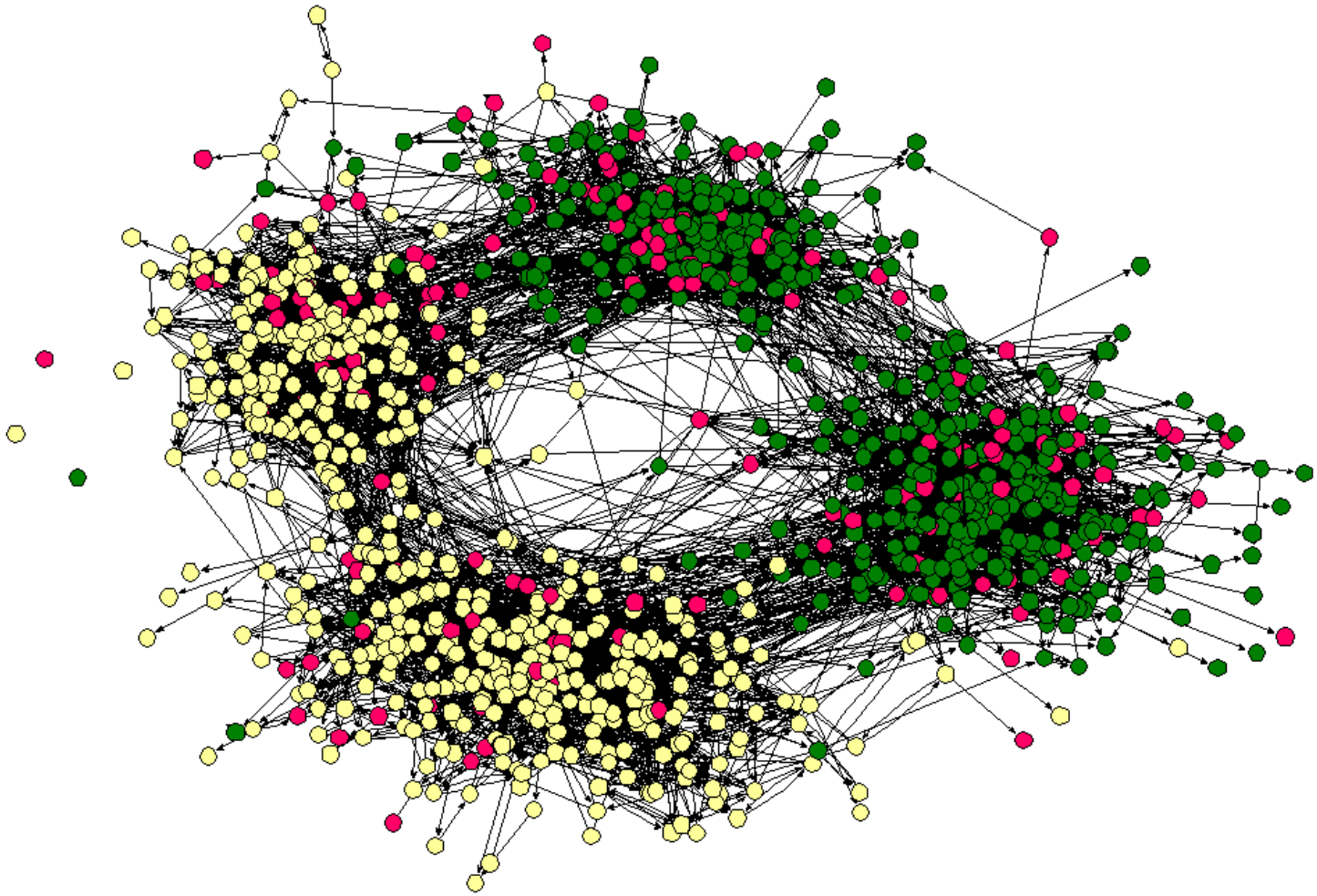
Verbondenheid

Het linker netwerk is veel meer verbonden dan het rechter netwerk:



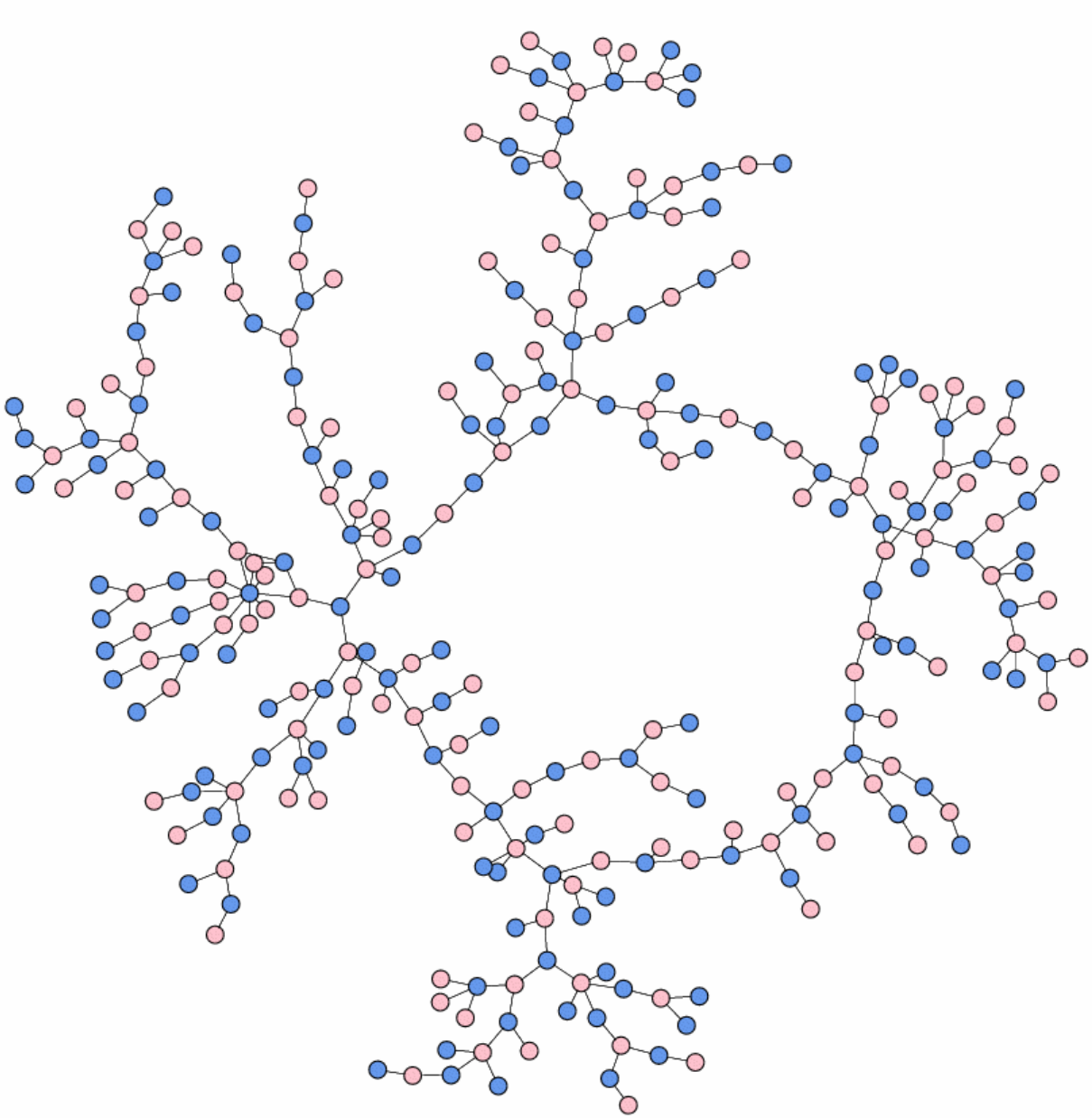


Vriendschap

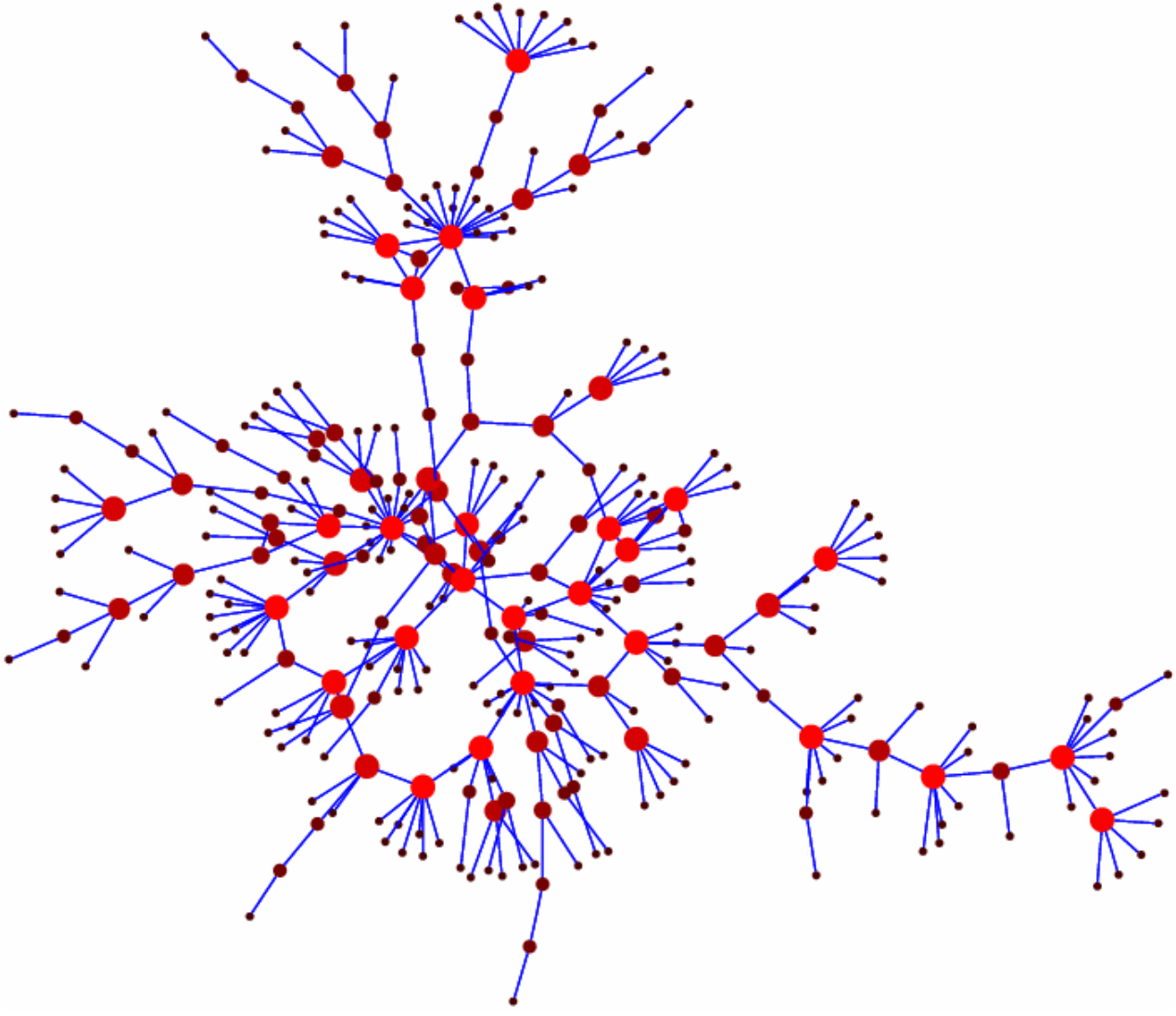



facebook
December 2010

Relaties

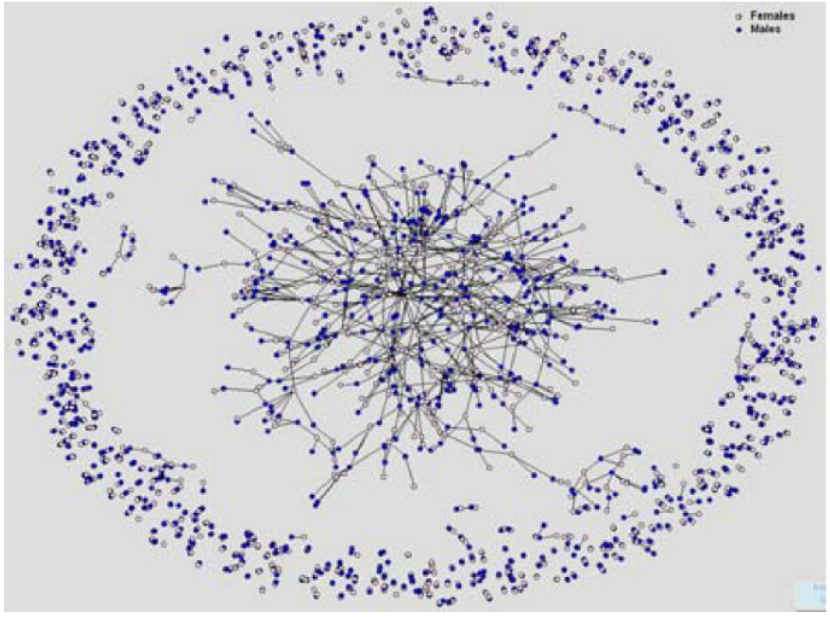


Sexuele contacten

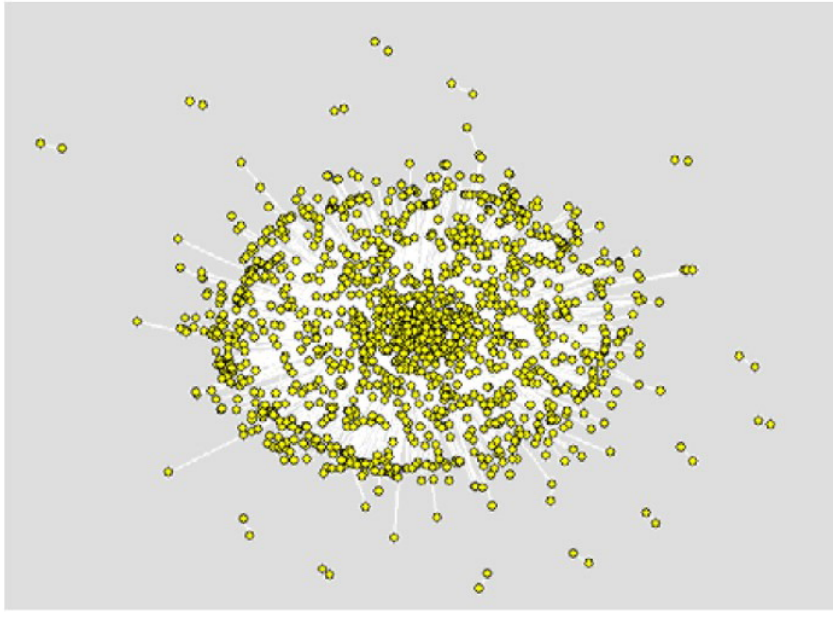


We kunnen ook netwerken simuleren:

(a)



(b)

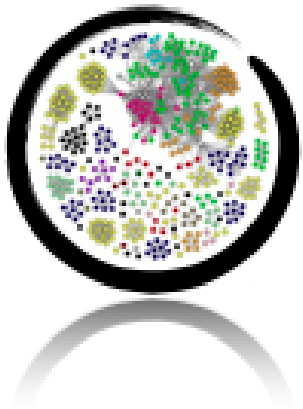


Preferential Attachment

Psychopathologie als een virus...

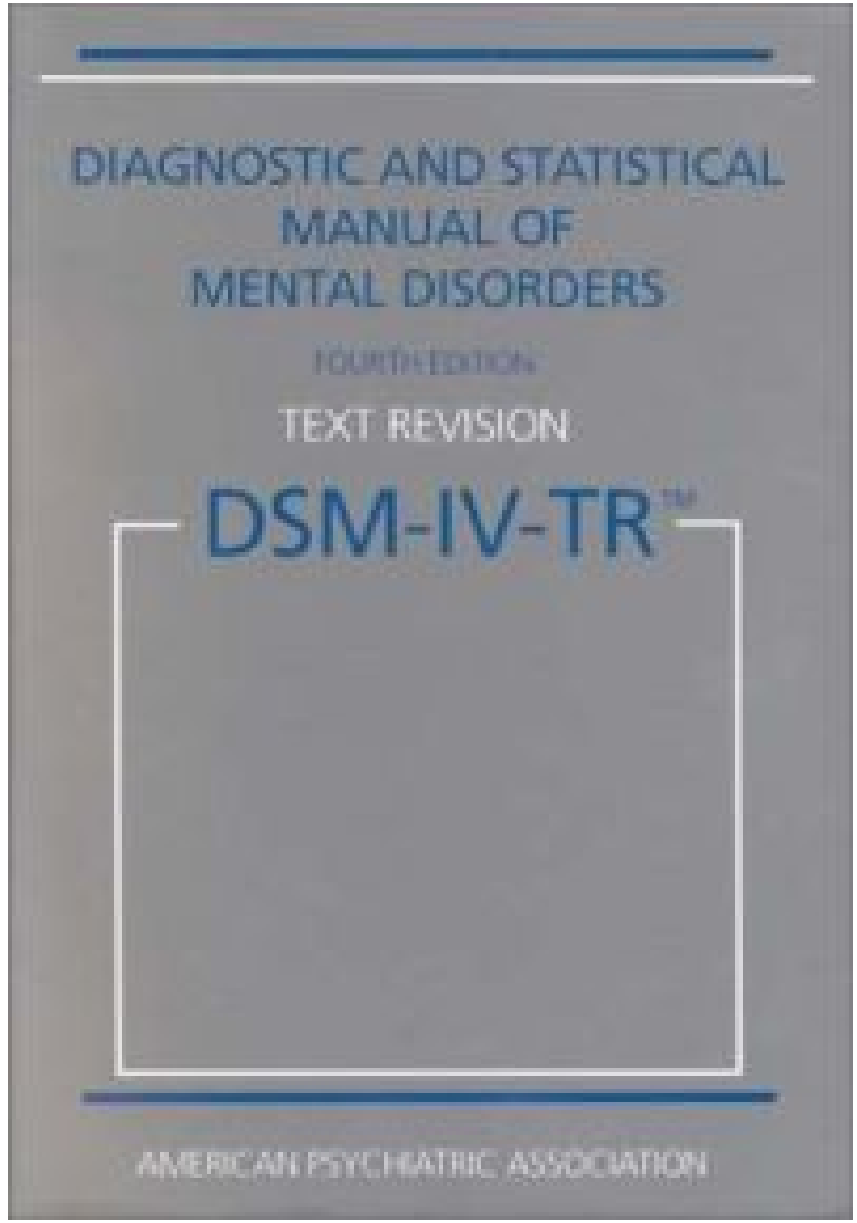
Hoe doen we dit?

The Psych Systems Project



http://www.psychosystems.org/

Theoretisch



Comorbidity

Generalized Anxiety:

- Chronic Anxiety
- Anxiety about more than one event
- Irritability
- No control of anxiety
- Muscle tension
- Sleep Disturbances
- Concentration problems
- Restlessness
- Fatigue

Major Depression:

- Depressed mood
- Loss of interest in pleasurable things
- Weight problems
- Self-reproach
- (thoughts of) suicide
- Sleep disturbances
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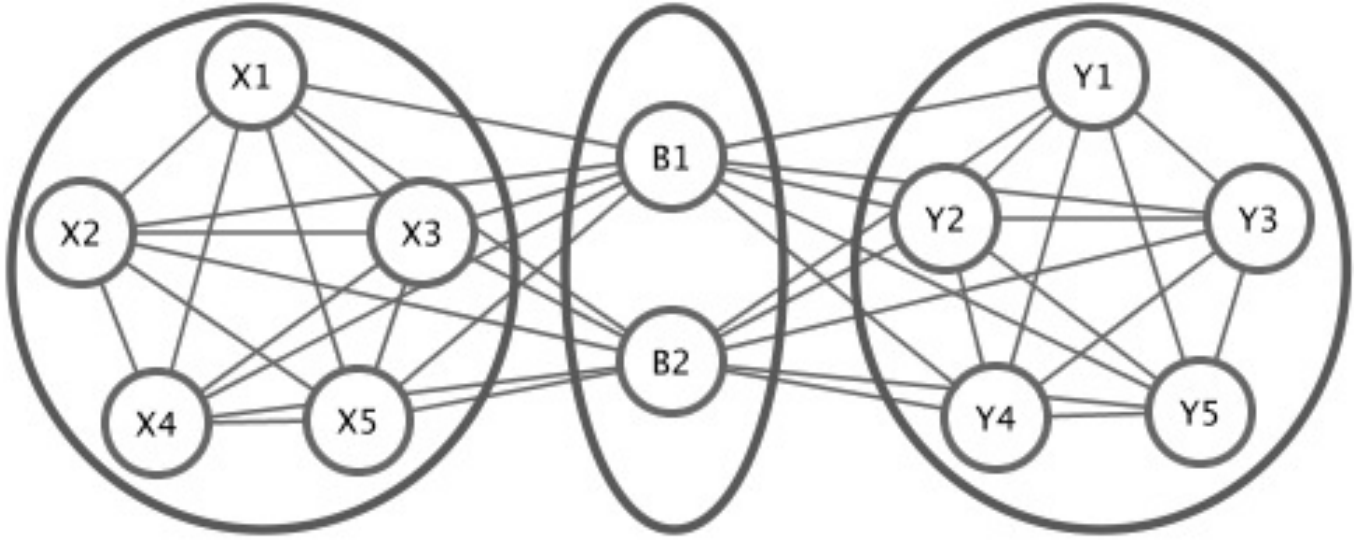
X1
X2
X3
X4
X5
B1
B2
Y1
Y2
Y3
Y4
Y5
Disorder A
Bridge symptoms
Disorder B

BEHAVIORAL AND BRAIN SCIENCES (2010) **33**, 137–193
doi:10.1017/S0140525X09991567

Comorbidity: A network perspective

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Denny Borsboom
Department of Psychology, University of Amsterdam, 1018 WB Amsterdam, The Netherlands
D.Borsboom@uva.nl
http://sites.google.com/site/borsboomdenny/dennyborsboom

Abstract: The pivotal problem of comorbidity research lies in the psychometric foundation it rests on, that is, *latent variable theory*, in which a mental disorder is viewed as a latent variable that *causes* a constellation of symptoms. From this perspective, comorbidity is a (bi)directional relationship between multiple latent variables. We argue that such a latent variable perspective encounters serious problems in the study of comorbidity, and offer a radically different conceptualization in terms of a *network approach*, where comorbidity is hypothesized to arise from direct relations between symptoms of multiple disorders. We propose a method to

OPEN ACCESS Freely available online

PLoS one

The Small World of Psychopathology

Denny Borsboom*, Angélique O. J. Cramer, Verena D. Schmittmann, Sacha Epskamp, Lourens J. Waldorp

Department of Psychology, University of Amsterdam, Amsterdam, The Netherlands

Abstract

Background: Mental disorders are highly comorbid: people having one disorder are likely to have another as well. We explain empirical comorbidity patterns based on a network model of psychiatric symptoms, derived from an analysis of symptom overlap in the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV).

Principal Findings: We show that a) half of the symptoms in the DSM-IV network are connected, b) the architecture of these connections conforms to a small world structure, featuring a high degree of clustering but a short average path length, and c) distances between disorders in this structure predict empirical comorbidity rates. Network simulations of Major Depressive Episode and Generalized Anxiety Disorder show that the model faithfully reproduces empirical population statistics for these disorders.

Conclusions: In the network model, mental disorders are inherently complex. This explains the limited successes of genetic, neuroscientific, and etiological approaches to unravel their causes. We outline a psychosystems approach to investigate the structure and dynamics of mental disorders.

Citation: Borsboom D, Cramer AOJ, Schmittmann VD, Epskamp S, Waldorp LJ (2011) The Small World of Psychopathology. PLoS ONE 6(11): e27407. doi:10.1371/journal.pone.0027407

Editor: Rochelle E. Tractenberg, Georgetown University Medical Center, United States of America

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Competing Interests: The authors have declared that no competing interests exist.

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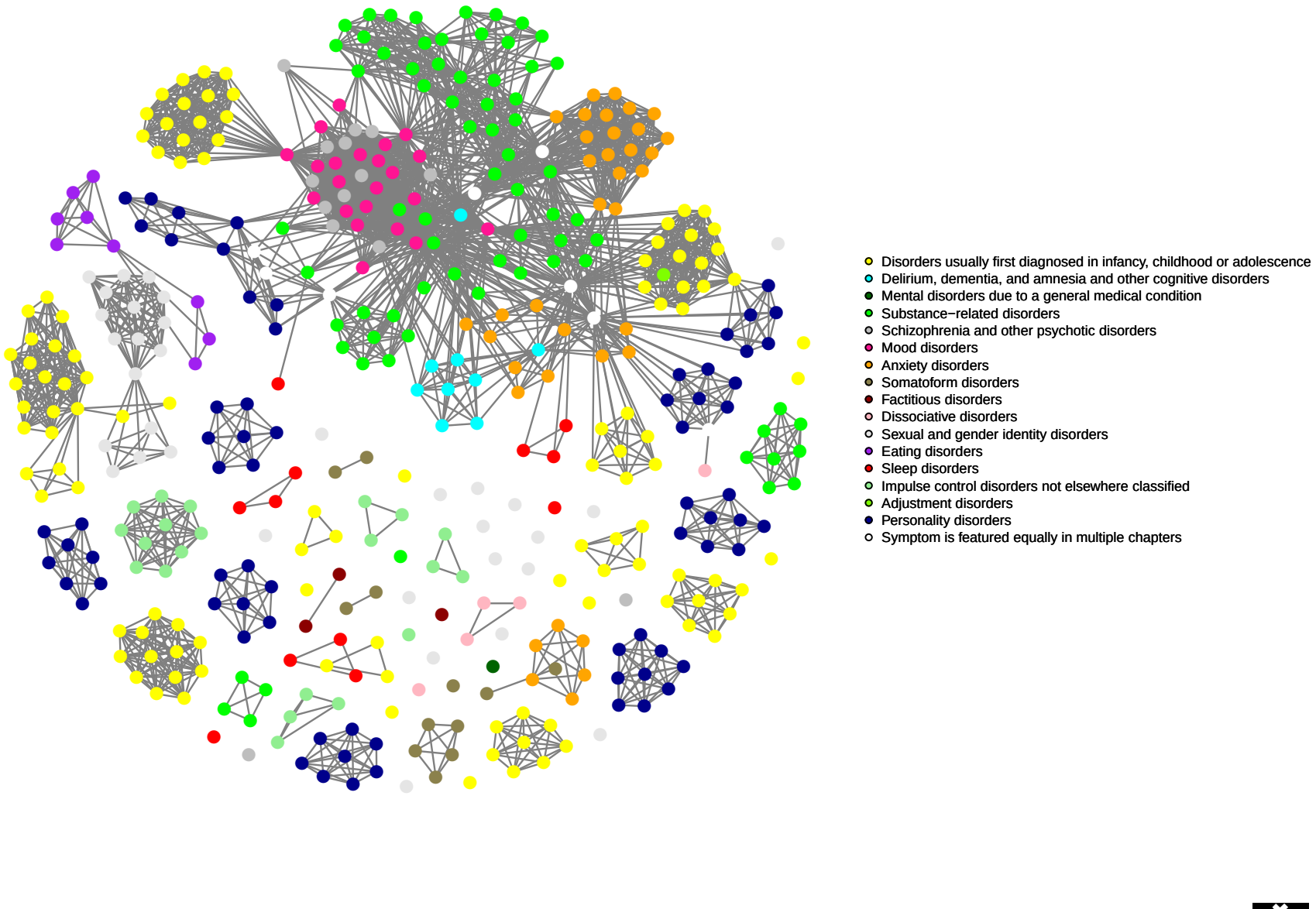
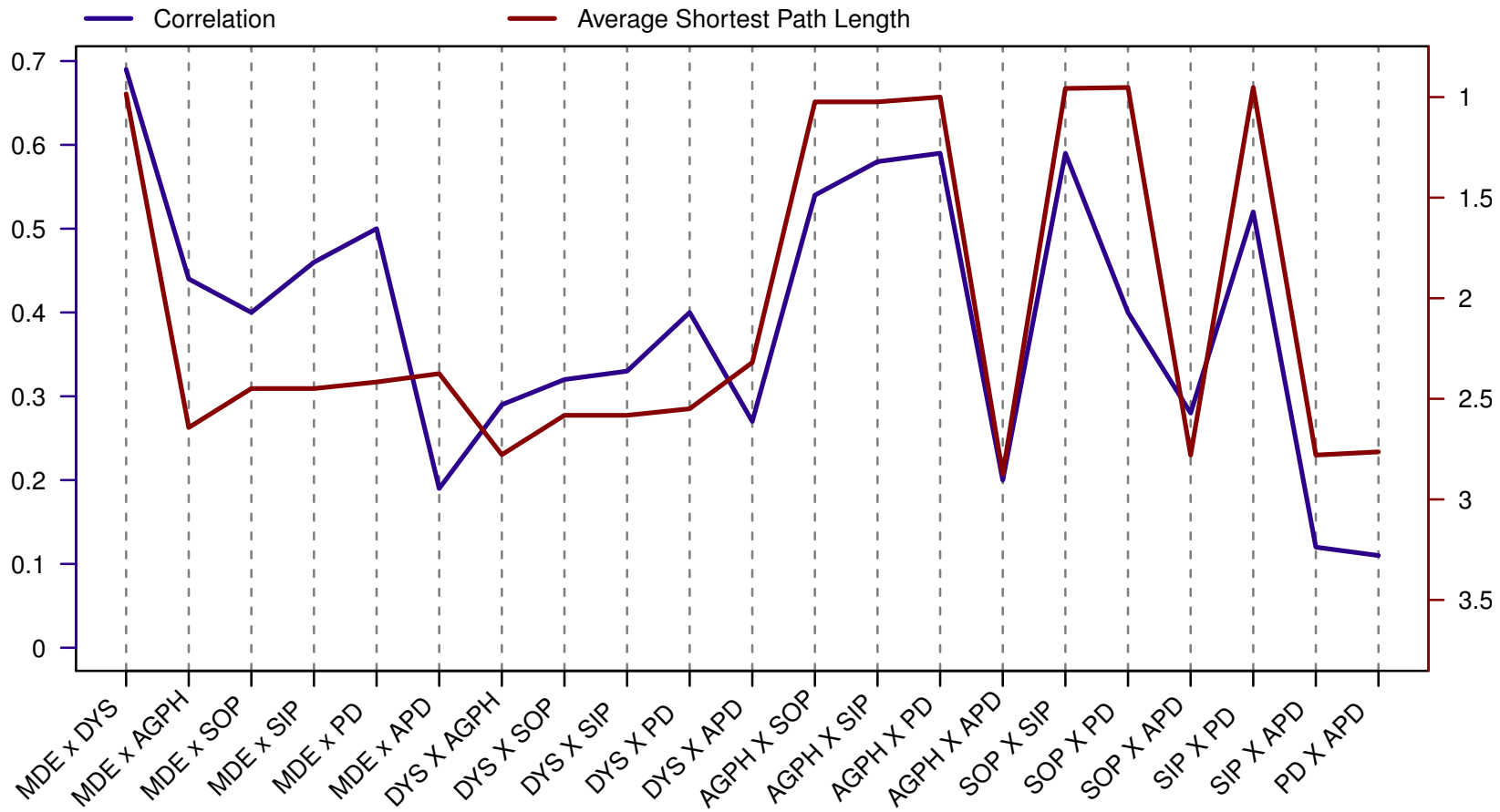

Disorders usually first diagnosed in infancy, childhood or adolescence
Delirium, dementia, and amnesia and other cognitive disorders
Mental disorders due to a general medical condition
Substance−related disorders
Schizophrenia and other psychotic disorders
Mood disorders
Anxiety disorders
Somatoform disorders
Factitious disorders
Dissociative disorders
Sexual and gender identity disorders
Eating disorders
Sleep disorders
Impulse control disorders not elsewhere classified
Adjustment disorders
Personality disorders
Symptom is featured equally in multiple chapters


Correlation
Average Shortest Path Length
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
1
1.5
2
2.5
3
3.5
MDE x DYS
MDE x AGPH
MDE x SOP
MDE x SIP
MDE x PD
MDE x APD
DYS X AGPH
DYS X SOP
DYS X SIP
DYS X PD
DYS X APD
AGPH X SOP
AGPH X SIP
AGPH X PD
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SOP X SIP
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SIP X PD
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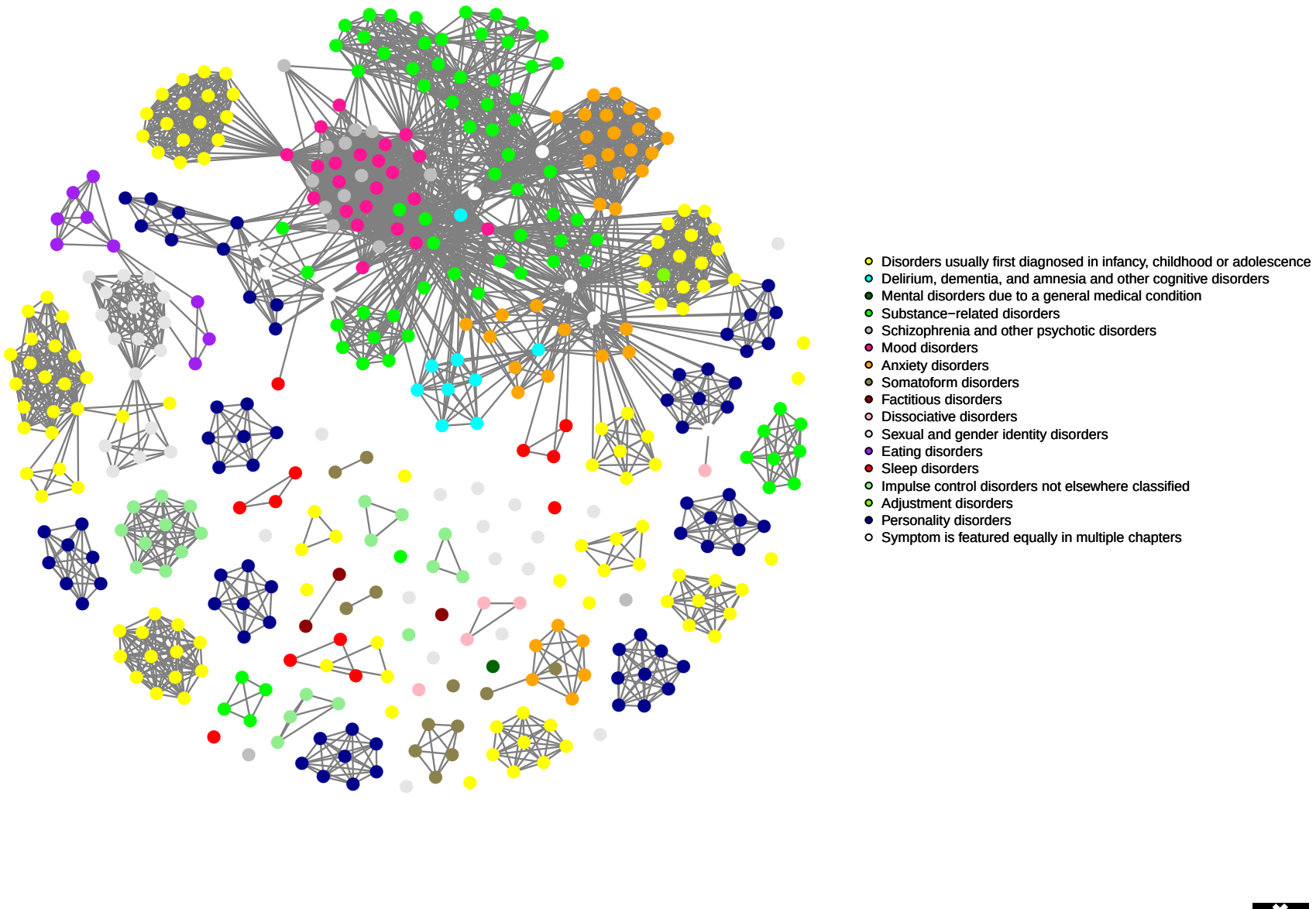
PD X APD


Disorders usually first diagnosed in infancy, childhood or adolescence
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Factitious disorders
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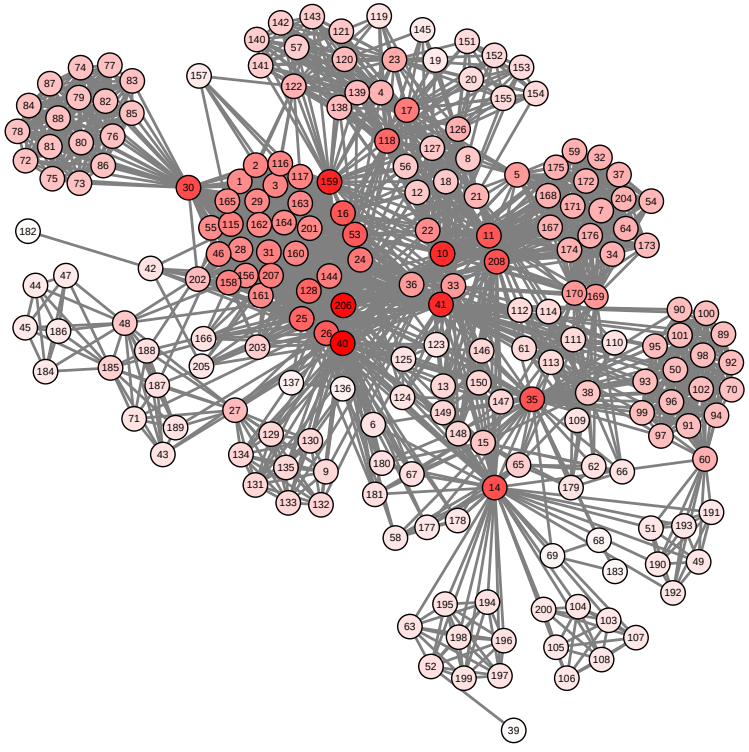
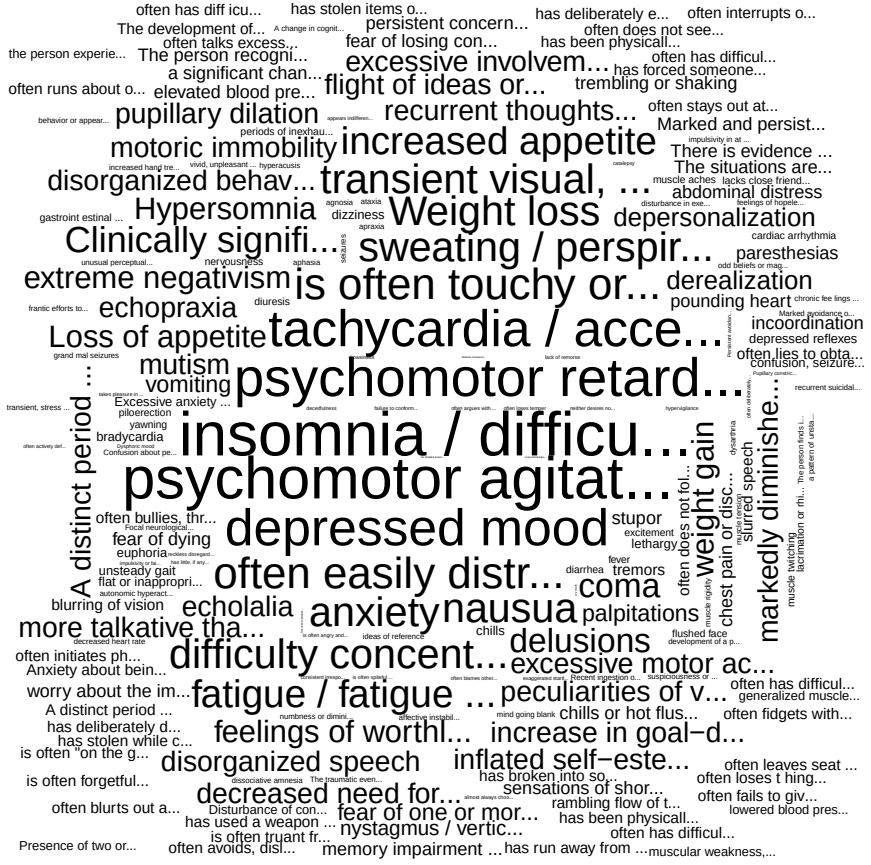
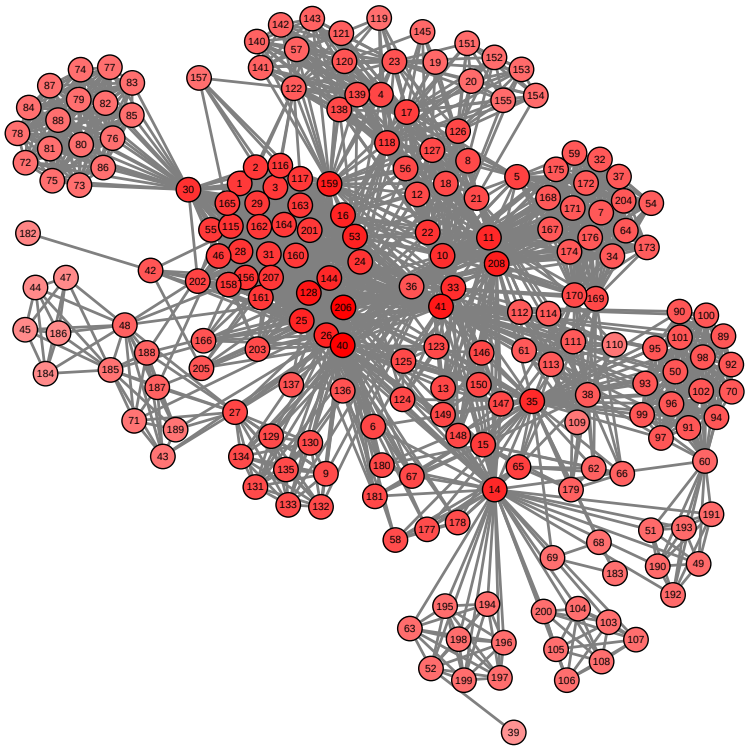
Sexual and gender identity disorders
Eating disorders
Sleep disorders
Impulse control disorders not elsewhere classified
Adjustment disorders
Personality disorders
Symptom is featured equally in multiple chapters

Degree



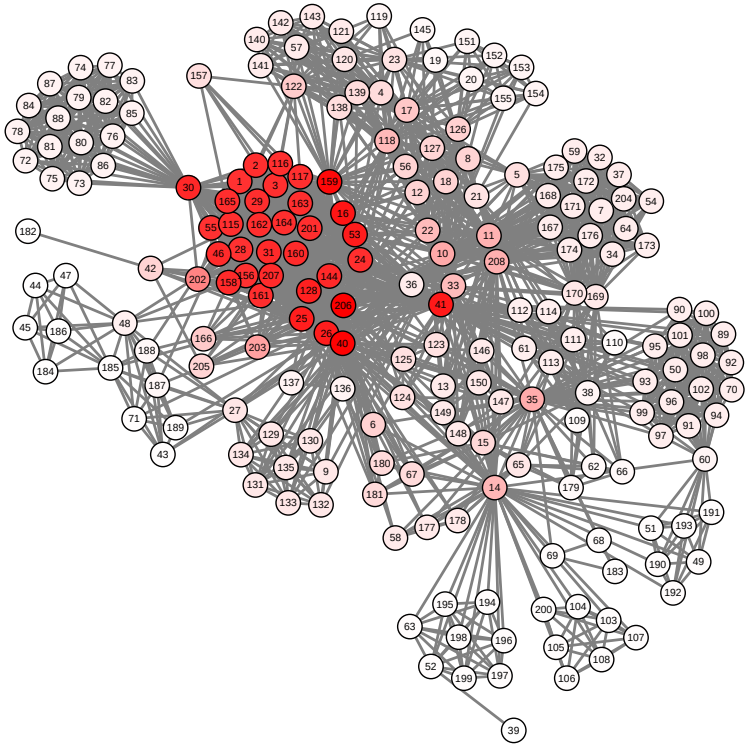

often has diff icu...
has stolen items o...
has deliberately e...
often interrupts o...
The development of...
persistent concern...
often does not see...
often talks excess...
fear of losing con...
has been physicall...
the person experie...
The person recogni...
excessive involvem...
often has difficul...
a significant chan...
has forced someone...
often runs about o...
elevated blood pre...
flight of ideas or...
trembling or shaking
pupillary dilation
recurrent thoughts...
often stays out at...
Marked and persist...
periods of inexhau...
motoric immobility
increased appetite
There is evidence ...
The situations are...
disorganized behav...
transient visual, ...
muscle aches
lacks close friend...
abdominal distress
Hypersomnia
Weight loss
depersonalization
gastroint estinal ...
dizziness
Clinically signifi...
sweating / perspir...
paresthesias
cardiac arrhythmia
nervousness
extreme negativism
is often touchy or...
derealization
pounding heart
echopraxia
tachycardia / acce...
incoordination
depressed reflexes
Loss of appetite
often lies to obta...
confusion, seizure...
mutism
vomiting
psychomotor retard...
recurrent suicidal...
Excessive anxiety ...
piloerection
yawning
bradycardia
insomnia / difficu...
A distinct period ...
psychomotor agitat...
weight gain
slurred speech
markedly diminishe...
often bullies, thr...
depressed mood
stupor
excitement
lethargy
fear of dying
euphoria
often easily distr...
diarrhea
tremors
coma
unsteady gait
flat or inappropri...
blurring of vision
echolalia
anxiety
nausua
palpitations
more talkative tha...
chills
delusions
chest pain or disc...
difficulty concent...
excessive motor ac...
often initiates ph...
Anxiety about bein...
worry about the im...
fatigue / fatigue ...
peculiarities of v...
often has difficul...
generalized muscle...
A distinct period ...
has deliberately d...
has stolen while c...
feelings of worthl...
increase in goal−d...
is often "on the g...
disorganized speech
inflated self−este...
often leaves seat ...
is often forgetful...
has broken into so...
often loses t hing...
decreased need for...
sensations of shor...
often fails to giv...
often blurts out a...
Disturbance of con...
fear of one or mor...
rambling flow of t...
lowered blood pres...
has used a weapon ...
nystagmus / vertic...
has been physicall...
is often truant fr...
often has difficul...
Presence of two or...
often avoids, disl...
memory impairment ...
has run away from ...
muscular weakness,...

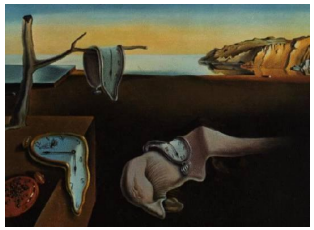
Closeness



echopraxia
extreme negativism
palpitations
pupillary dilation
excitement
Hypersomnia
vomiting
yawning
ataxia
delusions
Weight loss
diarrhea
stupor
mutism
difficulty concent...
chills
weight gain
nausua
fever
tremors
depressed mood
anxiety
increased appetite
insomnia / difficu...
psychomotor agitat...
psychomotor retard...
transient visual, ...
fatigue / fatigue ...
sweating / perspir...
is often touchy or...
often easily distr...
disorganized speech
unexpected travel ...
incoordination
echolalia
coma
lethargy
tachycardia / acce...
disorganized behav...
muscular weakness,...
feelings of worthl...
flushed face
muscle aches

Eigenvector Centraliteit





Journal of Statistical Software

May 2012, Volume 48, Issue 4. *http://www.jstatsoft.org/*

qgraph: Network Visualizations of Relationships in Psychometric Data

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University of Amsterdam

Angélique O. J. Cramer
University of Amsterdam

Lourens J. Waldorp
University of Amsterdam

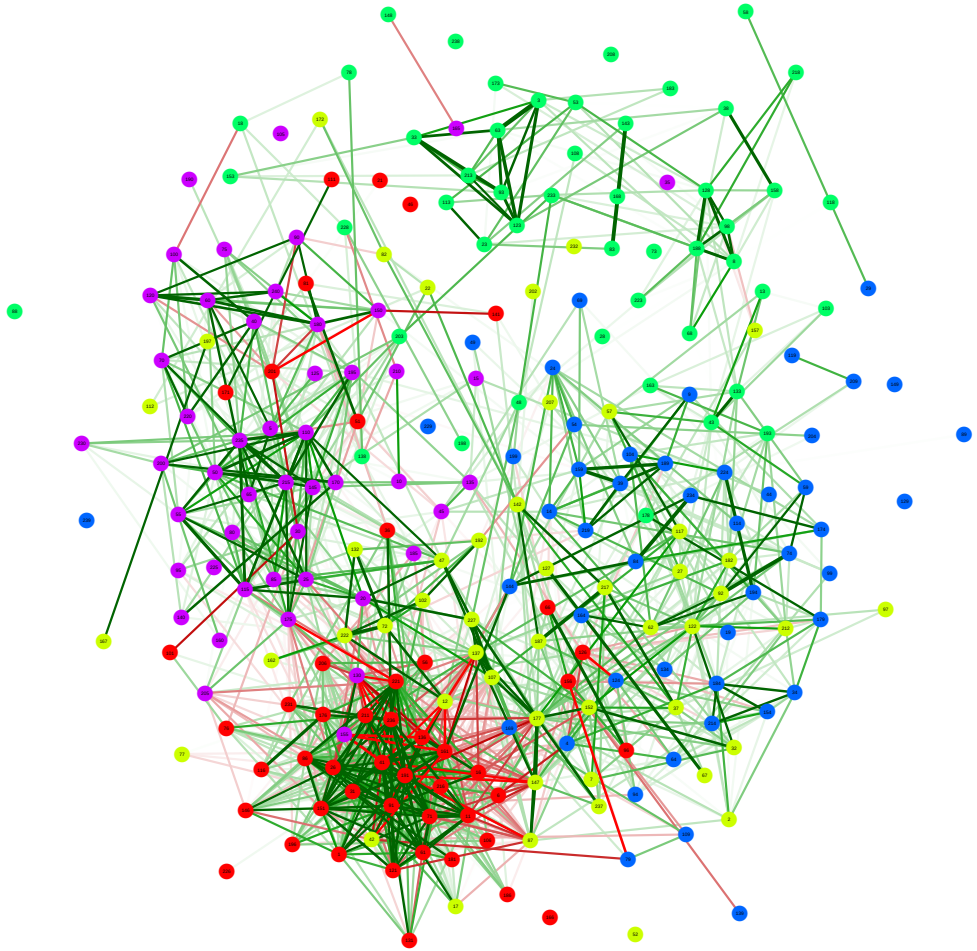
Verena D. Schmittmann
University of Amsterdam

Denny Borsboom
University of Amsterdam

Abstract

We present the **qgraph** package for R, which provides an interface to visualize data through network modeling techniques. For instance, a correlation matrix can be represented as a network in which each variable is a node and each correlation an edge; by

Correlaties



Minimum: 0.25 Cutoff: 0.4 Maximum: 0.77

- Neuroticism
- Extraversion
- Openness
- Agreeableness
- Conscientiousness

European Journal of Personality, *Eur. J. Pers.* **26**: 414–431 (2012)
Published online in Wiley Online Library (wileyonlinelibrary.com) **DOI**: 10.1002/per.1866

Dimensions of Normal Personality as Networks in Search of Equilibrium: You Can't Like Parties if You Don't Like People

ANGÉLIQUE O. J. CRAMER[1]*, SOPHIE VAN DER SLUIS[1,2], ARJEN NOORDHOF[1], MARIEKE WICHERS[3], NICOLE GESCHWIND[3,4], STEVEN H. AGGEN[5,6], KENNETH S. KENDLER[5,6] and DENNY BORSBOOM[1]

[1]*Department of Psychology, University of Amsterdam, The Netherlands*
[2]*Complex Trait Genetics, Department of Functional Genomics and Department Clinical Genetics, Center for Neurogenomics and Cognitive Research (CNCR), FALW-VUA, Neuroscience Campus Amsterdam, VU University Medical Center (VUmc), The Netherlands*
[3]*European Graduate School for Neuroscience, SEARCH, Department of Psychiatry and Psychology, Maastricht University Medical Centre, The Netherlands*
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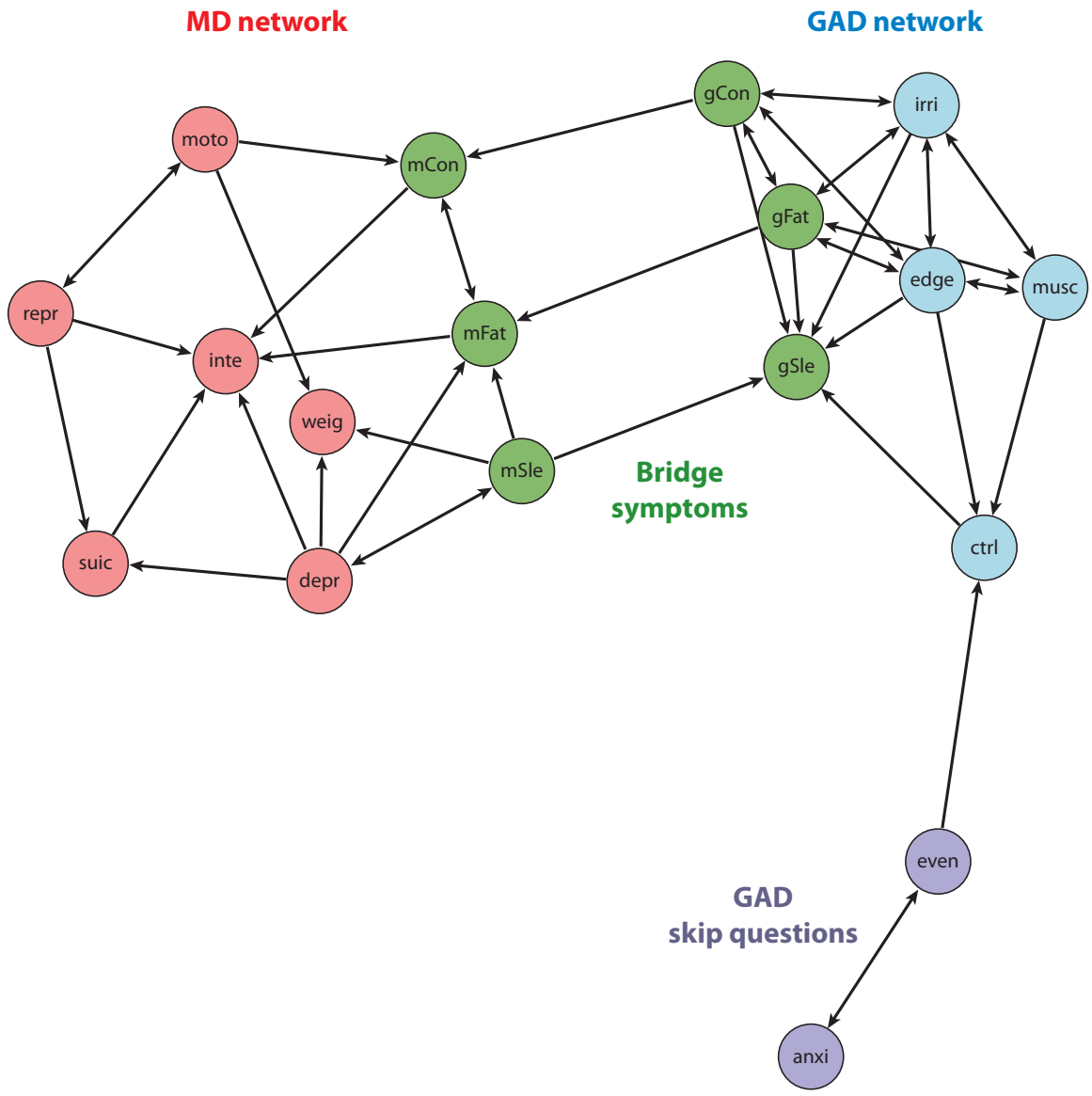
[5]*Virginia Institute for Psychiatric and Behavioral Genetics, USA*
[6]*Department of Psychiatry, Virginia Commonwealth University, USA*

Abstract: In one currently dominant view on personality, personality dimensions (e.g. extraversion) are causes of human behaviour, and personality inventory items (e.g. 'I like to go to parties' and 'I like people') are measurements of these dimensions. In this view, responses to extraversion items correlate because they measure the same latent dimension. In this paper, we challenge this way of thinking and offer an alternative perspective on personality as a system of connected affective, cognitive and behavioural components. We hypothesize that these components do not hang together because they measure the same underlying dimension; they do so because they depend on one another directly for causal, homeostatic or logical reasons (e.g. if one does not like people and it is harder to enjoy parties). From this 'network perspective', personality dimensions emerge out of the connectivity structure that exists between the various components of personality. After outlining the network theory, we illustrate how it applies to personality research in four domains: (i) the overall organization of personality components; (ii) the distinction between state and trait; (iii) the genetic architecture of personality; and (iv) the relation between personality and psychopathology.

Key words: normal personality; networks; latent variable models; personality traits

Causaliteit detectie algoritmes



Journal of Statistical Software

MMMMMM YYYY, Volume VV, Issue II. *http://www.jstatsoft.org/*

Causal Inference using Graphical Models with the R Package pcalg

Markus Kalisch
ETH Zurich

Martin Mächler
ETH Zurich

Diego Colombo
ETH Zurich

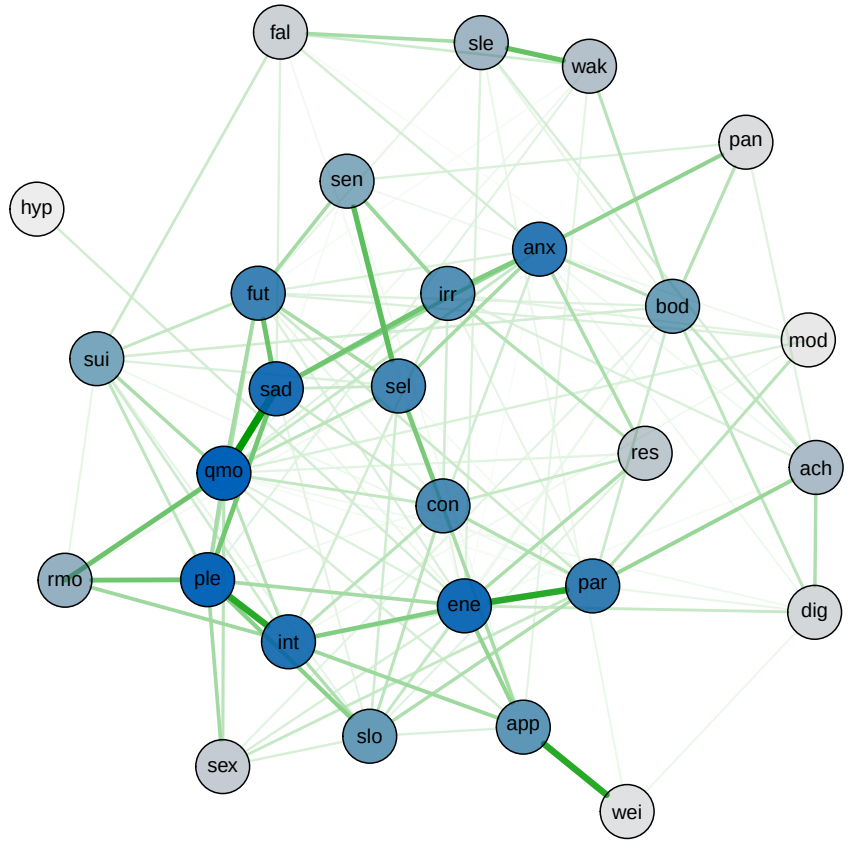
Marloes H. Maathuis
ETH Zurich

Peter Bühlmann
ETH Zurich

Abstract

The **pcalg** package for R (R Development Core Team (2010)) can be used for the following two purposes: Causal structure learning and estimation of causal effects from observational data. In this document, we give a brief overview of the methodology, and

Natuurkundige modellen



Paper door Claudia D. van Borkulo, Denny Borsboom, Sacha Epskamp
Tessa F. Blanken, Lynn Boschloo, Robert A. Schoevers & Lourens J. Waldorp
in voorbereiding.

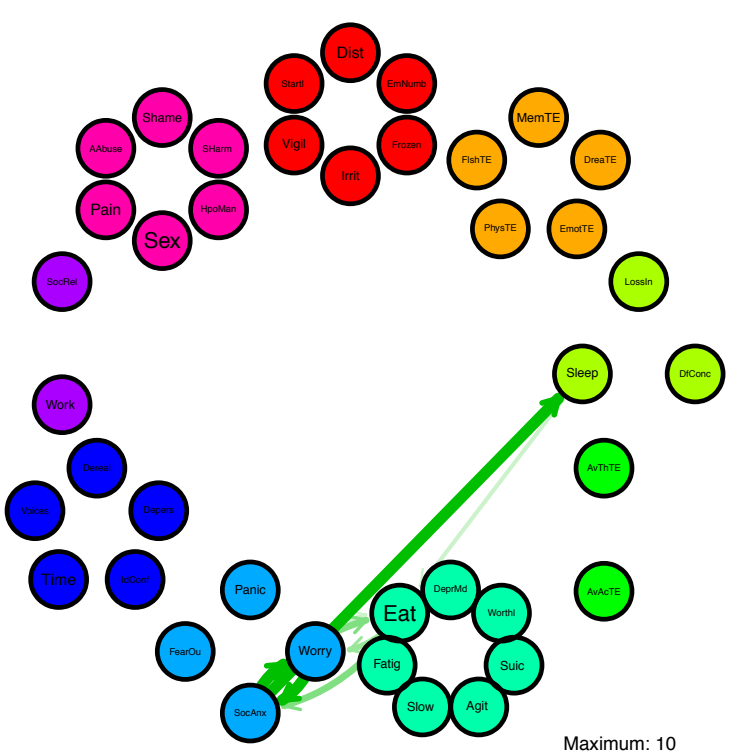
Individuele netwerken

Individuele netwerken

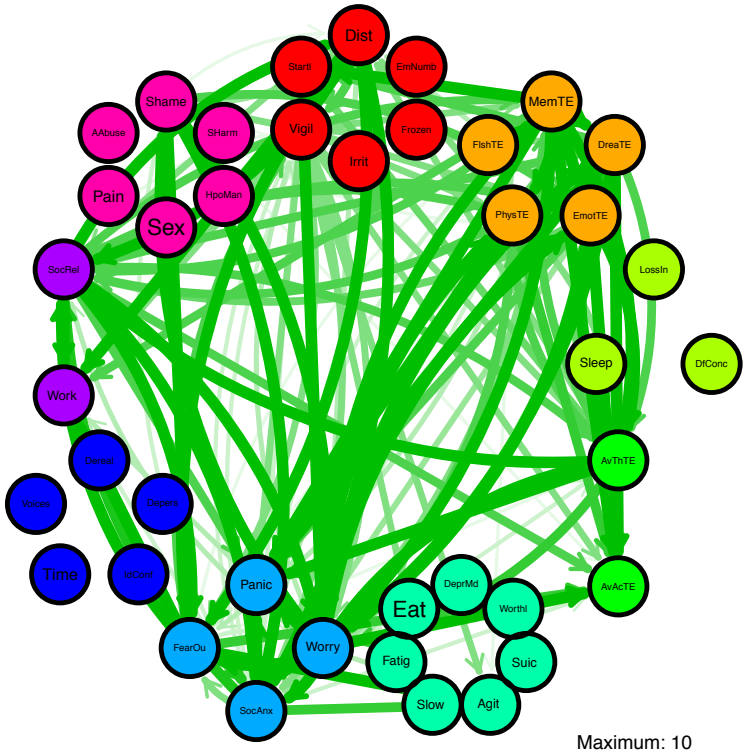
Er zijn verschillende methoden om een idee te krijgen van persoonlijke netwerken:

- Vraag het!
- Tijdserie analyse
- Cluster analyse

Individual PCR graphs

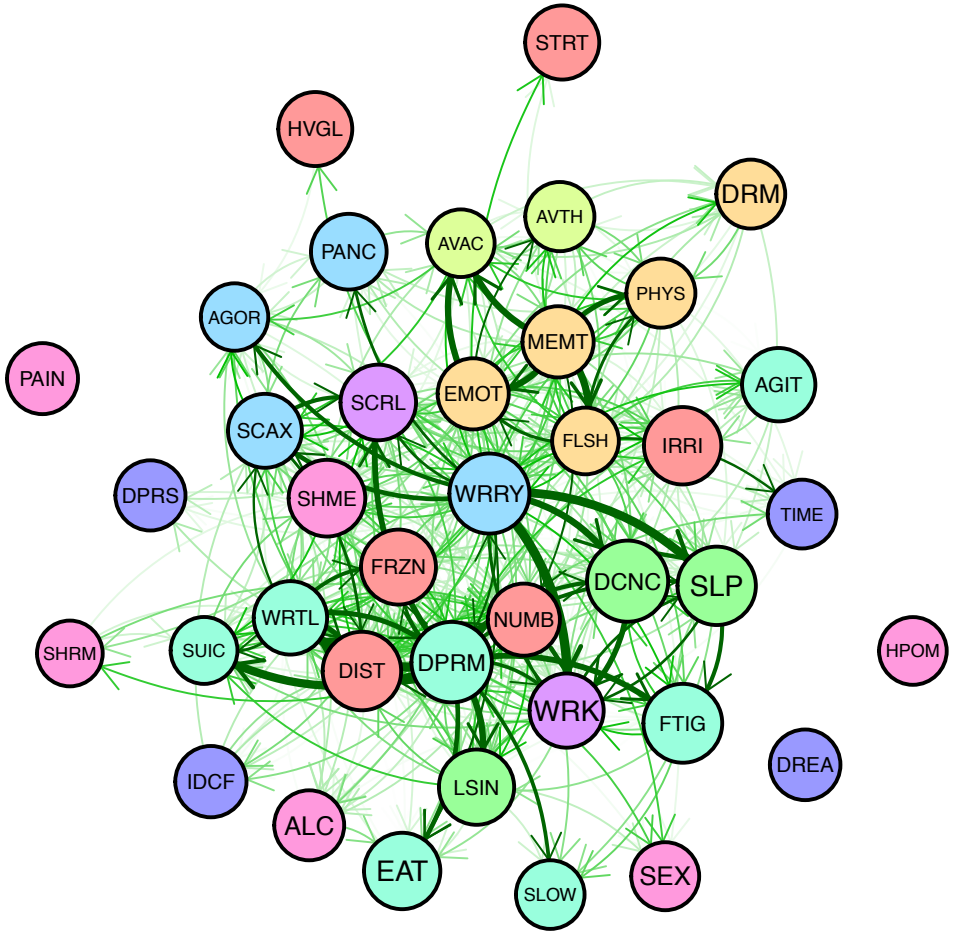


Maximum: 10



Maximum: 10

Average PCR graph



- PTSD other
- PTSD reexp
- PTSD avoid
- PTSD and MDD
- MDD
- Anxiety
- Dissoc
- Impairment
- Other

Frewen, P.A., Schmittmann, V. D., Bringmann, L. F., & Borsboom, D. (submitted). Perceived Causal Relations between Posttraumatic Stress, Anxiety, and Depression.

CLINICAL RESEARCH ARTICLE

COACTION PUBLISHING

Perceived causal relations between anxiety, posttraumatic stress and depression: extension to moderation, mediation, and network analysis

Paul A. Frewen[1]*, Verena D. Schmittmann[2], Laura F. Bringmann[3] and Denny Borsboom[2]

[1]Department of Psychiatry and Psychology, Graduate Program in Neuroscience, Western University Canada, London, Ontario, Canada; [2]Department of Psychological Methods, University of Amsterdam, Amsterdam, The Netherlands; [3]Department of Quantitative Psychology and Individual Differences, University of Leuven, Leuven, Belgium

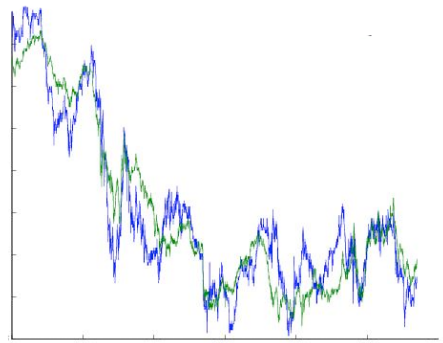
Background: Previous research demonstrates that posttraumatic memory reexperiencing, depression, anxiety, and guilt-shame are frequently co-occurring problems that may be causally related.

Objectives: The present study utilized Perceived Causal Relations (PCR) scaling in order to assess participants' own attributions concerning whether and to what degree these co-occurring problems may be causally interrelated.

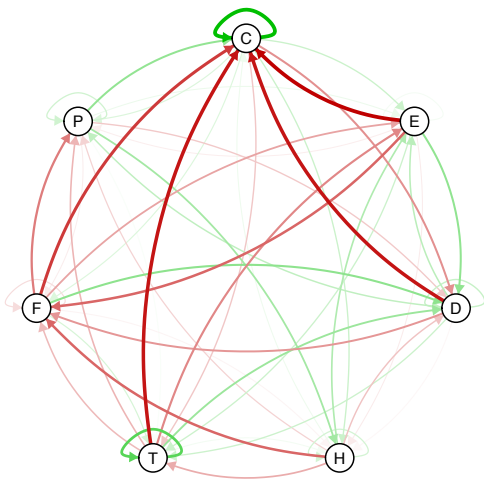
Methods: 288 young adults rated the frequency and respective PCR scores associating their symptoms of posttraumatic reexperiencing, depression, anxiety, and guilt-shame.

Results: PCR scores were found to moderate associations between the frequency of posttraumatic memory reexperiencing, depression, anxiety, and guilt-shame. Network analyses showed that the number of feedback loops between PCR scores was positively associated with symptom frequencies.

Conclusion: Results tentatively support the interpretation of PCR scores as moderators of the association between different psychological problems, and lend support to the hypothesis that increased symptom frequencies are observed in the presence of an increased number of causal feedback loops between symptoms. Additionally, a perceived causal role for the reexperiencing of traumatic memories in exacerbating emotional disturbance was identified.



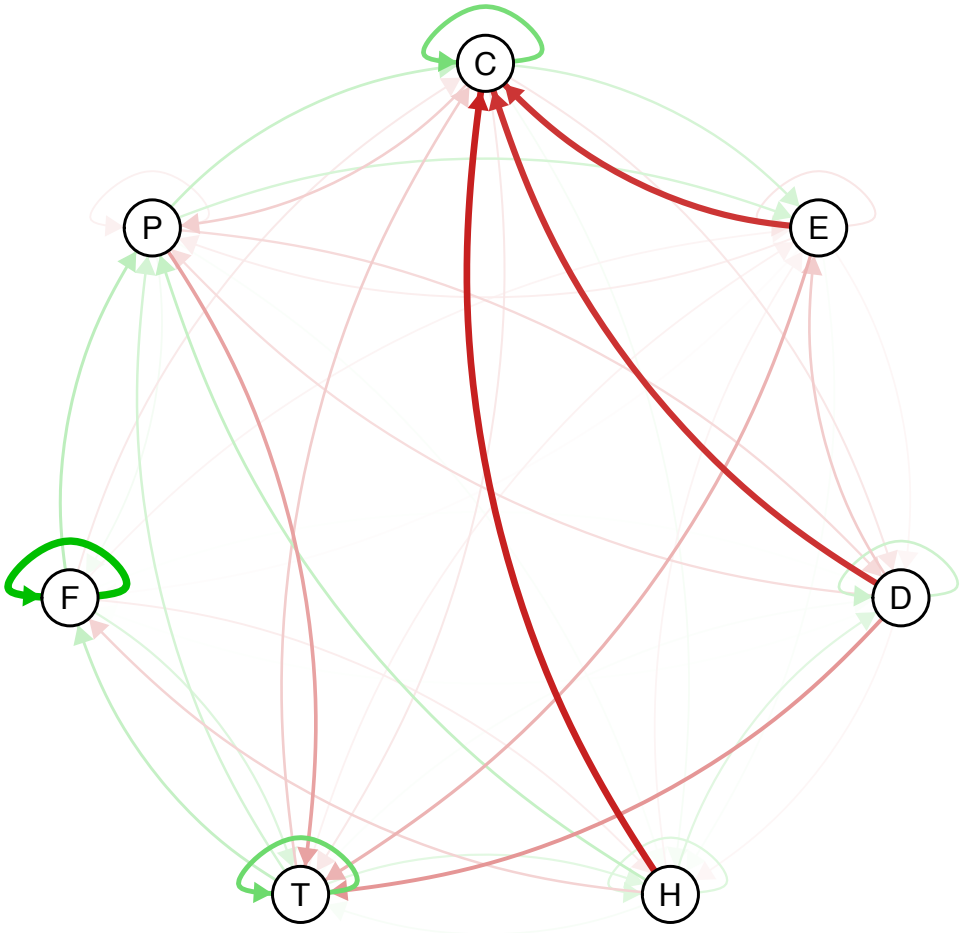
$$Y_{ijt} = \alpha + \beta_1 X_{1,t-1} + \beta_2 X_{2,t-1} + \ldots + \varepsilon$$



Bringmann, L., Vissers, N., Wichers, M., Geschwind, N., Kuppens, P., Peeters, F., Borsboom, D., & Tuerlinckx, F. (2013). A network approach to psychopathology: New insights into clinical longitudinal data. *PLoS ONE*.

Dynamical networks

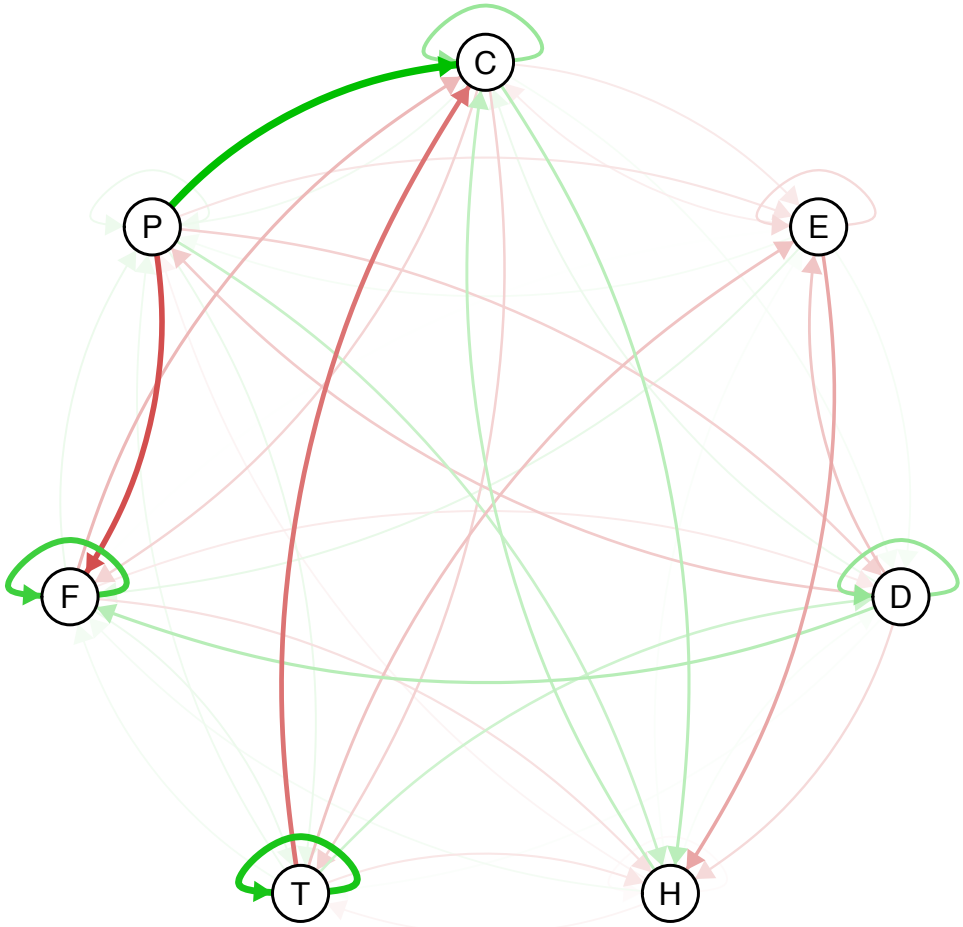
Subject 31



C = Cheerful
E = Would prefer doing something else
D = What I am doing takes a lot of effort
H = I am hungry
T = I am tired
F = I am not feeling well
P = Pleasantness of prior event

Dynamical networks

Subject 41



C = Cheerful
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F = I am not feeling well
P = Pleasantness of prior event

OPEN ACCESS Freely available online

PLOS ONE

A Network Approach to Psychopathology: New Insights into Clinical Longitudinal Data

Laura F. Bringmann[1]*, Nathalie Vissers[1], Marieke Wichers[2], Nicole Geschwind[3], Peter Kuppens[1], Frenk Peeters[2], Denny Borsboom[4], Francis Tuerlinckx[1]

1 Department of Psychology, University of Leuven, Leuven, Belgium, **2** Department of Psychiatry and Neuropsychology, Maastricht University, Maastricht, The Netherlands, **3** Department of Clinical Psychological Science, Maastricht University, Maastricht, The Netherlands, **4** Department of Psychology, University of Amsterdam, Amsterdam, The Netherlands

Abstract

In the network approach to psychopathology, disorders are conceptualized as networks of mutually interacting symptoms (e.g., depressed mood) and transdiagnostic factors (e.g., rumination). This suggests that it is necessary to study how symptoms dynamically interact over time in a network architecture. In the present paper, we show how such an architecture can be constructed on the basis of time-series data obtained through Experience Sampling Methodology (ESM). The proposed methodology determines the parameters for the interaction between nodes in the network by estimating a multilevel vector autoregression (VAR) model on the data. The methodology allows combining between-subject and within-subject information in a multilevel framework. The resulting network architecture can subsequently be analyzed through network analysis techniques. In the present study, we apply the method to a set of items that assess mood-related factors. We show that the analysis generates a plausible and replicable network architecture, the structure of which is related to variables such as neuroticism; that is, for subjects who score high on neuroticism, worrying plays a more central role in the network. Implications and extensions of the methodology are discussed.

Citation: Bringmann LF, Vissers N, Wichers M, Geschwind N, Kuppens P, et al. (2013) A Network Approach to Psychopathology: New Insights into Clinical Longitudinal Data. PLoS ONE 8(4): e60188. doi:10.1371/journal.pone.0060188

Editor: Gabriel Alejandro de Erausquin, University of South Florida, United States of America

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Competing Interests: The authors have declared that no competing interests exist.

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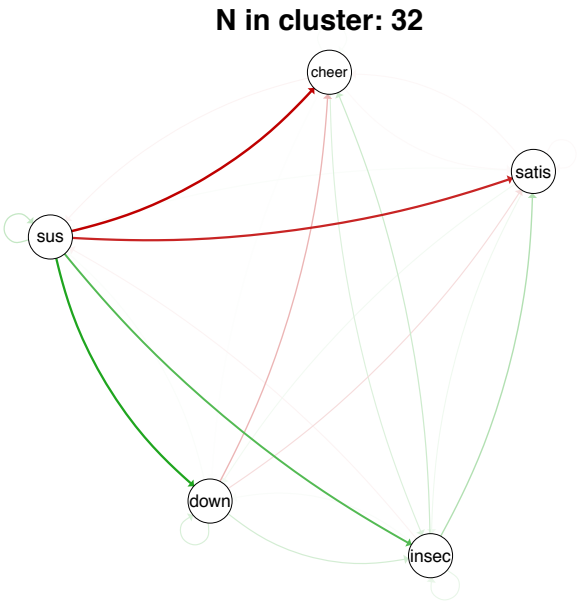
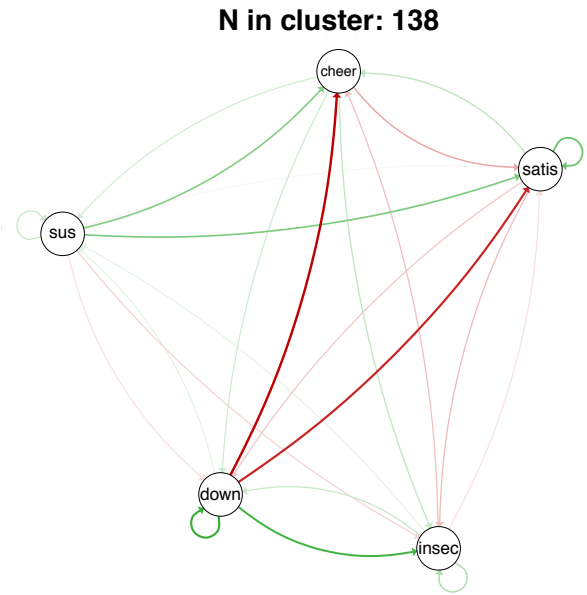
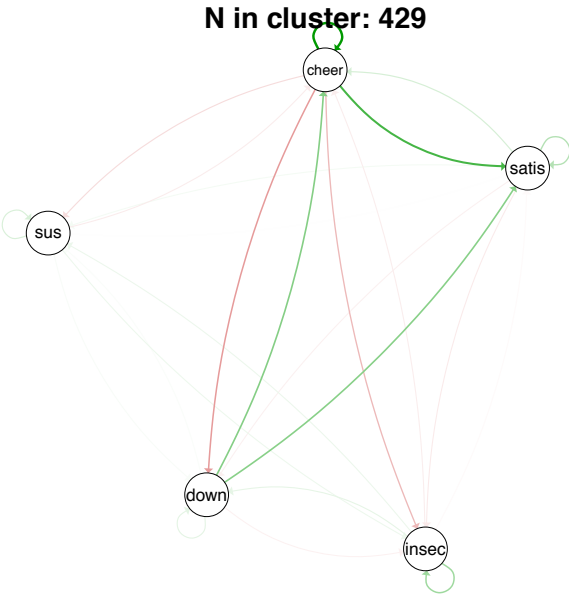
Individual differences



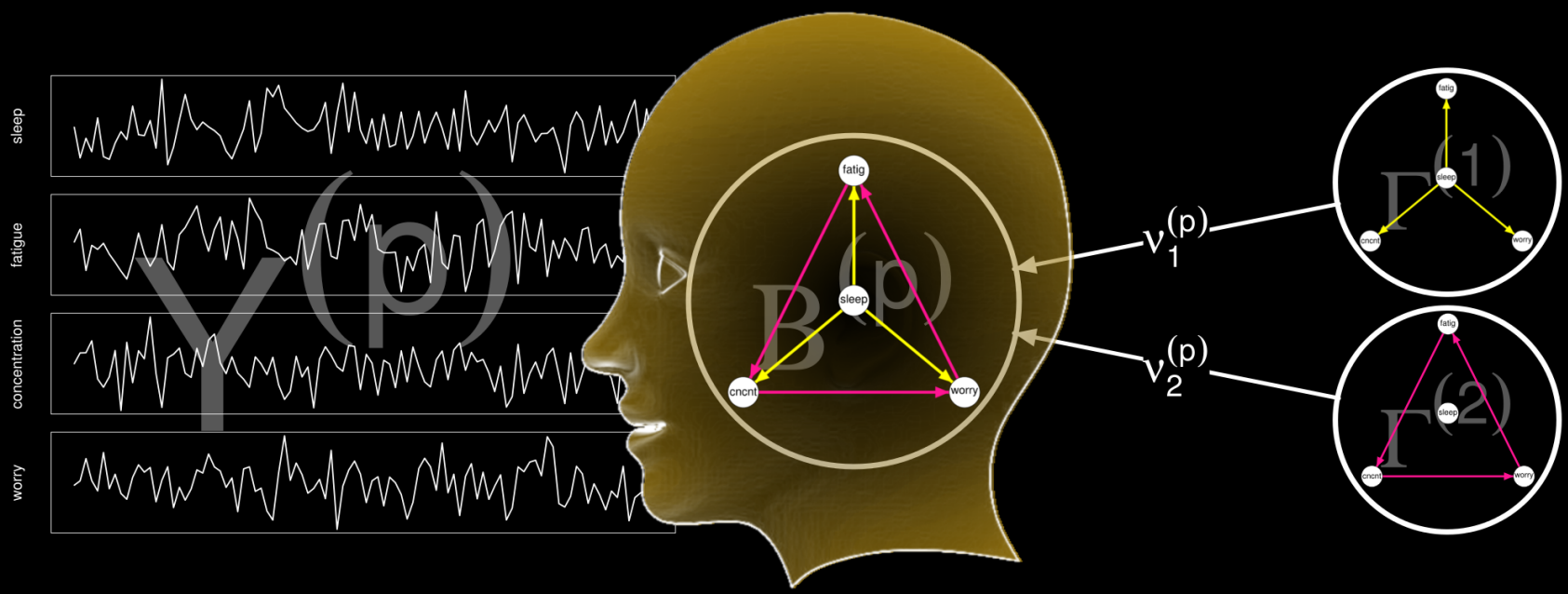
Network driven by suspicion



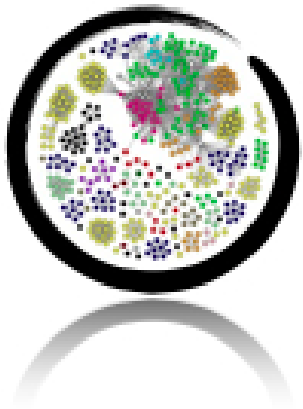
Network driven by mood



Healthy network


sleep
fatigue
concentration
worry
Y(p)
B(p)
fatig
sleep
cncnt
worry
$\nu_1^{(p)}$
$\nu_2^{(p)}$
$\Gamma^{(1)}$
$\Gamma^{(2)}$

The Psych Systems Project



http://www.psychosystems.org/

Network Analysis: An Integrative Approach to the Structure of Psychopathology

Denny Borsboom and Angélique O.J. Cramer

Department of Psychology, University of Amsterdam, Amsterdam 1018 XA, The Netherlands; email: D.Borsboom@uva.nl

Annu. Rev. Clin. Psychol. 2013. 9:91–121

The *Annual Review of Clinical Psychology* is online at http://clinpsy.annualreviews.org

This article's doi: 10.1146/annurev-clinpsy-050212-185608

Keywords

network analysis, psychopathology, latent variable models, psychometrics, measurement, philosophy of science

Abstract

In network approaches to psychopathology, disorders result from the causal interplay between symptoms (e.g., worry → insomnia → fatigue), possibly involving feedback loops (e.g., a person may engage in substance abuse to forget the problems that arose due to substance abuse). The present review examines methodologies suited to identify such symptom networks and discusses network analysis techniques that may be used to extract clinically and scientifically useful information from such networks (e.g., which symptom is most central in a person's network). The authors also show how network analysis techniques may be used to construct simulation models that mimic symptom dynamics. Network approaches naturally explain the limited success of traditional research strategies, which are typically based on the idea that symptoms are manifestations of some common underlying fac-

Bedankt voor uw aandacht!