

# Biomarkerji depresije pri izbiri ustreznega zdravljenja

Predavatelj:  
Grega Repovš

Teden  
možganov 2018

Na sanjah  
svet stoji



VZAJEMNA  
zdravstvena zavarovalnica

FENS | Federation of  
European  
Neuroscience  
Societies



TEDEN  
MOŽGANOV



SiNAPSA  
SLOVENSKO DRUŠTVO ZA NEUROZNAKOSLOVJE  
SLOVENIAN NEUROSCIENCE ASSOCIATION



za možgane

THE  
DANA  
FOUNDATION

12.–18. marec



# ARTICLES

## Resting-state connectivity biomarkers define neurophysiological subtypes of depression

Andrew T Drysdale<sup>1-3</sup>, Logan Groesenick<sup>4,5</sup>, Jonathan Downar<sup>6</sup>, Katharine Dunlop<sup>6</sup>, Farrokh Mansouri<sup>6</sup>, Yue Meng<sup>1</sup>, Robert N Fetcho<sup>1</sup>, Benjamin Zebley<sup>7</sup>, Desmond J Oathes<sup>8</sup>, Amit Etkin<sup>9,10</sup>, Alan F Schatzberg<sup>9</sup>, Keith Sudheimer<sup>9</sup>, Jennifer Keller<sup>9</sup>, Helen S Mayberg<sup>11</sup>, Faith M Gunning<sup>2,12</sup>, George S Alexopoulos<sup>2,12</sup>, Michael D Fox<sup>13</sup>, Alvaro Pascual-Leone<sup>13</sup>, Henning U Voss<sup>14</sup>, BJ Casey<sup>15</sup>, Marc J Dubin<sup>1,2</sup> & Conor Liston<sup>1-3</sup>

**Biomarkers have transformed modern medicine but remain largely elusive in psychiatry, partly because there is a weak correspondence between diagnostic labels and their neurobiological substrates. Like other neuropsychiatric disorders, depression is not a unitary disease, but rather a heterogeneous syndrome that encompasses varied, co-occurring symptoms and divergent responses to treatment. By using functional magnetic resonance imaging (fMRI) in a large multisite sample ( $n = 1,188$ ), we show here that patients with depression can be subdivided into four neurophysiological subtypes ('biotypes') defined by distinct patterns of dysfunctional connectivity in limbic and frontostriatal networks. Clustering patients on this basis enabled the development of diagnostic classifiers (biomarkers) with high (82–93%) sensitivity and specificity for depression subtypes in multisite validation ( $n = 711$ ) and out-of-sample replication ( $n = 477$ ) data sets. These biotypes cannot be differentiated solely on the basis of clinical features, but they are associated with differing clinical-symptom profiles. They also predict responsiveness to transcranial magnetic stimulation therapy ( $n = 154$ ). Our results define novel subtypes of depression that transcend current diagnostic boundaries and may be useful for identifying the individuals who are most likely to benefit from targeted neurostimulation therapies.**



# psihopatologija

# psihopatologija



vedenje

doživljanje

znaki in simptomi

# psihopatologija



# psihopatologija





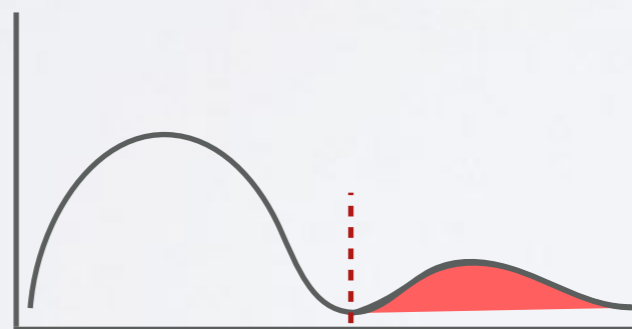


**psihopatologija**

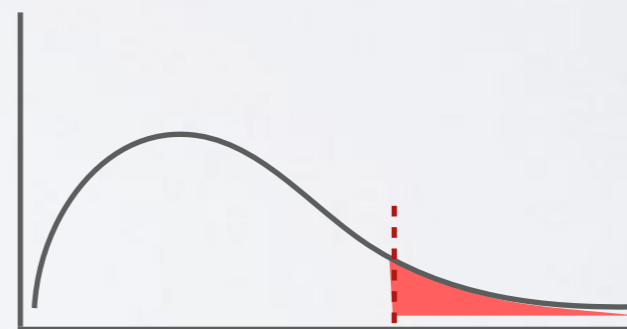
# psihopatologija



# psihopatologija



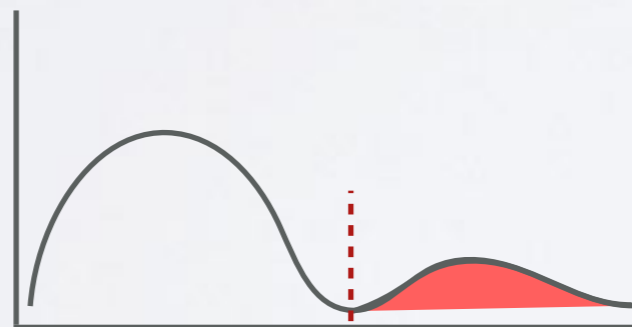
kategorično različna od normalnosti



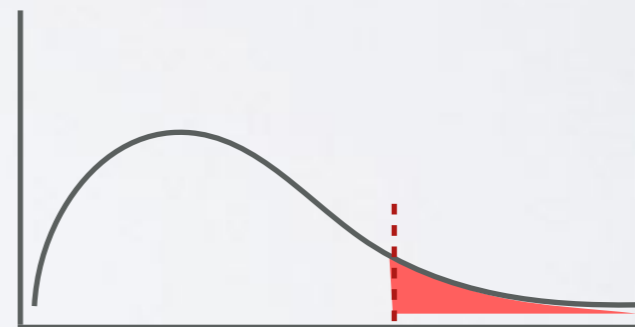
kontinuum brez jasnih prehodov

**standard**

**psihopatologija**



kategorično različna od normalnosti



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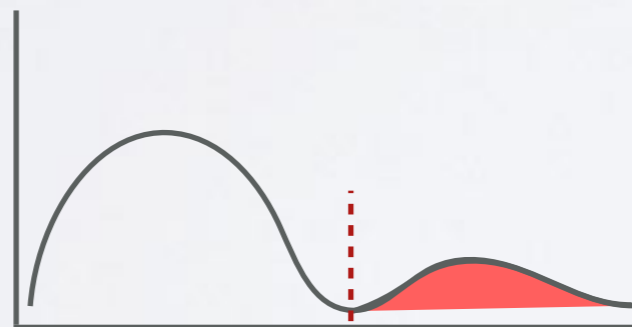
opredelitev  
duševne motnje



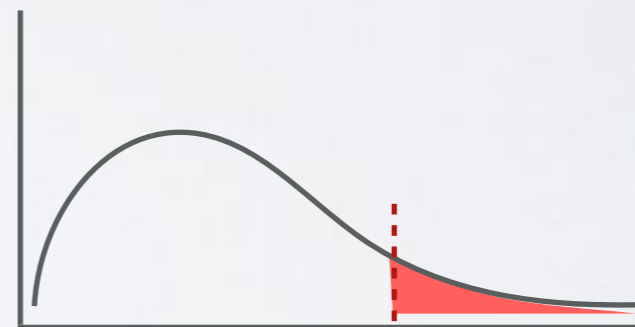
iskanje  
patofiziologije

**standard**

**psihopatologija**



kategorično različna od normalnosti



kontinuum brez jasnih prehodov



opredelitev  
duševne motnje

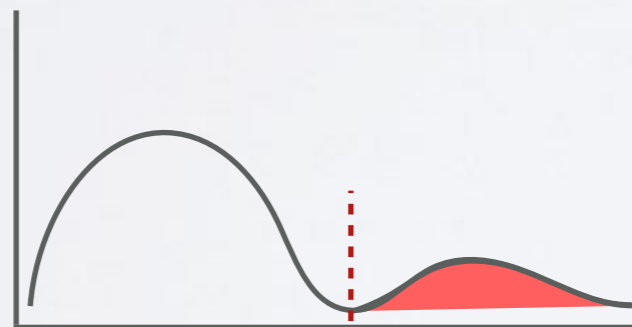


iskanje  
patofiziologije

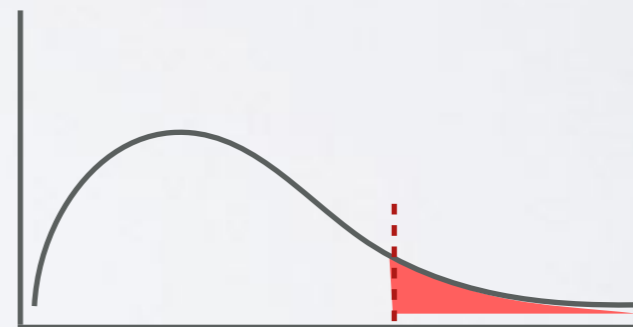
**standard**

**RDoC**

**psihopatologija**



kategorično različna od normalnosti



kontinuum brez jasnih prehodov

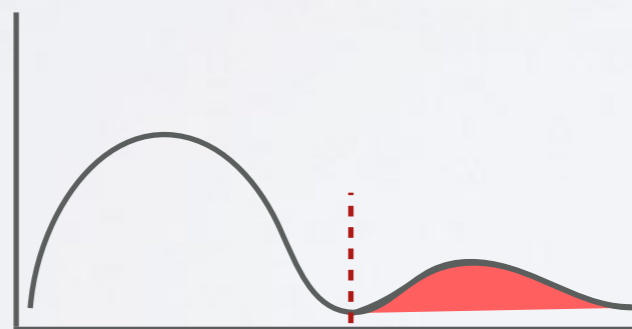
opredelitev duševne motnje → iskanje patofiziologije

**standard**

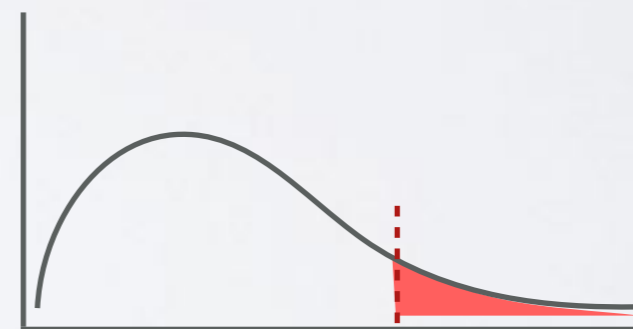
normalna distribucija lastnosti → zadolžen možganski sistem → razumevanje motnje

**RDoC**

**psihopatologija**



kategorično različna od normalnosti



kontinuum brez jasnih prehodov

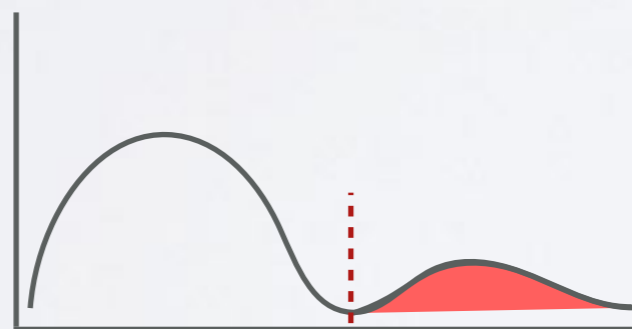
opredelitev duševne motnje → iskanje patofiziologije

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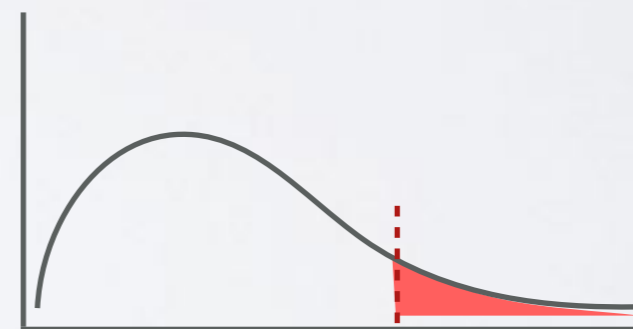
PREVEDBENI PRISTOP



**psihopatologija**



kategorično različna od normalnosti



kontinuum brez jasnih prehodov

**psihopatologija**

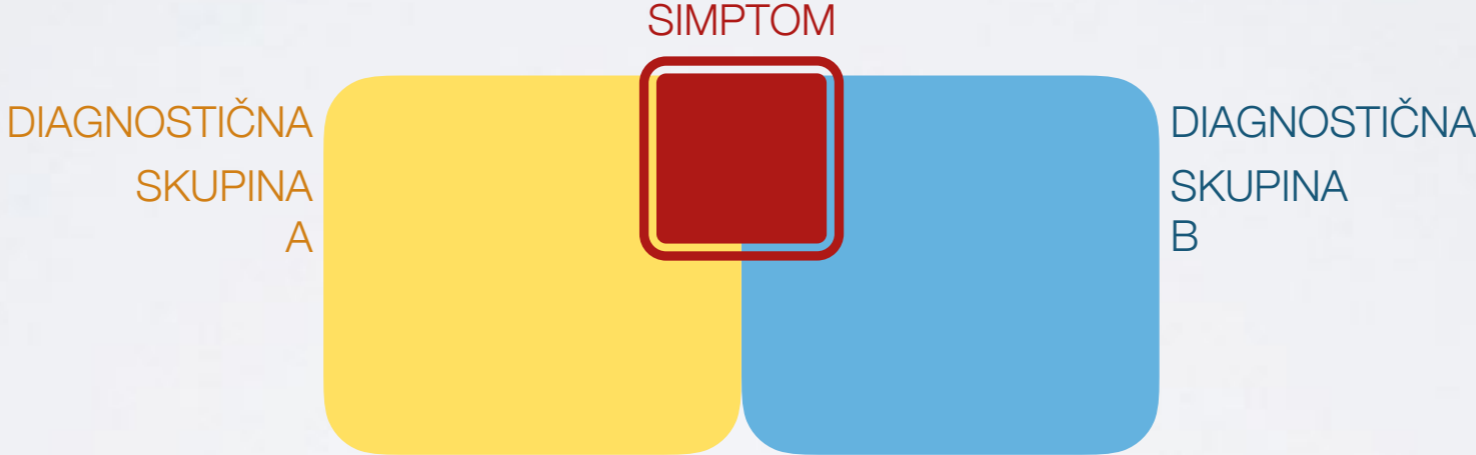
# psihopatologija

SIMPTOM



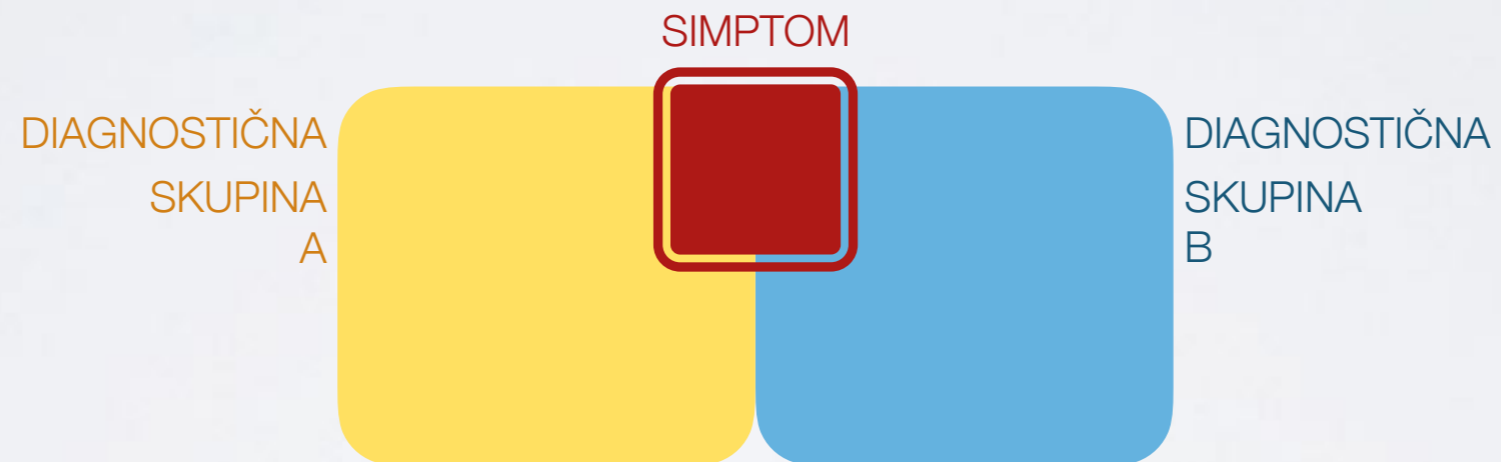


# psihopatologija



**zdravljenje**

**psihopatologija**



razvoj novih  
terapij

**zdravljenje**

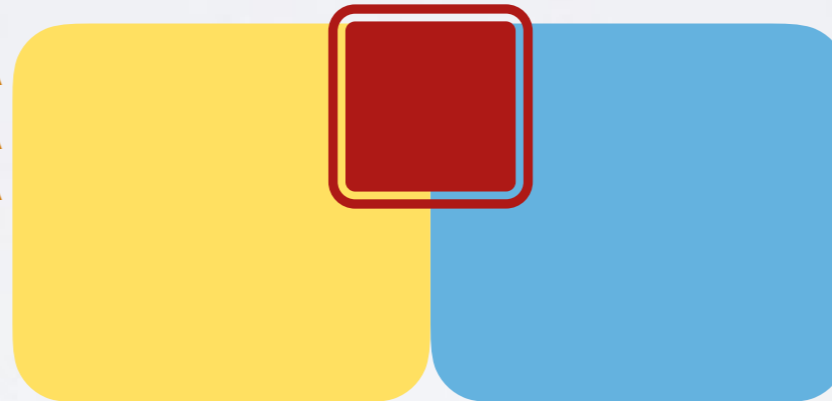
ujemanje bolnikov  
in zdravljenj

**psihopatologija**

DIAGNOSTIČNA  
SKUPINA  
A

SIMPTOM

DIAGNOSTIČNA  
SKUPINA  
B

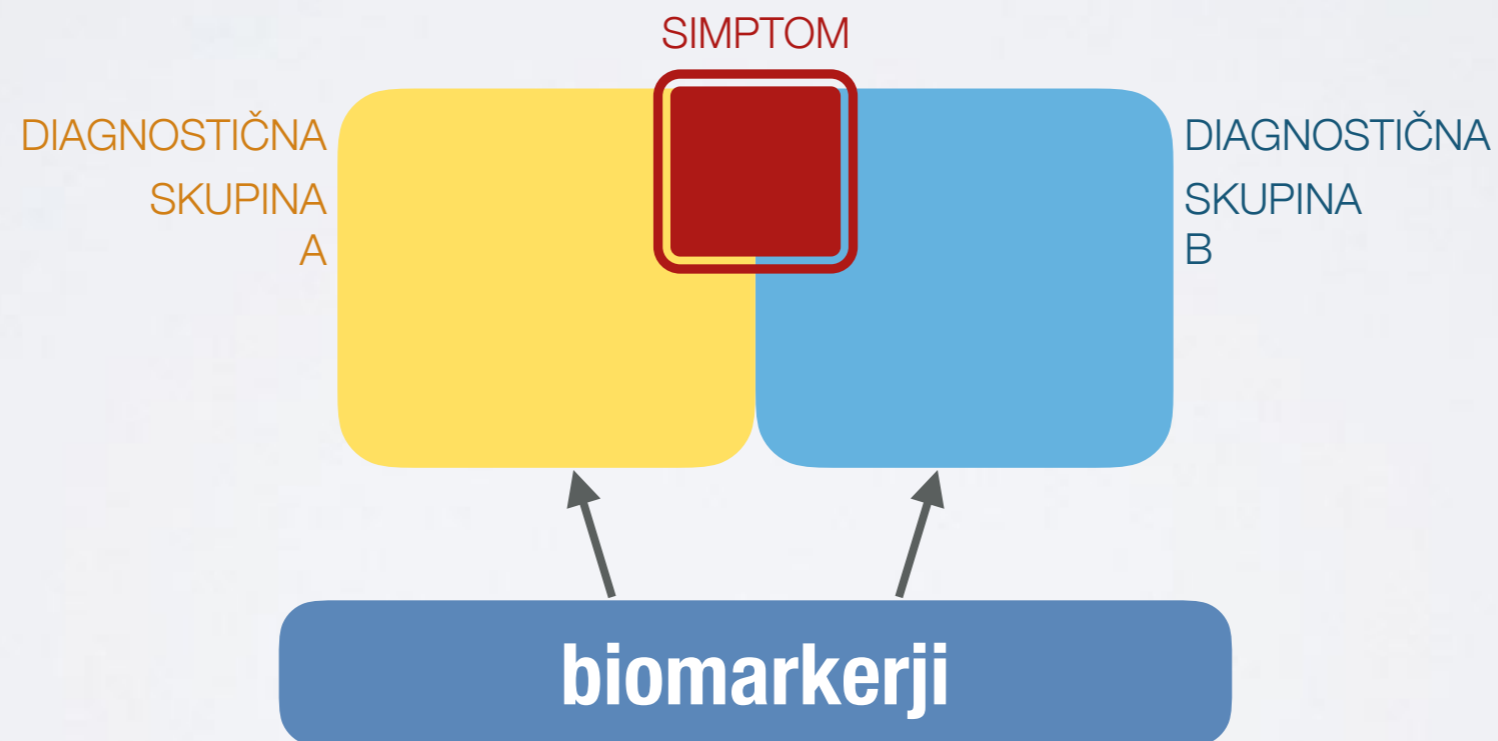


razvoj novih  
terapij

**zdravljenje**

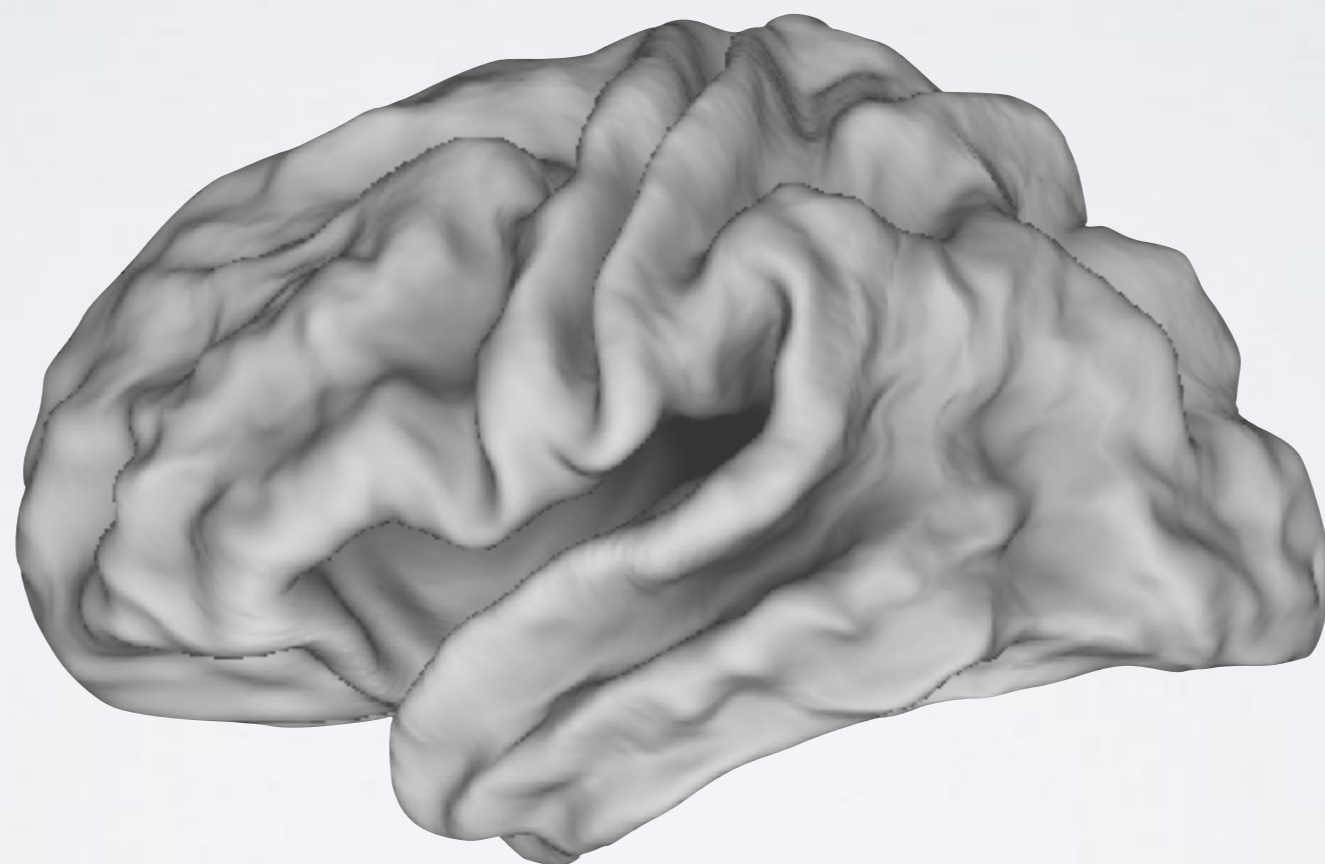
ujemanje bolnikov  
in zdravljenj

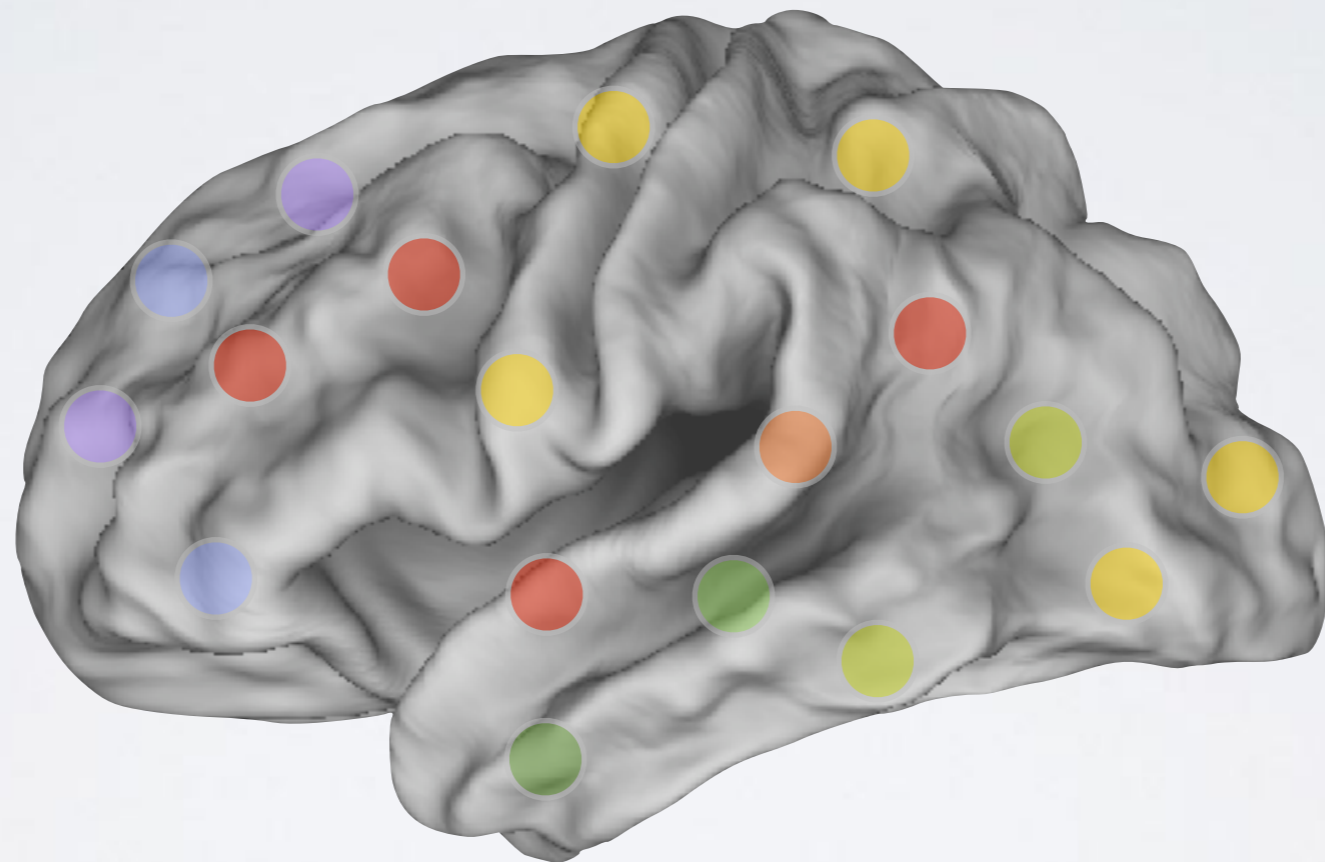
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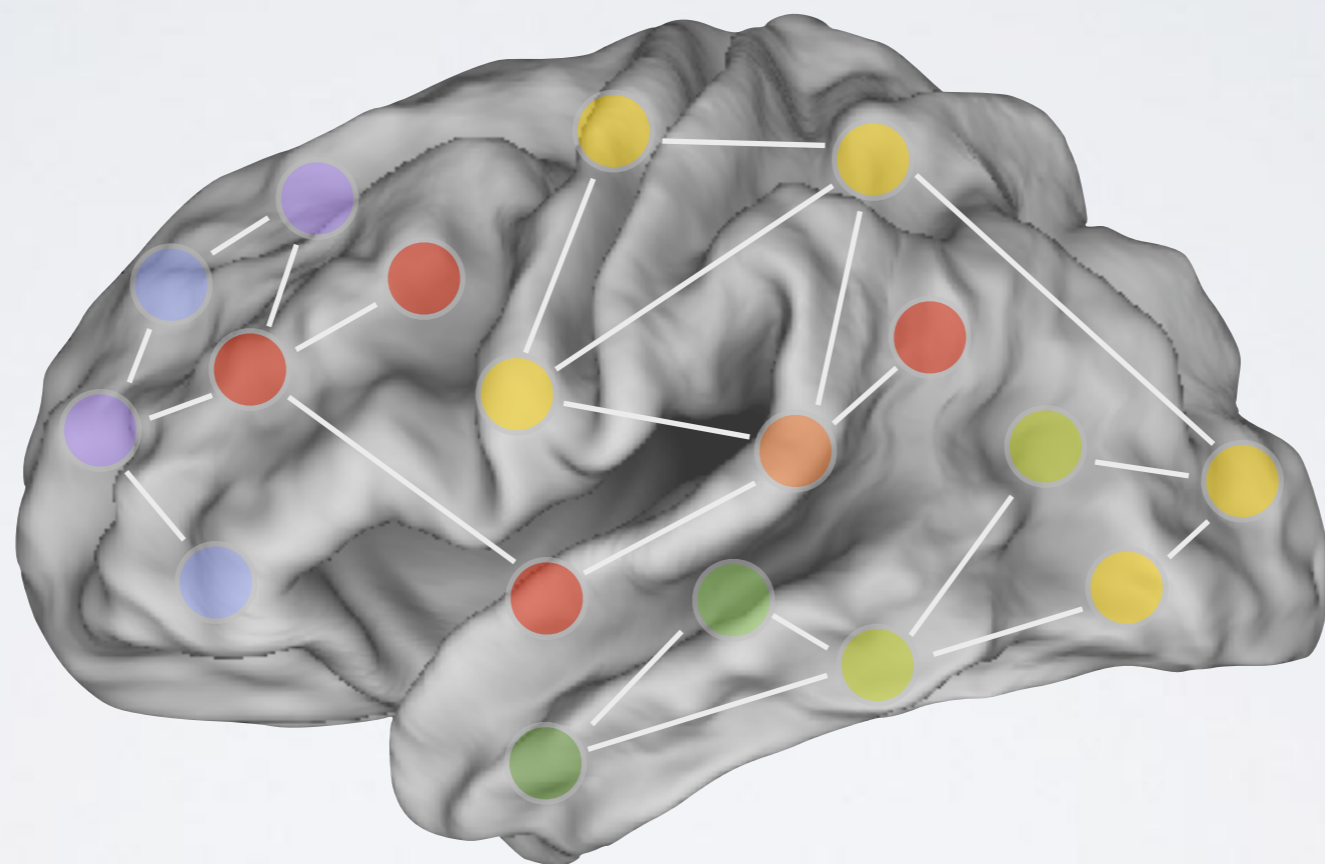


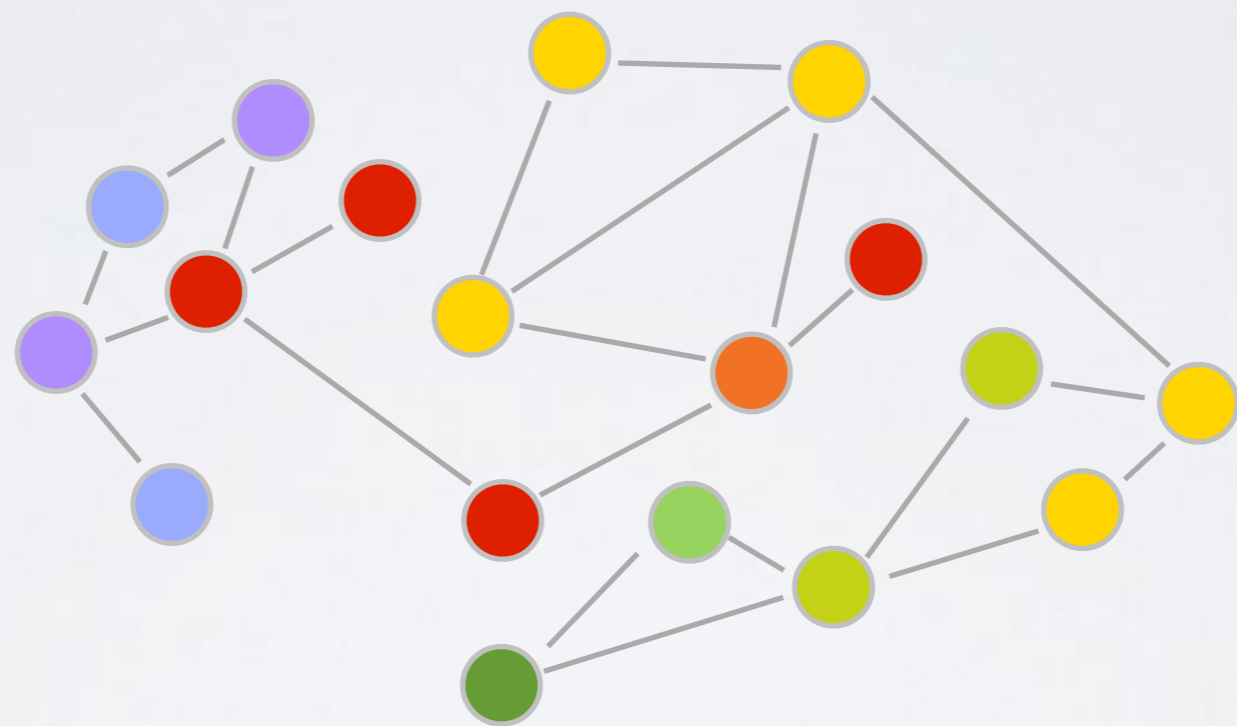


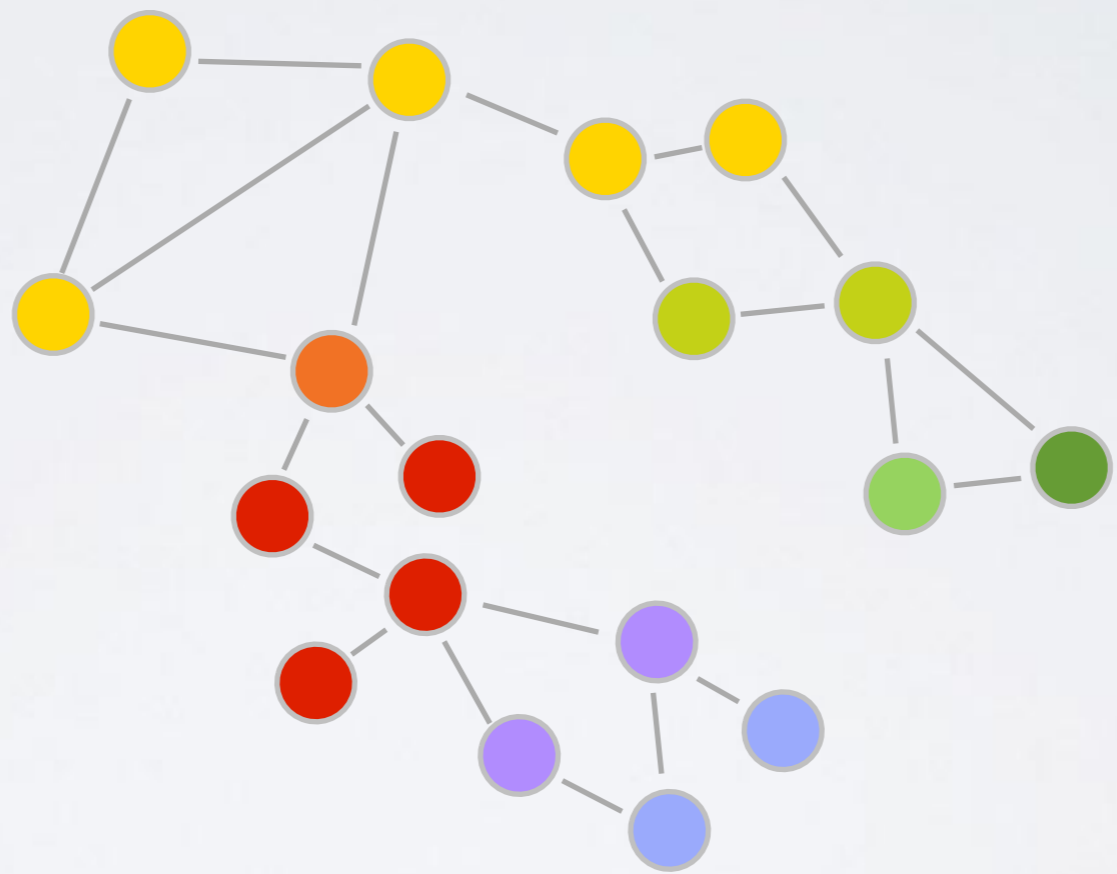






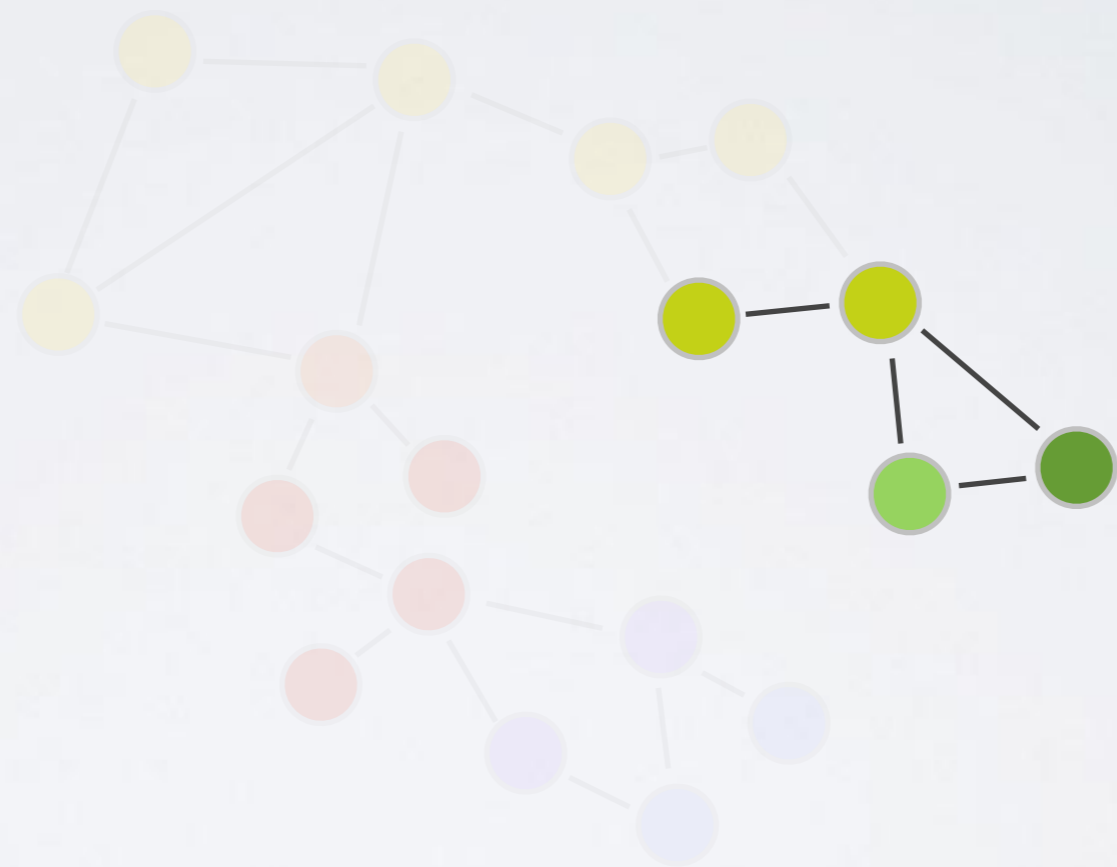




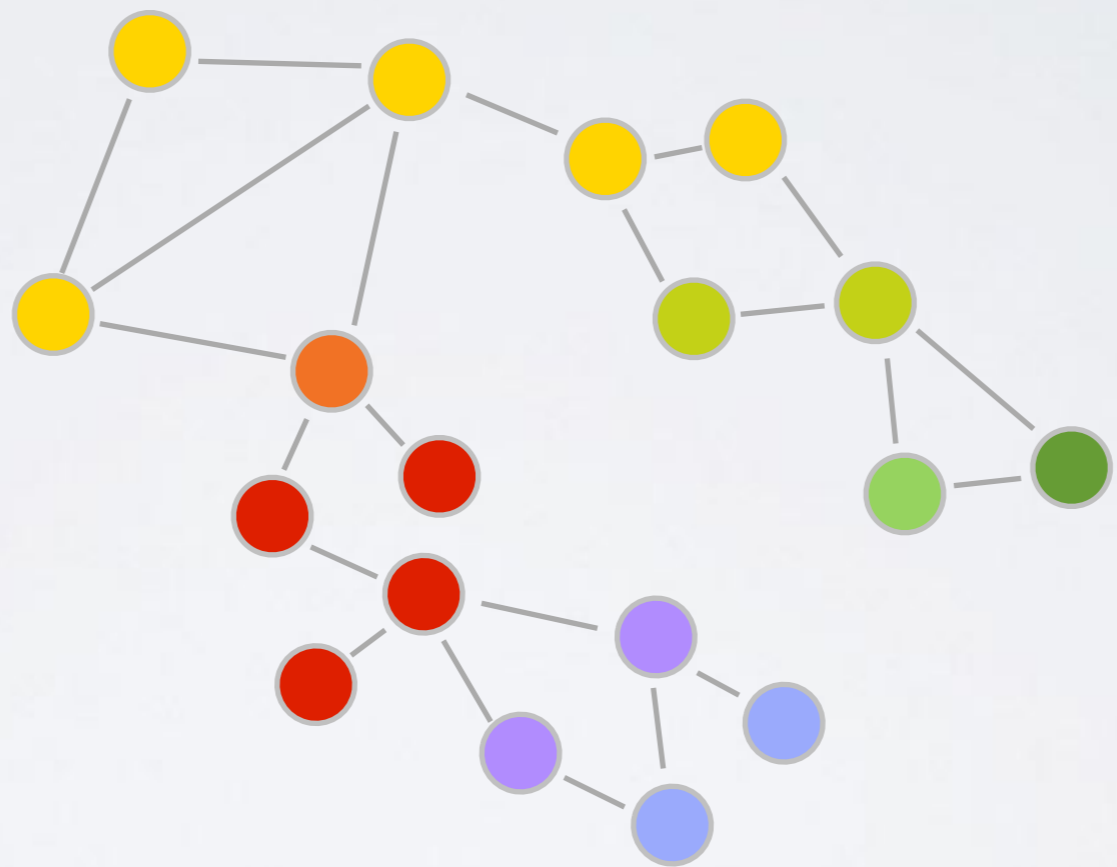


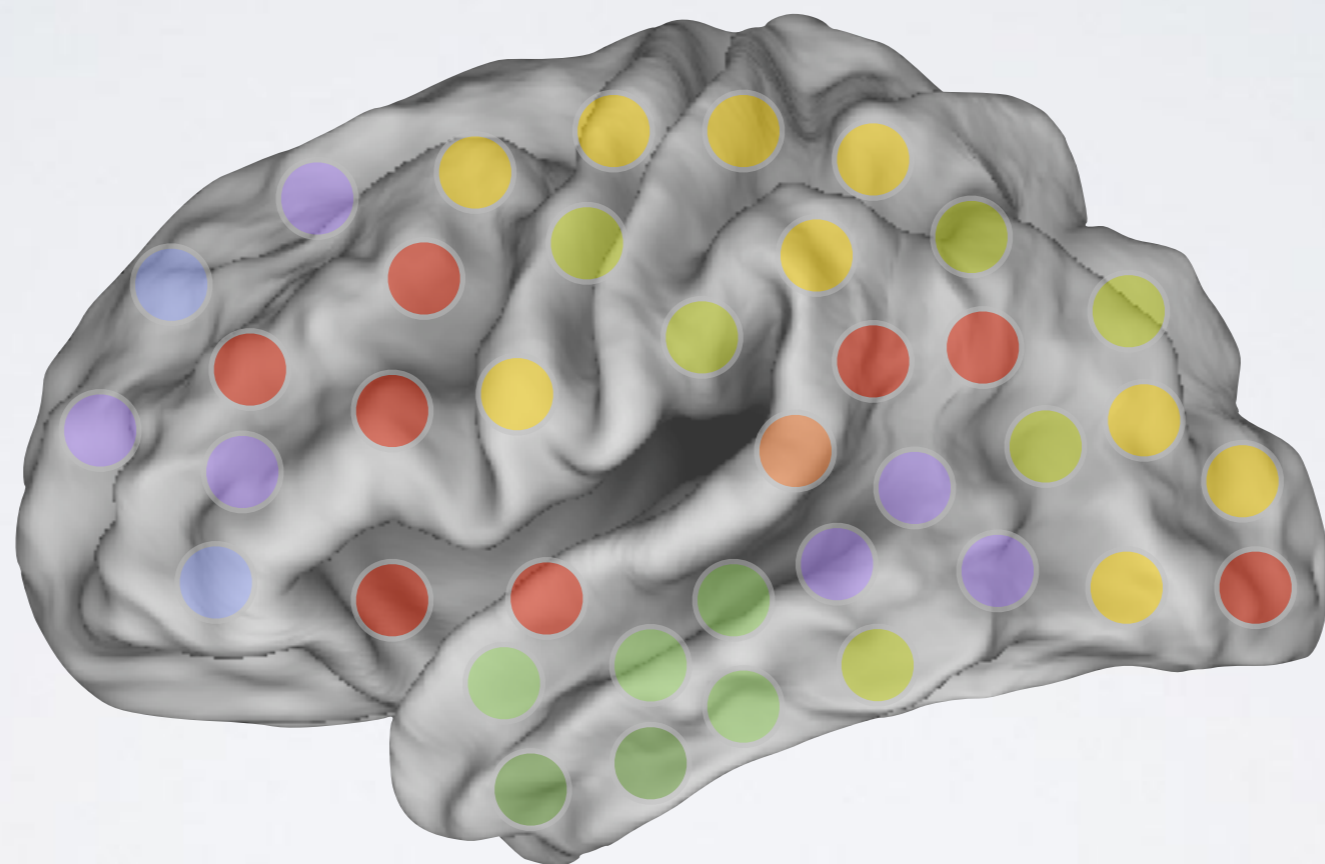


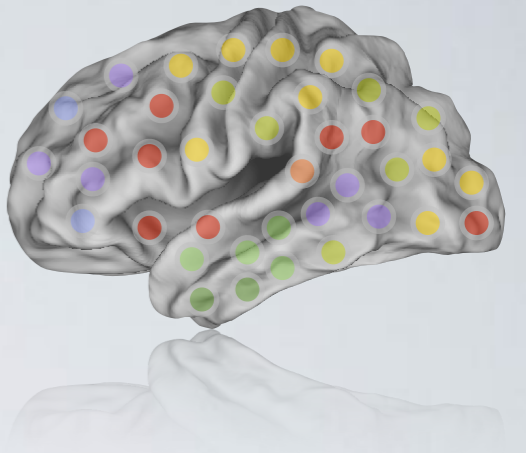




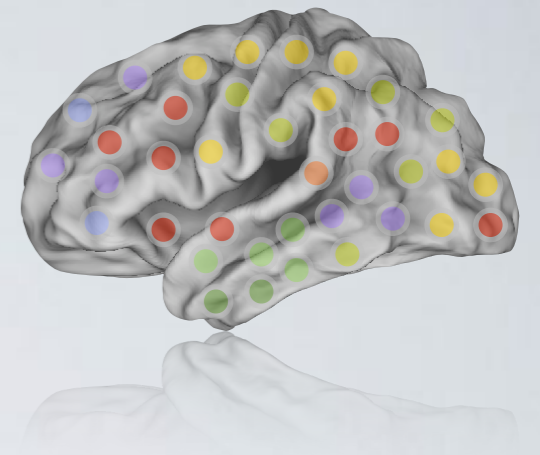




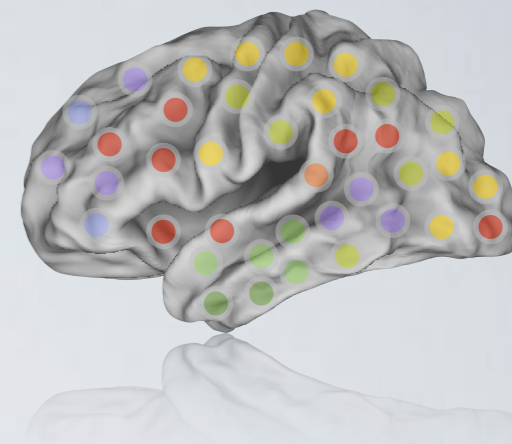
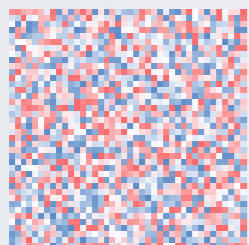
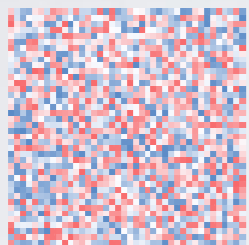
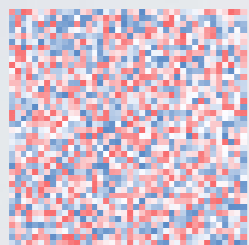
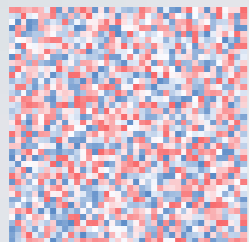




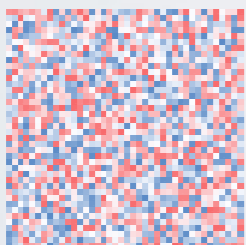
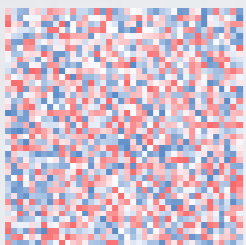
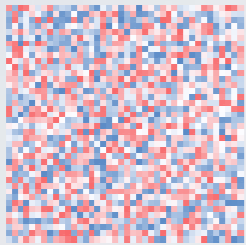
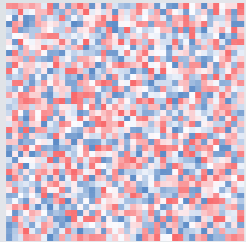
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funkcijske  
povezanosti



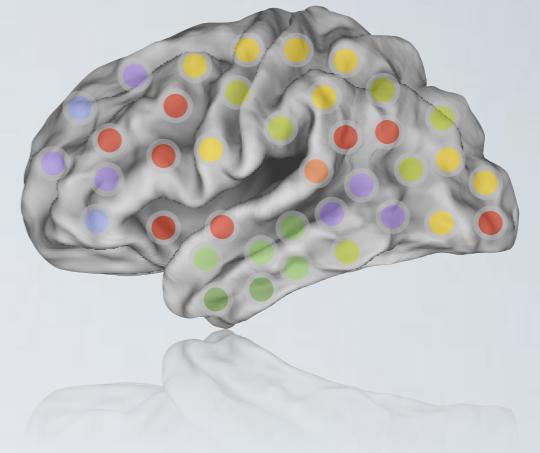
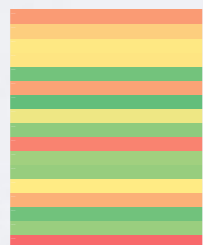
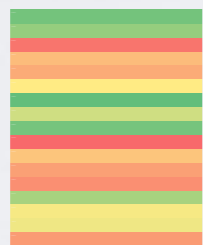
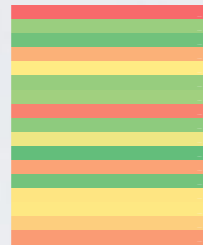
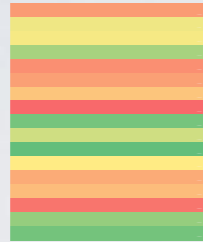
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funkcijske  
povezanosti



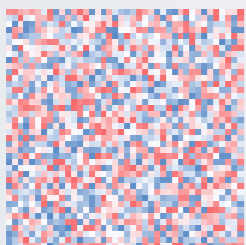
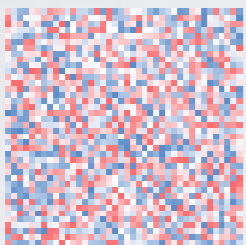
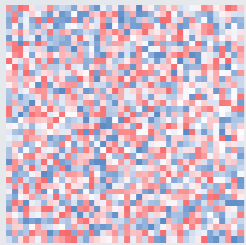
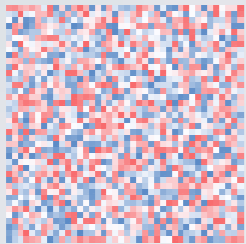
vzorec  
funkcijske  
povezanosti



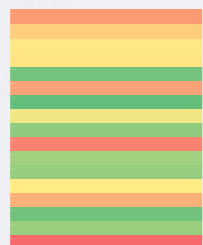
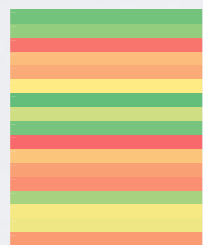
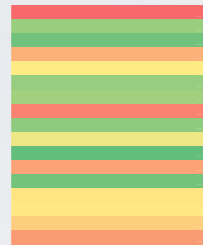
izraženost  
simptomov  
depresije



vzorec  
funkcijske  
povezanosti



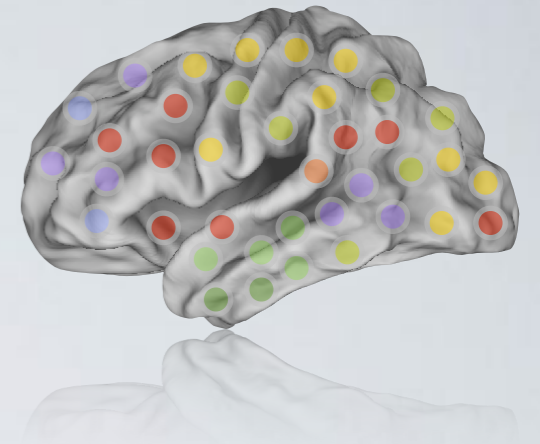
izraženost  
simptomov  
depresije

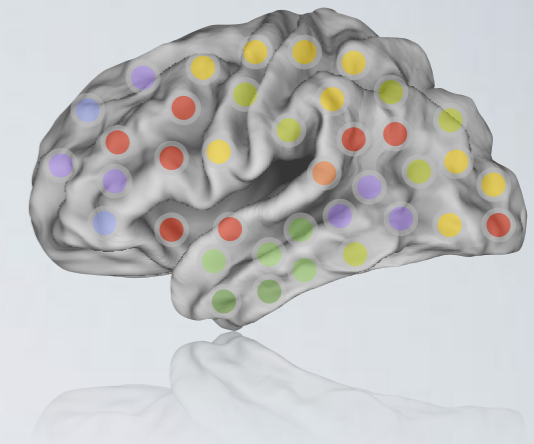


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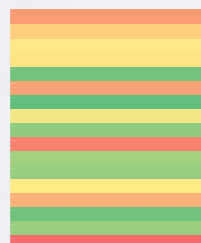
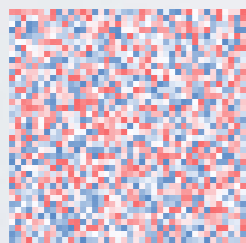
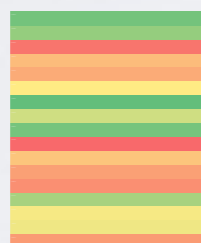
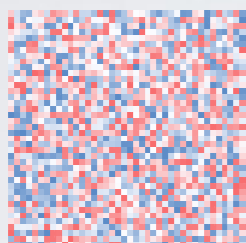
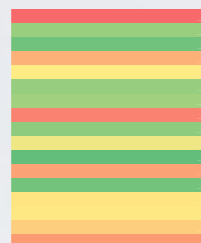
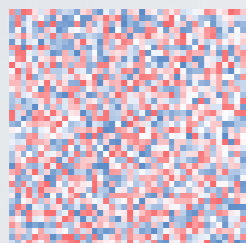
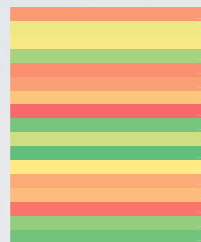
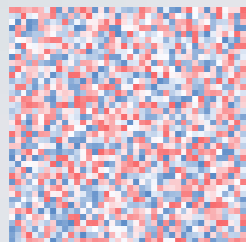
2 dimenziji





vzorec  
funkcijske  
povezanosti

izraženost  
simptomov  
depresije



## 2 dimenziji

frontostriatalna in  
orbitofrontalna  
konektivnost



anhedonija  
psihomotorna  
retardiranost

limbična in lateralno  
prefrontalna  
konektivnost

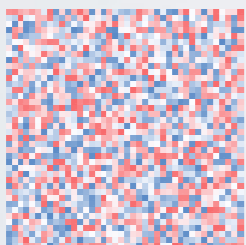
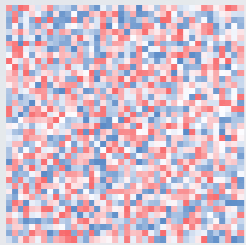
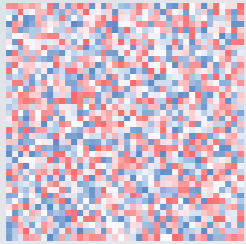


anksioznost  
nespečnost

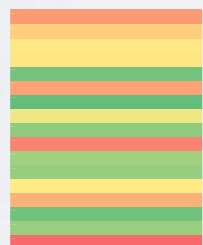
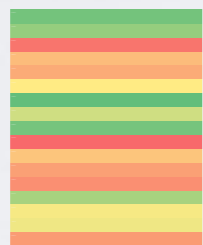
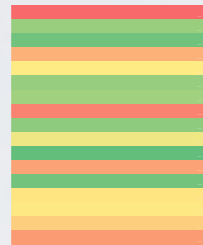
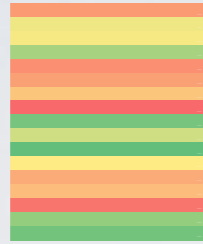
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vzorec  
funkcijske  
povezanosti



izraženost  
simptomov  
depresije



220



**2 dimenziji**

frontostriatalna in  
orbitofrontalna  
konektivnost



anhedonija  
psihomotorna  
retardiranost

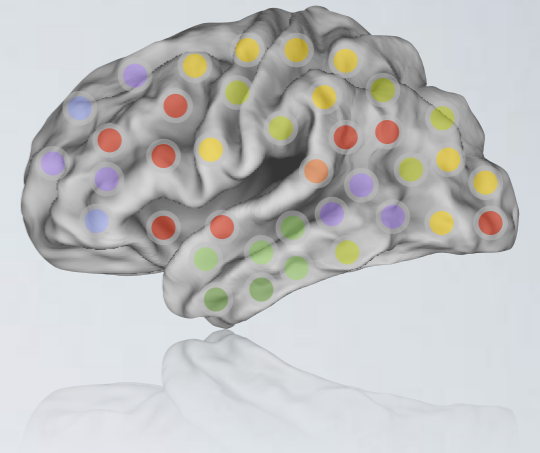
limbična in lateralno  
prefrontalna  
konektivnost



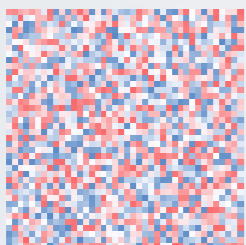
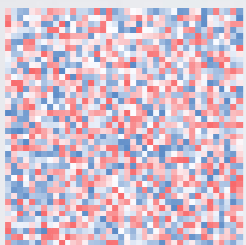
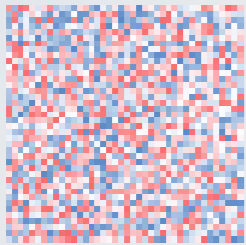
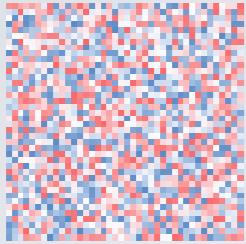
anksioznost  
nespečnost



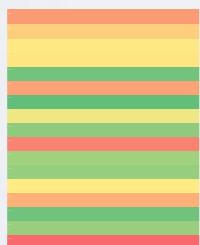
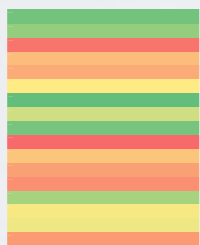
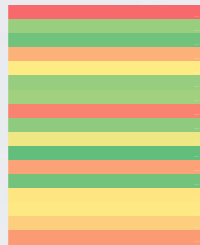
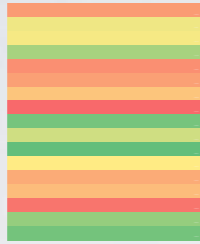
**4 podskupine**



vzorec  
funkcijske  
povezanosti



izraženost  
simptomov  
depresije



**220**



**2 dimenziji**

frontostriatalna in  
orbitofrontalna  
konektivnost



anhedonija  
psihomotorna  
retardiranost

limbična in lateralno  
prefrontalna  
konektivnost



anksioznost  
nespečnost



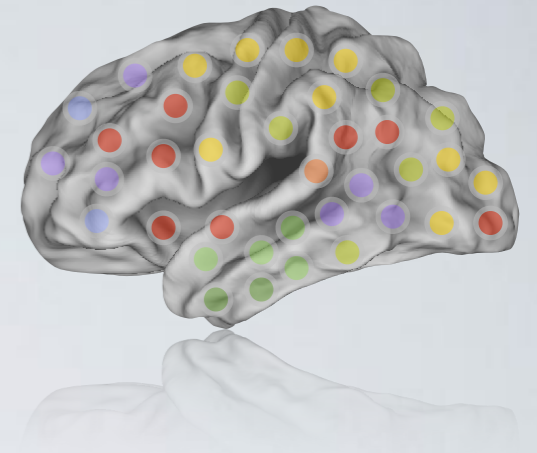
**4 podskupine**



**strojno učenje**

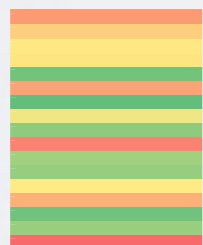
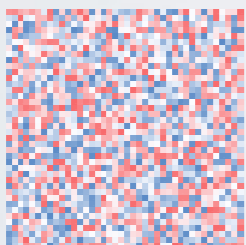
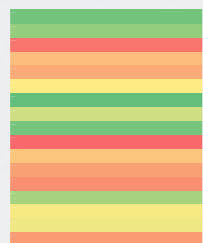
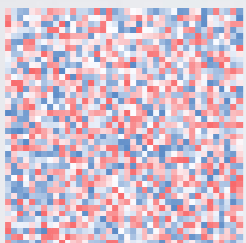
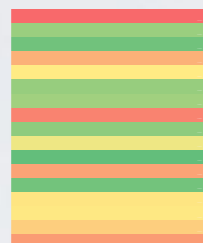
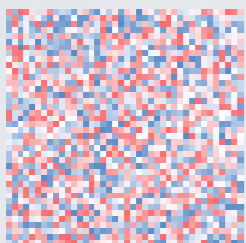
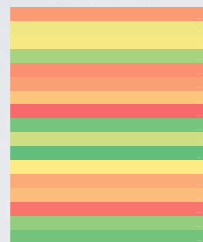
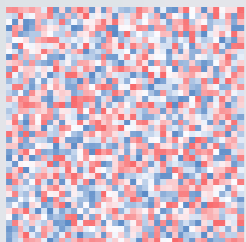
**333 | 378**

**89%**



vzorec  
funkcijske  
povezanosti

izraženost  
simptomov  
depresije



**220**



**2 dimenziji**

frontostriatalna in  
orbitofrontalna  
konektivnost



anhedonija  
psihomotorna  
retardiranost

limbična in lateralno  
prefrontalna  
konektivnost



anksioznost  
nespečnost



**4 podskupine**



**strojno učenje**

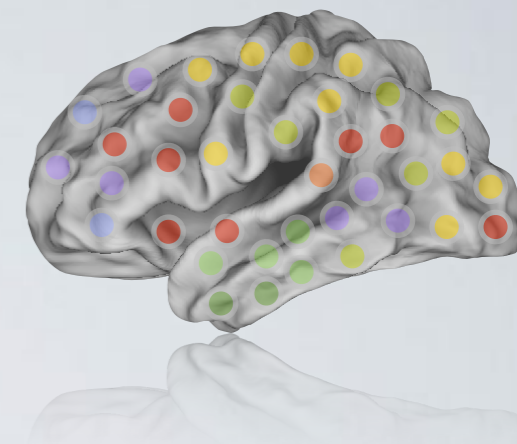
**333 | 378**

**89%**

ponovitev

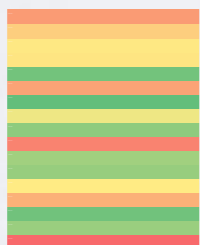
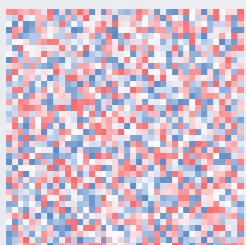
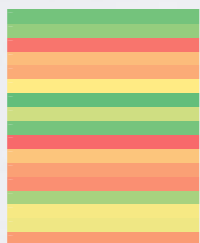
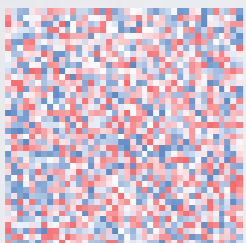
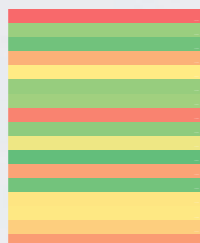
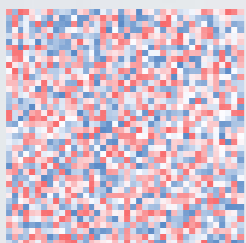
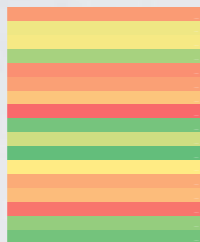
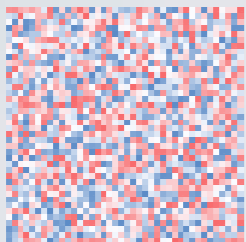
**50**

**90%**



vzorec  
funkcijske  
povezanosti

izraženost  
simptomov  
depresije



**220**



**2 dimenziji**

frontostriatalna in  
orbitofrontalna  
konektivnost



anhedonija  
psihomotorna  
retardiranost

limbična in lateralno  
prefrontalna  
konektivnost



anksioznost  
nespečnost



**4 podskupine**



**strojno učenje**

**333 | 378**

89%

ponovitev

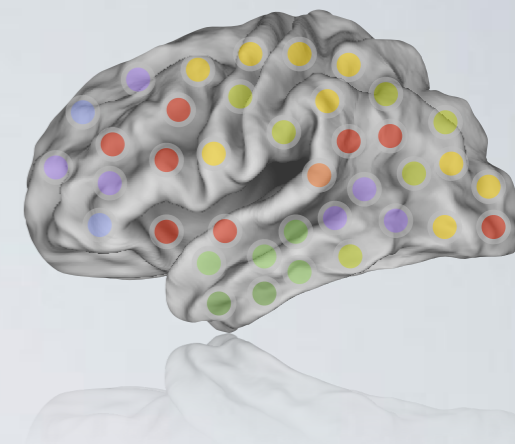
**50**

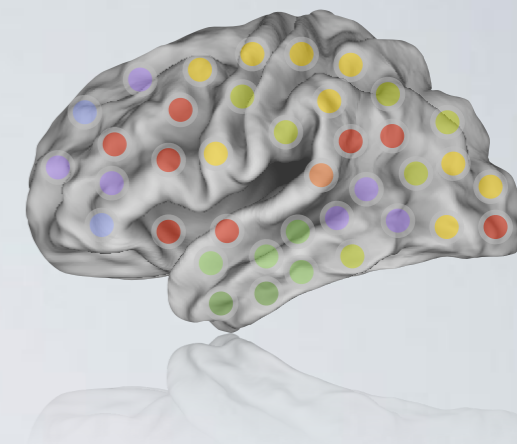
90%

nov vzorec

**125 | 352**

86%

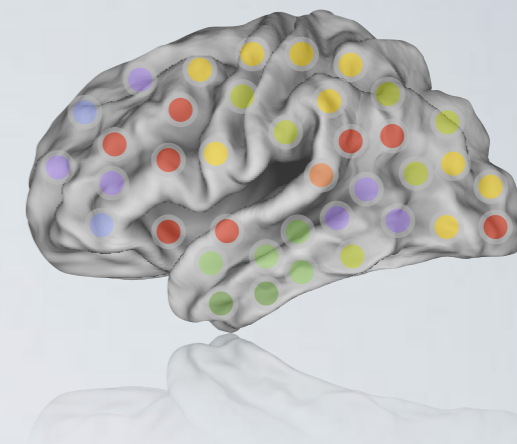




**4 podskupine**



**strojno učenje**



**4 podskupine**



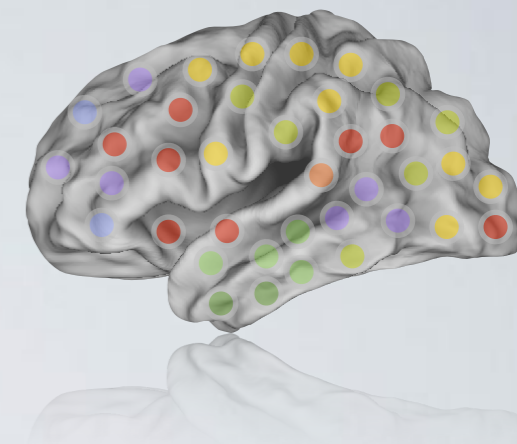
**strojno učenje**



generalizirana  
motnja anksioznosti

**39**

**69% (59%)**

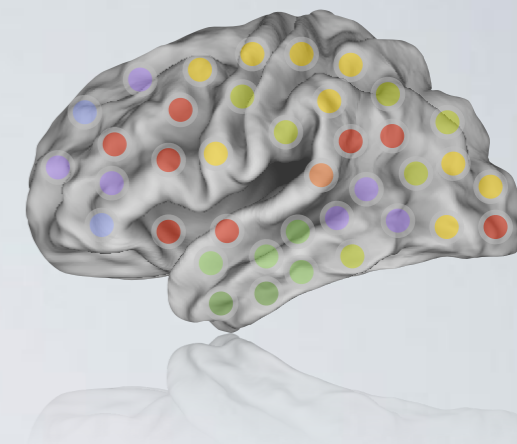


## 4 podskupine



### strojno učenje



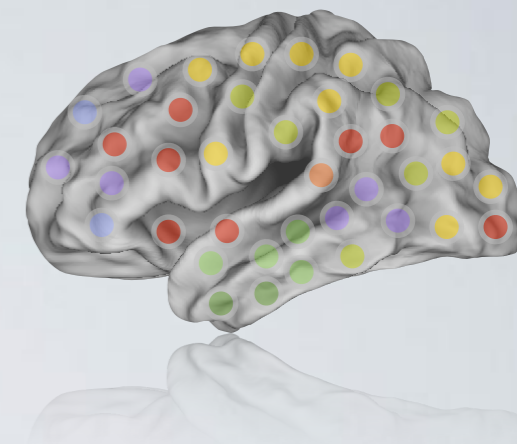


**4 podskupine**



**strojno učenje**





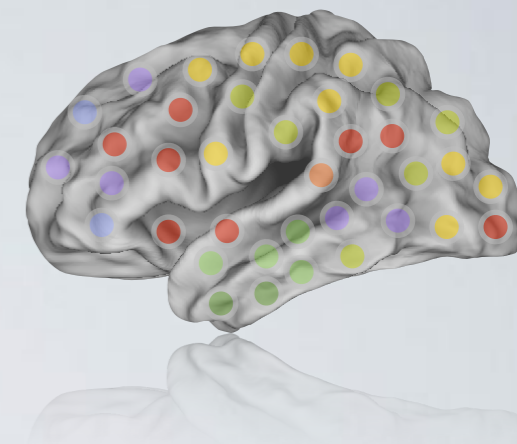
**4 podskupine**



strojno učenje



**rTMS**  
**124**



**4 podskupine**

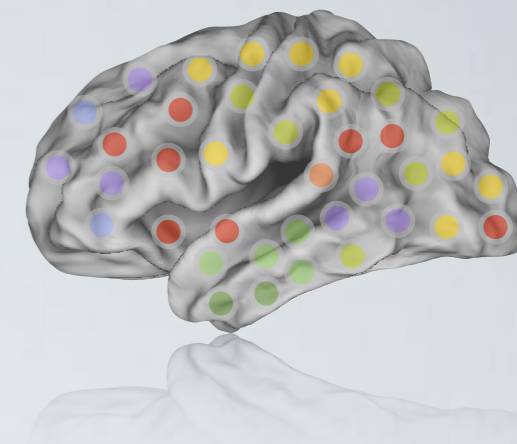


strojno učenje



**rTMS**  
**124**

<b>82%</b>	<b>25%</b>
<b>61%</b>	<b>29%</b>



**4 podskupine**



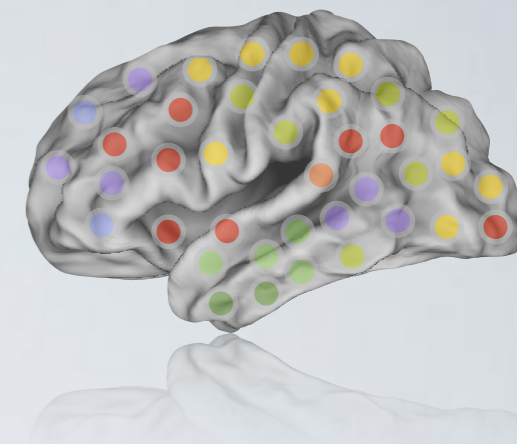
strojno učenje



**rTMS**  
**124**

vzorec  
povezanosti  
**89%**

<b>82%</b>	<b>25%</b>
<b>61%</b>	<b>29%</b>



**4 podskupine**



strojno učenje



**rTMS**  
**124**

vzorec  
povezanosti  
**89%**

<b>82%</b>	<b>25%</b>
<b>61%</b>	<b>29%</b>

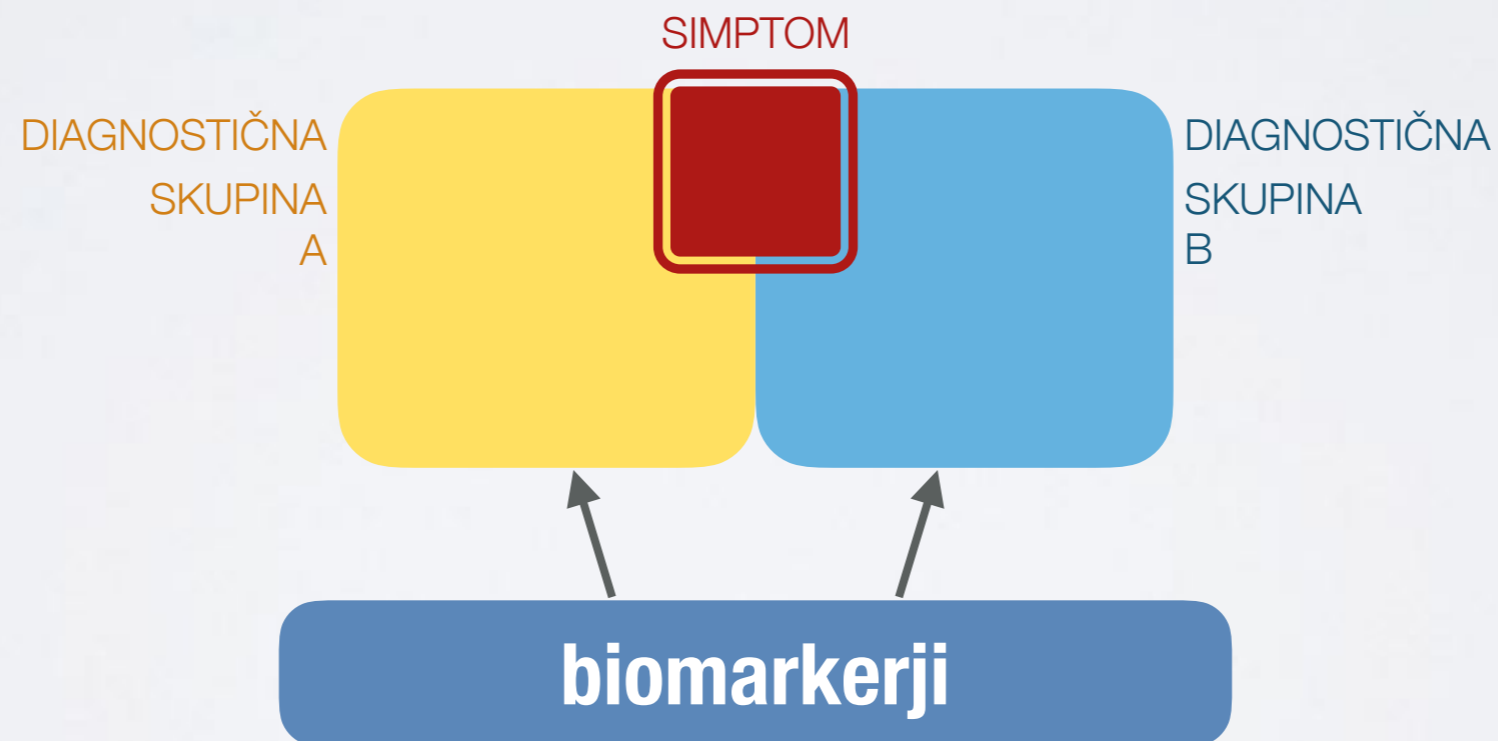
simptomi  
**62%**

razvoj novih  
terapij

**zdravljenje**

ujemanje bolnikov  
in zdravljenj

**psihopatologija**



razvoj novih  
terapij

**zdravljenje**

ujemanje bolnikov  
in zdravljenj

**psihopatologija**

DIAGNOSTIČNA  
SKUPINA  
A

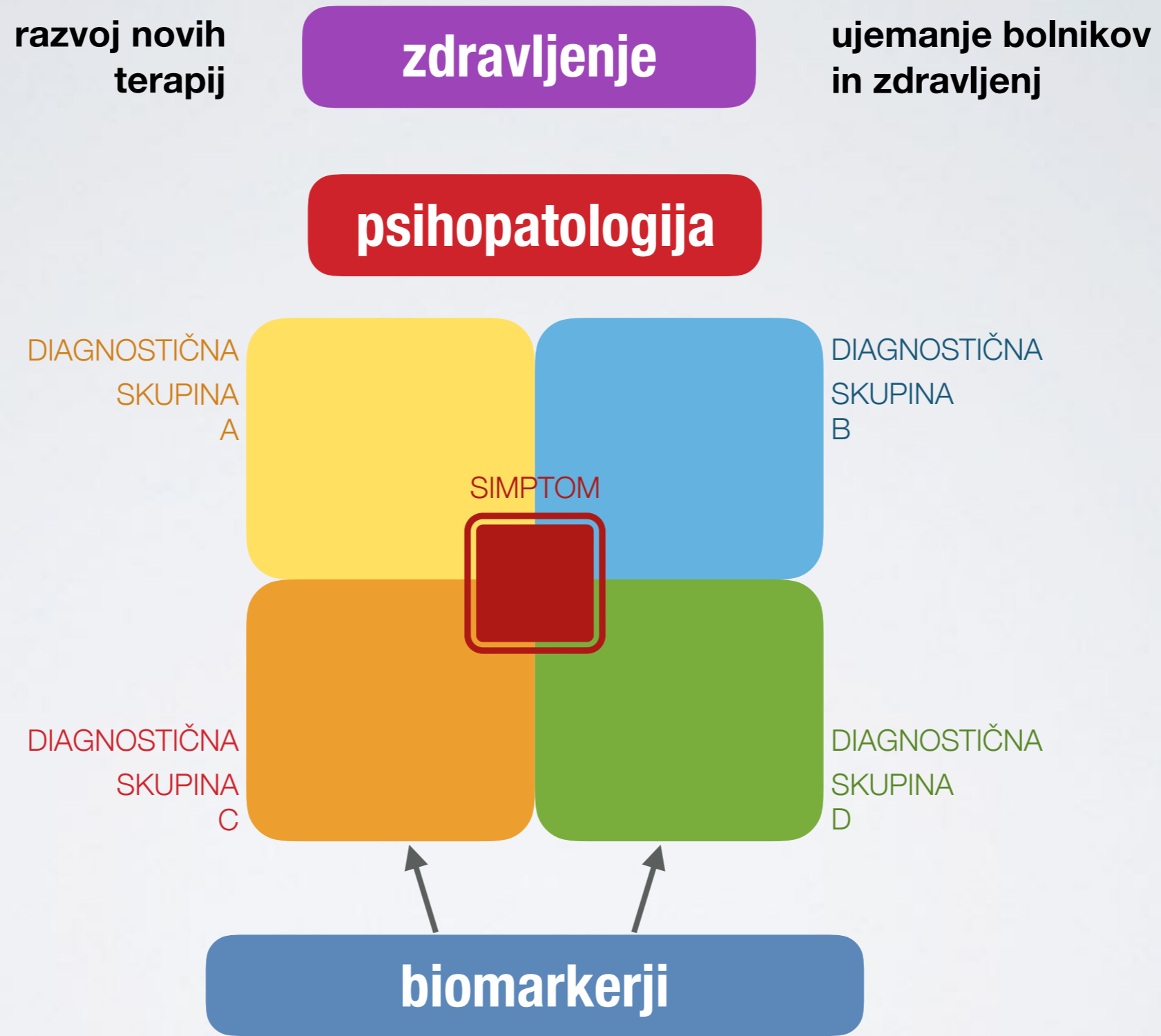
DIAGNOSTIČNA  
SKUPINA  
B

SIMPTOM

DIAGNOSTIČNA  
SKUPINA  
C

DIAGNOSTIČNA  
SKUPINA  
D

**biomarkerji**





# Biomarkerji depresije pri izbiri ustreznega zdravljenja

Predavatelj:  
Grega Repovš

Teden  
možganov 2018

Na sanjah  
svet stoji



VZAJEMNA  
zdravstvena zavarovalnica

FENS | Federation of  
European  
Neuroscience  
Societies



TEDEN  
MOŽGANOV



SiNAPSA  
SLOVENSKO DRUŠTVO ZA NEUROZNAKOSLOVJE  
SLOVENIAN NEUROSCIENCE ASSOCIATION



za možgane

THE  
DANA  
FOUNDATION

12.–18. marec