JAMA Psychiatry | Original Investigation

Prediction Models of Functional Outcomes for Individuals in the Clinical High-Risk State for Psychosis or With Recent-Onset Depression

A Multimodal, Multisite Machine Learning Analysis

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Soyeon Kim

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Structural neuroimaging as clinical predictor: A review of machine learning applications

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Montreal Neurological Institute, McGill University, Montreal, Quebec, Canada

A R T I C L E I N F O

Keywords:
Neuroimaging
Structural magnetic resonance imaging
Machine learning
Predictive modeling
Alzheimer
Autism
Multiple sclerosis
Parkinson
SVMs
Ensembling
Cross-validation

A B S T R A C T

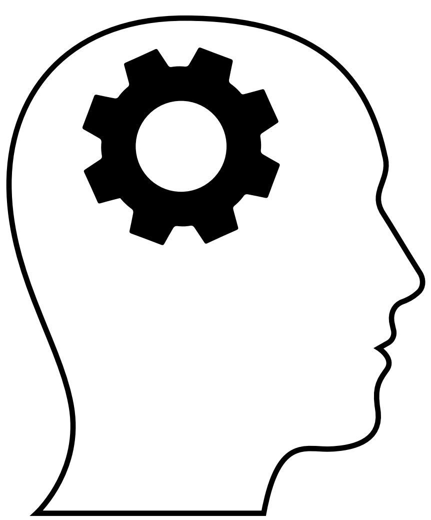
In this paper, we provide an extensive overview of machine learning techniques applied to structural magnetic resonance imaging (MRI) data to obtain clinical classifiers. We specifically address practical problems commonly encountered in the literature, with the aim of helping researchers improve the application of these techniques in future works. Additionally, we survey how these algorithms are applied to a wide range of diseases and disorders (e.g. Alzheimer's disease (AD), Parkinson's disease (PD), autism, multiple sclerosis, traumatic brain injury, etc.) in order to provide a comprehensive view of the state of the art in different fields.

Research

JAMA Psychiatry | Original Investigation

Use of Machine Learning to Determine Deviance in Neuroanatomical Maturity Associated With Future Psychosis in Youths at Clinically High Risk

Yoonho Chung, MS; Jean Addington, PhD; Carrie E. Bearden, PhD; Kristin Cadenhead, MD; Barbara Cornblatt, PhD; Daniel H. Mathalon, PhD, MD; Thomas McGlashan, MD; Diana Perkins, MD; Larry J. Seidman, PhD; Ming Tsuang, MD, PhD; Elaine Walker, PhD; Scott W. Woods, MD, PhD; Sarah McEwen, PhD; Theo G. M. van Erp, PhD; Tyrone D. Cannon, PhD; for the North American Prodrome Longitudinal Study (NAPLS) Consortium and the Pediatric Imaging, Neurocognition, and Genetics (PING) Study Consortium



Clinical research

+

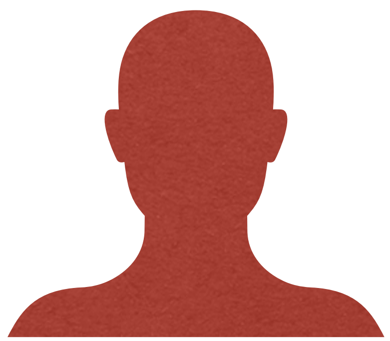
Machine Learning

Why do we use machine learning?

Diagnosis

Prognosis ➜ Intervention ➜ Prevention

Treatment decisions



Clinical high-risk (CHR)

nonpsychotic morbidity

neurocognitive & functional deficits

Major affective episode

risk for relapse

lifelong deficits

LinA,WoodSJ,NelsonB,BeavanA,McGorryP, Yung AR. Outcomes of nontransitioned cases in a sample at ultra-high risk for psychosis. *Am J Psychiatry*. 2015;172(3):249-258. doi:10.1176/appi.ajp .2014.13030418

BoraE,HarrisonBJ,YücelM,PantelisC. Cognitive impairment in euthymic major depressive disorder: a meta-analysis. *Psychol Med*. 2013;43 (10):2017-2026. doi:10.1017/S0033291712002085

Previous research

Clinical data

neurocognitive data

neurophysiological data

fMRI data

Psychosis

CannonTD,YuC,AddingtonJ,etal.An individualized risk calculator for research in prodromal psychosis. *Am J Psychiatry*. 2016;173 (10):980-988. doi:10.1176/appi.ajp.2016.15070890

Clinical baseline data

MRI model

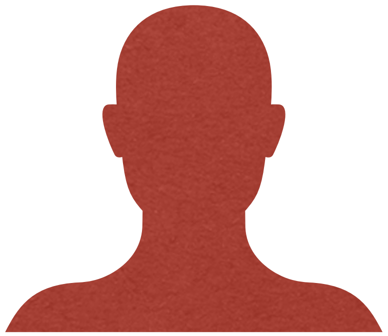
functional &
treatment
outcomes

global functioning

ChekroudAM,ZottiRJ,ShehzadZ,etal. Cross-trial prediction of treatment outcome in depression: a machine learning approach. *Lancet Psychiatry*. 2016;3(3):243-250. doi:10.1016/S2215 -0366(15)00471-X

Kambeitz-IlankovicL,MeisenzahlEM,CabralC, et al. Prediction of outcome in the psychosis prodrome using neuroanatomical pattern classification. *Schizophr Res*. 2016;173(3):159-165. doi:10.1016/j.schres.2015.03.005

Purpose



Clinical high-risk (CHR)

Recent-onset depression (ROD)

sMRI model

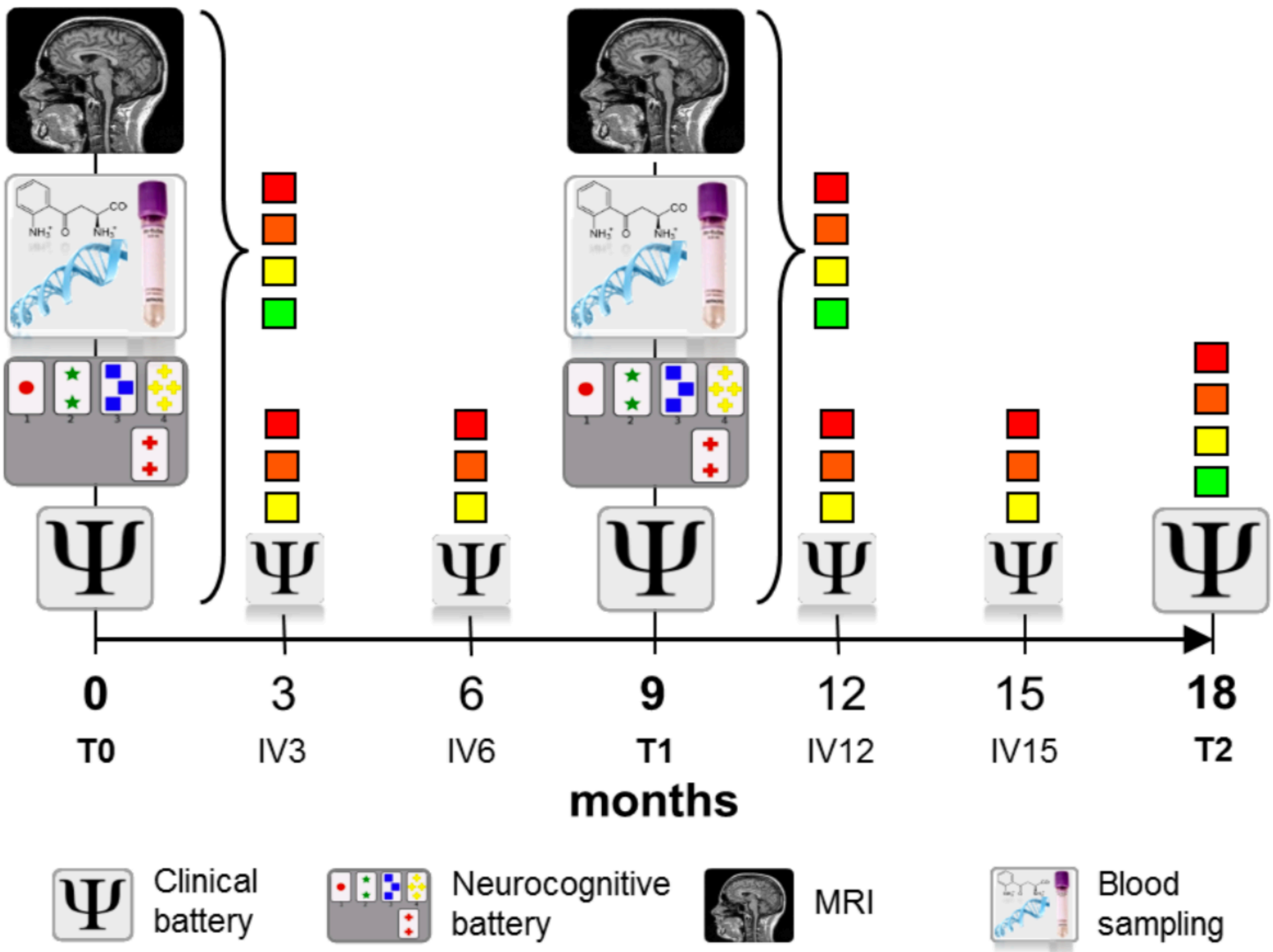
Clinical model

Combined model

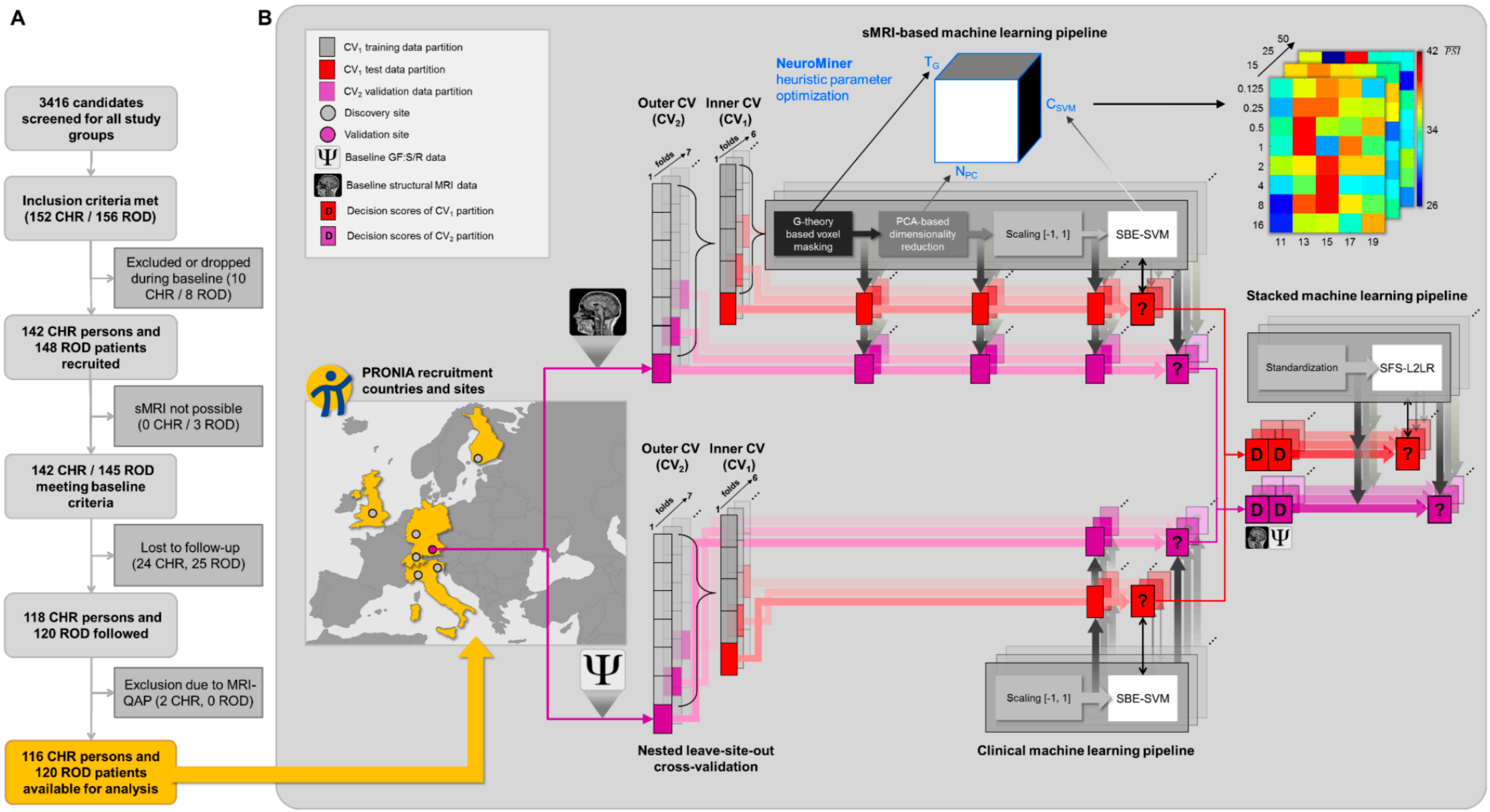
Social fucntioning

Role functioning

Methods


0
3
6
9
12
15
18
T0
IV3
IV6
T1
IV12
IV15
T2
months
Clinical battery
Neurocognitive battery
MRI
Blood sampling

Methods


A
B
3416 candidates screened for all study groups
Inclusion criteria met (152 CHR / 156 ROD)
Excluded or dropped during baseline (10 CHR / 8 ROD)
142 CHR persons and 148 ROD patients recruited
sMRI not possible (0 CHR / 3 ROD)
142 CHR / 145 ROD meeting baseline criteria
Lost to follow-up (24 CHR, 25 ROD)
118 CHR persons and 120 ROD followed
Exclusion due to MRI-QAP (2 CHR, 0 ROD)
116 CHR persons and 120 ROD patients available for analysis
CV_1 training data partition
CV_1 test data partition
CV_2 validation data partition
Discovery site
Validation site
Baseline GF:S/R data
Baseline structural MRI data
Decision scores of CV_1 partition
Decision scores of CV_2 partition
PRONIA recruitment countries and sites
sMRI-based machine learning pipeline
NeuroMiner heuristic parameter optimization
T_G
C_{SVM}
N_{PC}
Outer CV (CV_2)
Inner CV (CV_1)
folds
G-theory based voxel masking
PCA-based dimensionality reduction
Scaling [-1, 1]
SBE-SVM
Stacked machine learning pipeline
Standardization
SFS-L2LR
Nested leave-site-out cross-validation
Clinical machine learning pipeline

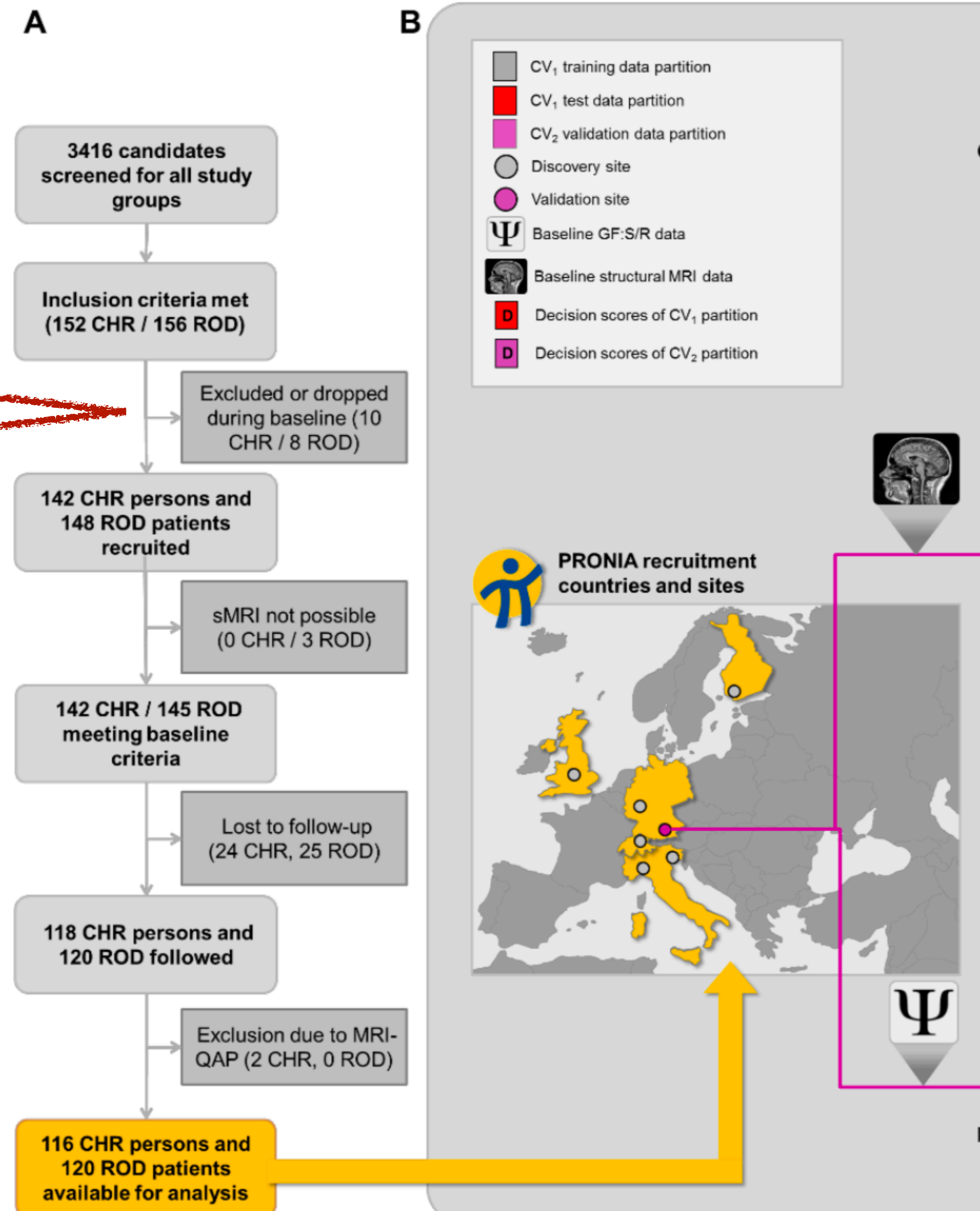
Methods

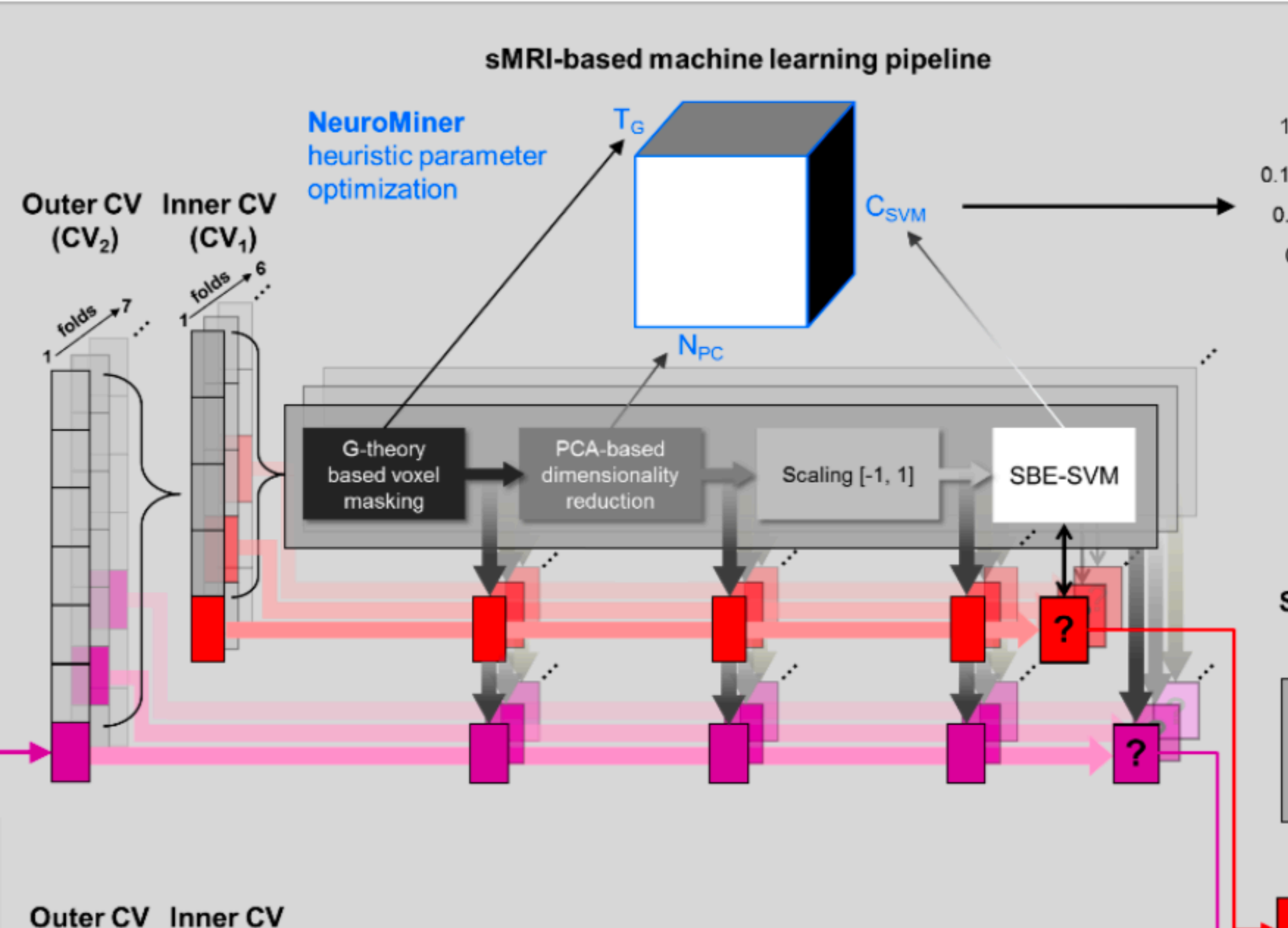
Recent Onset Depression (ROD)
- meet criteria for major depression fulfilled within the past 3 months

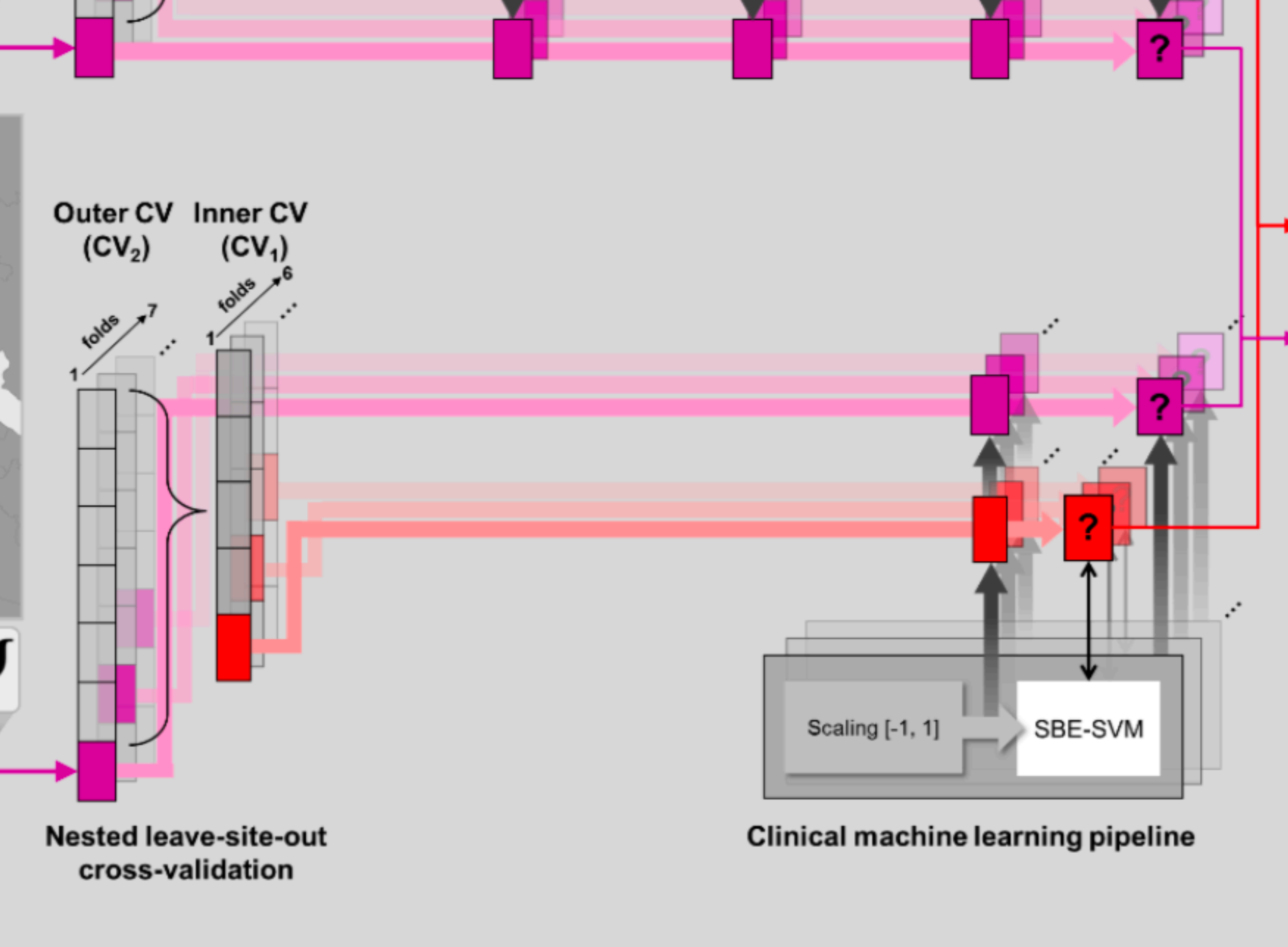
Clinical High Risk (CHR)
- Cognitive disturbances
- ultra-high-risk criteria for psychosis

1. IQ below 70
2. head trauma with loss of consciousness
3. neurological or somatic disorders
4. alcohol dependence

…




sMRI-based machine learning pipeline
NeuroMiner
heuristic parameter
optimization
Outer CV
(CV2)
Inner CV
(CV1)
folds
1
7
6
TG
CSVM
NPC
G-theory
based voxel
masking
PCA-based
dimensionality
reduction
Scaling [-1, 1]
SBE-SVM
?
?
Outer CV
Inner CV



Outer CV
(CV2)
Inner CV
(CV1)
folds
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7
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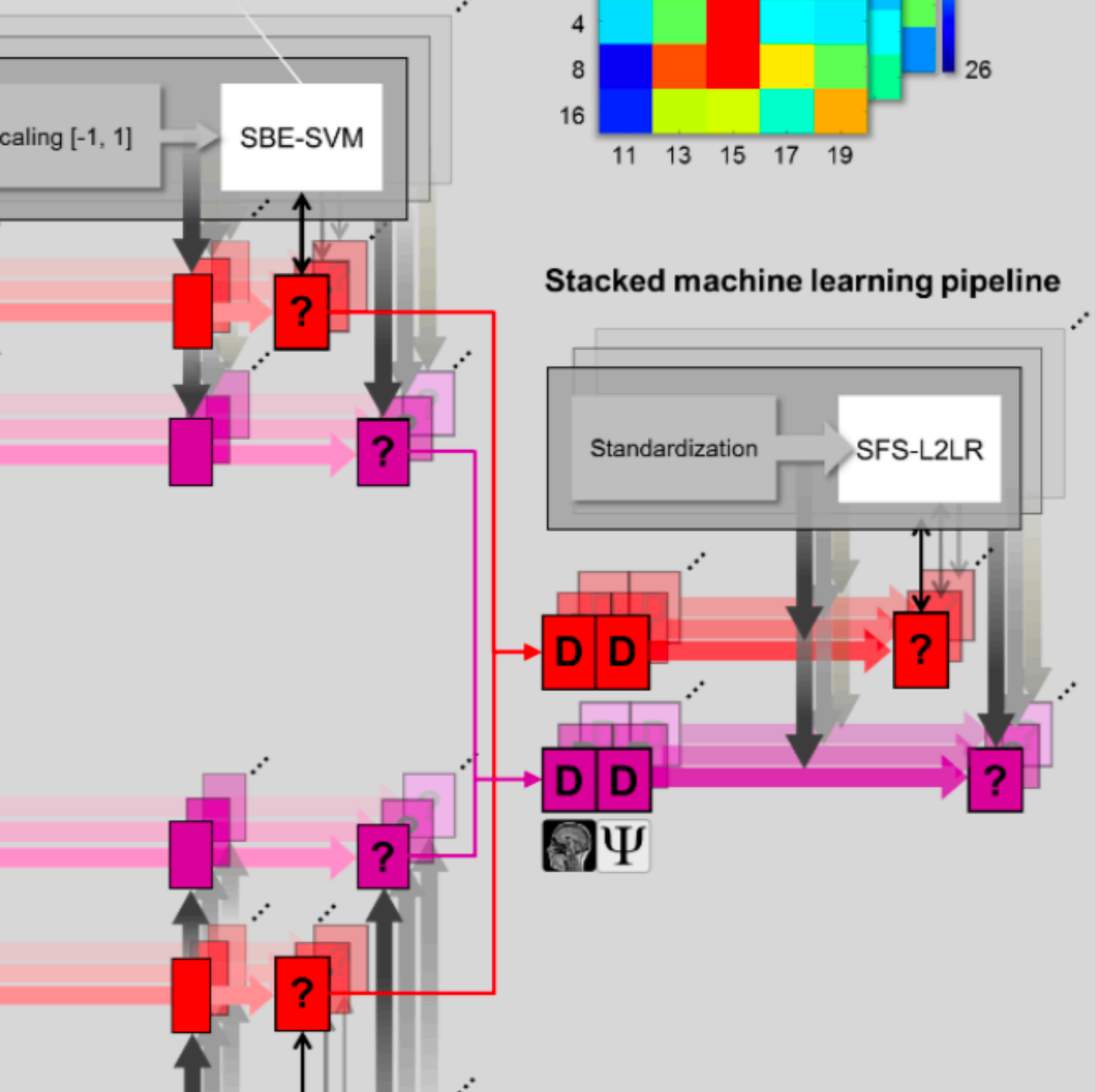
Nested leave-site-out
cross-validation
Clinical machine learning pipeline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caling [-1, 1]
SBE-SVM
Stacked machine learning pipeline
Standardization
SFS-L2LR
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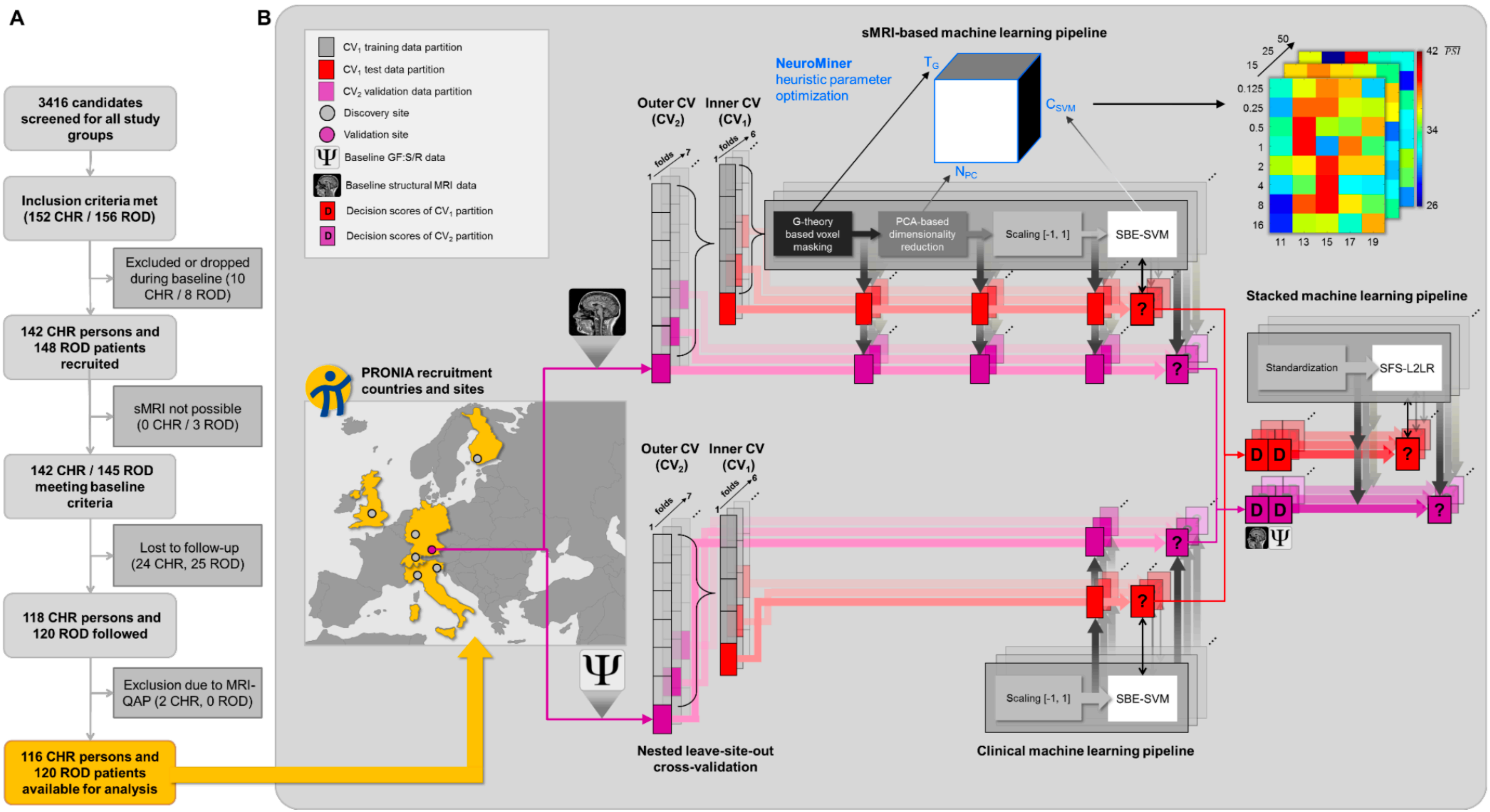
Ψ

Methods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Clinical machine learning pipeline

Methods

- **Clinical data**
  - Global functioning
  - Social functioning
  - Role scales
- **MRI data**
  - Gray matter volume

Methods

- **3 models**
  - Clinical data model
  - sMRI model
  - Combined model
- **Models vs Expert raters**
- **Transferability**

Methods

- MRI scanning

PRONIA Site	Model	Field Strength	Coil Channels	Flip Angle	TR [ms]	TE [ms]	Voxel Size [mm]	FOV	Slice Number
Munich	Philips Ingenia	3T	32	8	9.5	5.5	0.97 x 0.97 x 1.0	250 x 250	190
Milan Niguarda	Philips Achieva Intera	1.5T	8	12	Short-est (8.1)	Short-est (3.7)	0.93 x 0.93 x 1.0	240 x 240	170
Basel	SIEMENS Verio	3T	12	8	2000	3.4	1.0 x 1.0 x 1.0	256 x 256	176
Cologne	Philips Achieva	3T	8	8	9.5	5.5	0.97 x 0.97 x 1.0	250 x 250	190
Birmingham	Philips Achieva	3T	32	8	8.4	3.8	1.0 x 1.0 x 1.0	288 x 288	175
Turku	Philips Ingenuity	3T	32	7	8.1	3.7	1.0 x 1.0 x 1.0	256 x 256	176
Udine	Philips Achieva	3T	8	12	Short-est (8.1)	Short-est (3.7)	0.93 x 0.93 x 1.0	240 x 240	170

Latest News

No news available.

NeuroMiner (NM)

NeuroMiner Downloads

- Neurominer (Mac/Win/Linux; matlab R2016b or above)
- Neurominer Manual
- Example Data

PRONIA Team

About NeuroMiner

Machine learning techniques are poised to become clinically useful methods that may be used for diagnosis, prognosis, and treatment decisions. Despite this, they are currently underutilised in medical studies and, even more in psychiatric research because most current tools require strong programming and computational engineering skills (e.g., scikit-learn, caret, Weka, nilearn). While there are some great tools that do not require programming experience (e.g., PRoNTo), these are often focused on making predictions from specific data domains such as neuroimaging data. This highlights a pressing need for user-friendly machine learning software that makes advanced methods available to clinical researchers from different fields aiming at collaboratively developing diagnostic, predictive, and prognostic tools for precision medicine approaches.

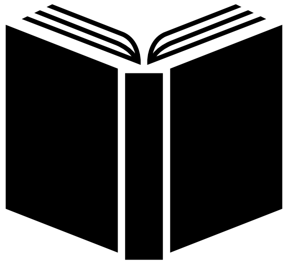
Results

- Social functioning

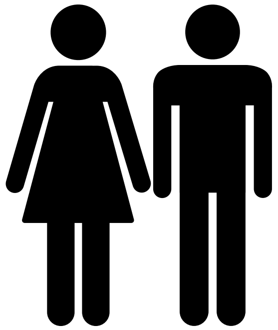
Impaired social functioning group

Age ↓

Education ↓



Having a partnership ↓



Results

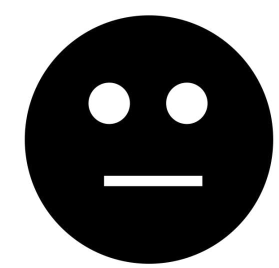
- Social functioning

Impaired social functioning group

Global functioning

SIPS
(Standardized interview
for prodromal symptoms)

PANSS
(Positive and negative syndrome scale)



Results

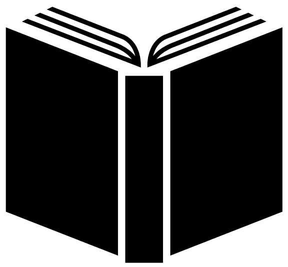
- Role functioning

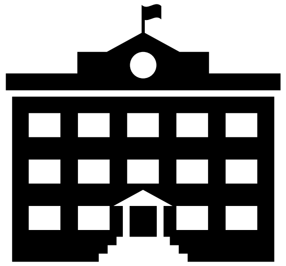
Impaired role functioning group

Age ↓

Education ↓

Education years repeated ↑





Results

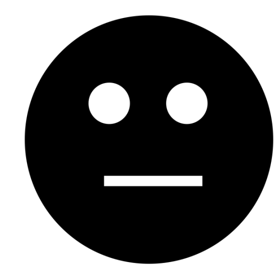
- Role functioning

Impaired role functioning group

Global functioning ↓

SIPS ↑
(Standardized interview
for prodromal symptoms)

PANSS ↑
(Positive and negative syndrome scale)



Results

- Machine learning analysis

	Social functioning	Role functioning
	Balanced Accuracy, %	Balanced Accuracy, %
CHR		
Clinical model	76.9	67.7
sMRI model	76.2	56.7
Combined model	82.7	64.8
Expert prognosis	71.8	70.4
ROD		
Clinical model	66.1	57.4
sMRI model	65.0	55.3
Combined model	70.3	62.6
Expert prognosis	59.6	57.9

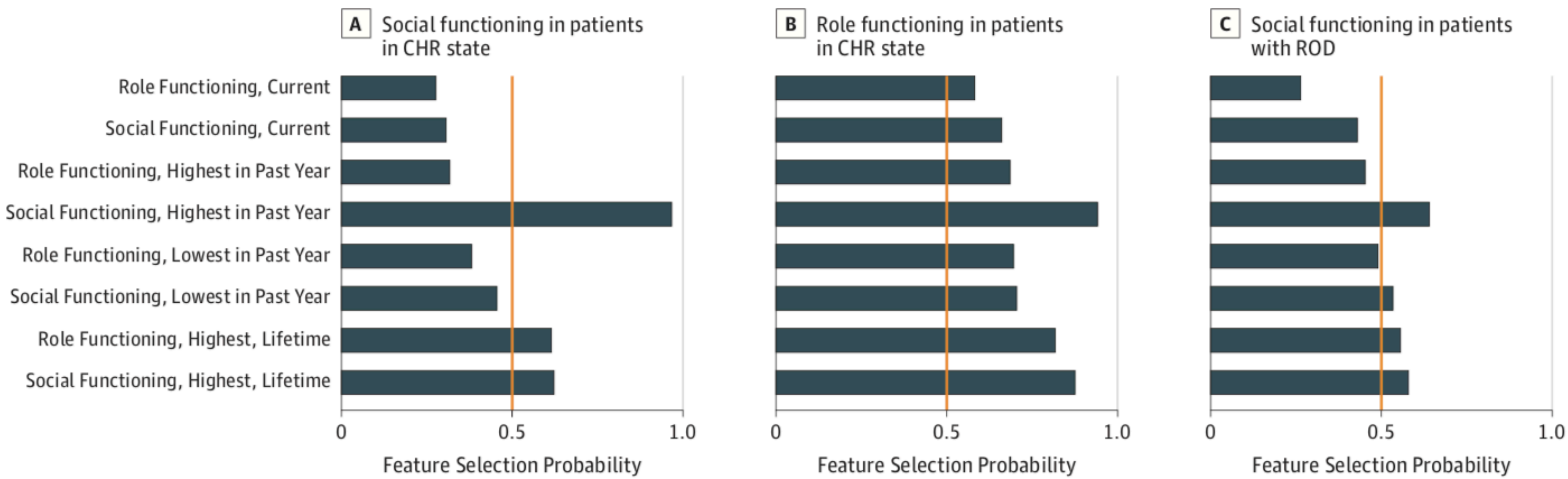
Results

- **Machine learning analysis : Transdiagnostic generalizability**

	Social functioning	Role functioning
	Balanced Accuracy, %	Balanced Accuracy, %
Clinical model	70.1	65.1
sMRI model	58.9	56.6
Combined model	66.8	64.9

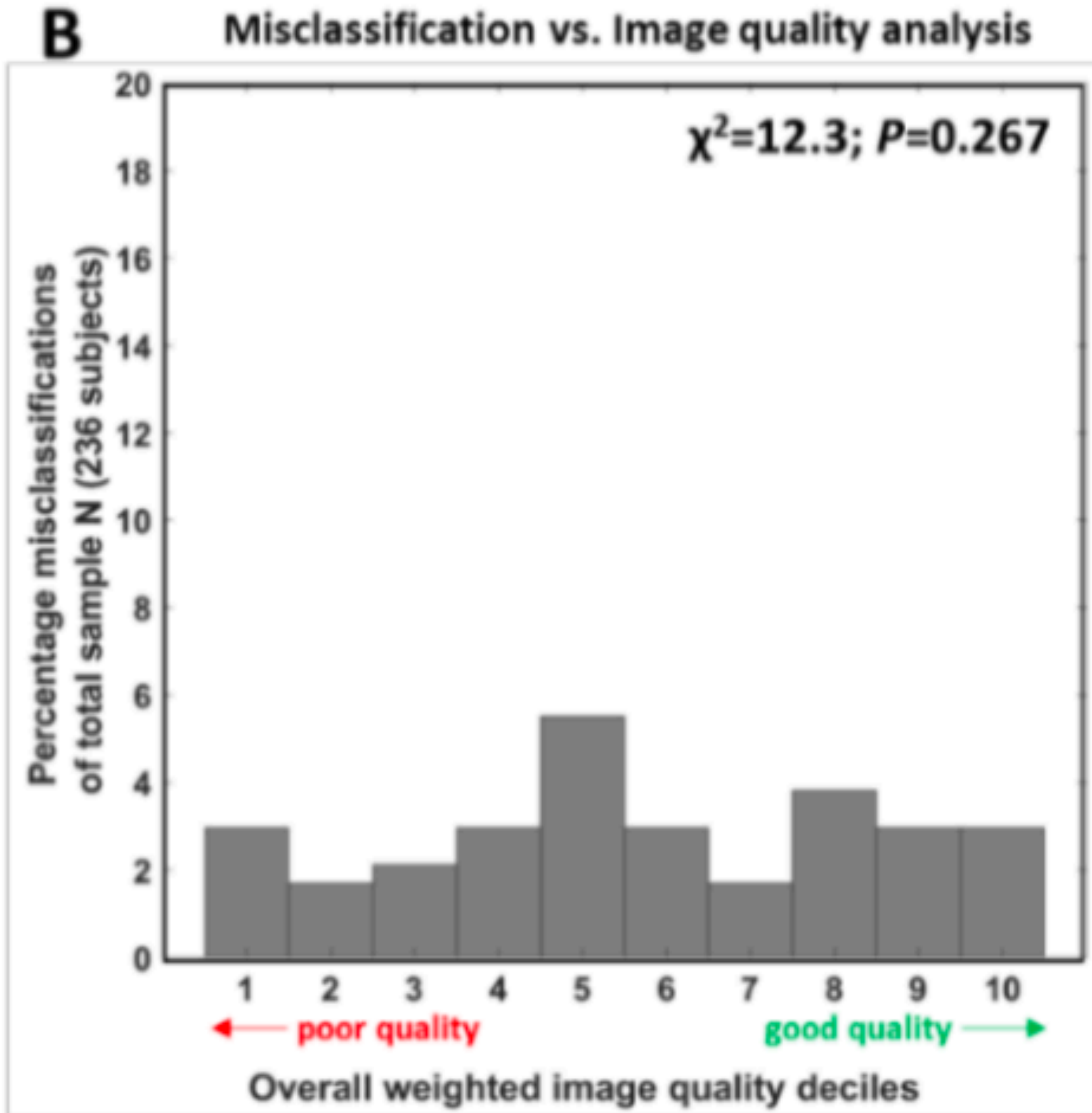
Results

- Machine learning analysis : Clinical data model



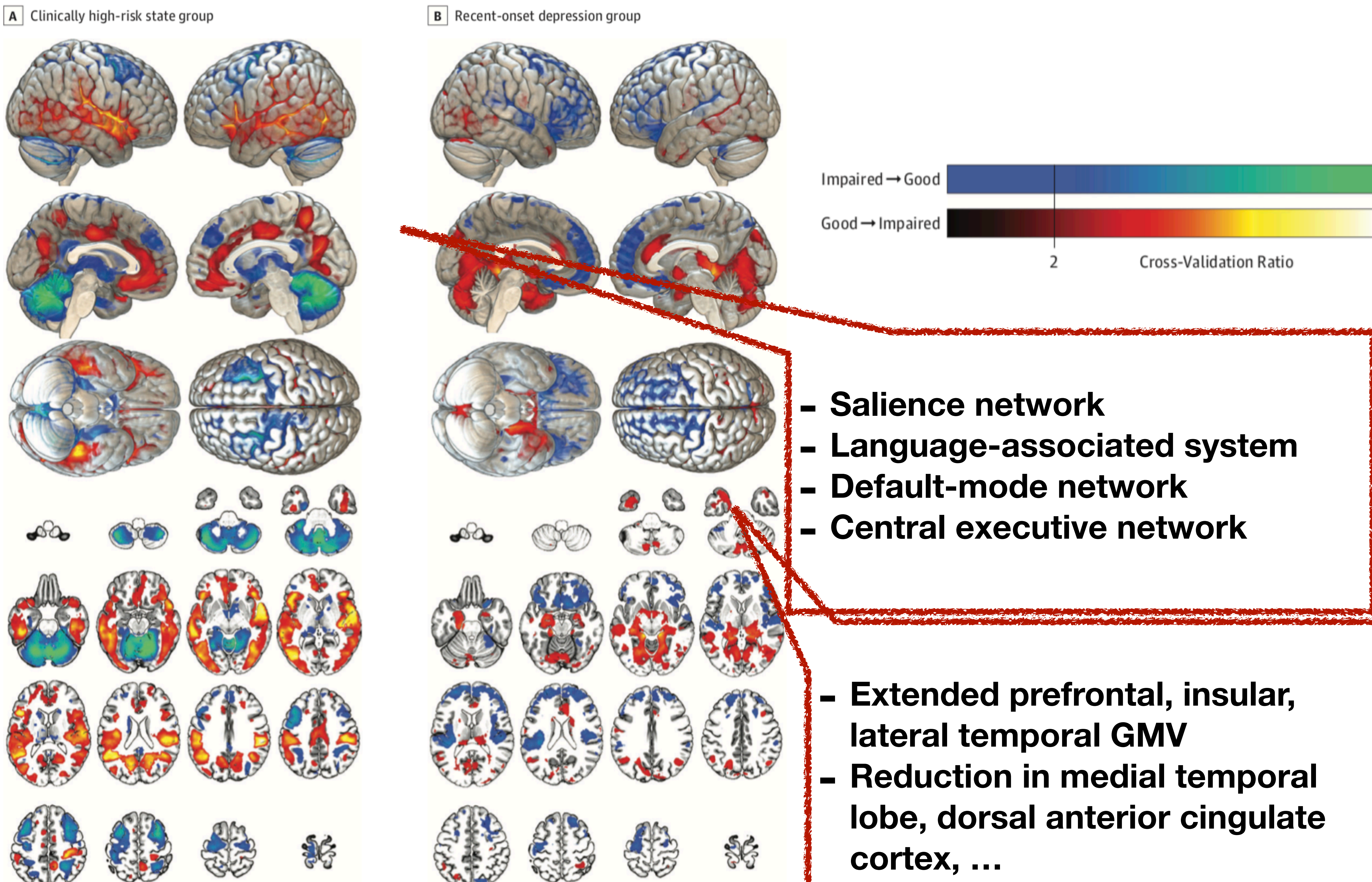
Results

- Machine learning analysis : sMRI model



Results

- Machine learning analysis : sMRI model



- Salience network
- Language-associated system
- Default-mode network
- Central executive network

- Extended prefrontal, insular, lateral temporal GMV
- Reduction in medial temporal lobe, dorsal anterior cingulate cortex, …

Results

- Transdiagnostic Prognostic Generalization

Modality	Study group	TP	TN	FP	FN	Sens	Spec	BAC	PPV	NPV	PSI	AUC	P_{PERM}
Models trained to predict impaired (≤7) vs. good (>7) GF:S outcomes at follow-up													
Generalization to the prediction of transition to psychosis													
Clinical classifiers	CHR	2	58	50	6	25.0	53.7	39.4	3.9	90.6	-5.5	0.39	0.910
sMRI classifiers	CHR	**8**	**49**	**59**	**0**	**100**	**45.4**	**72.7**	**11.9**	**100**	**11.9**	**0.73**	**0.014**
Combined classifi-ers	CHR	5	49	59	3	62.5	45.4	53.9	7.8	94.2	2.0	0.54	0.238
Generalization to the prediction of symptomatic depression													
Clinical classifiers	CHR	**13**	**52**	**36**	**0**	**100**	**59.1**	**79.5**	**26.5**	**100**	**26.5**	**0.79**	**<.001**
Clinical classifiers	ROD	15	45	30	10	60.0	60.0	60.0	33.3	81.8	15.2	0.58	0.243
sMRI classifiers	CHR	9	38	50	4	69.2	43.2	56.2	15.3	90.5	5.73	0.63	0.195
sMRI classifiers	ROD	15	40	35	10	60.0	53.3	56.7	30.0	80.0	10.0	0.56	0.243
Combined classifi-ers	CHR	**12**	**43**	**45**	**1**	**92.3**	**48.9**	**70.6**	**21.1**	**97.7**	**18.8**	**0.75**	**0.032**
Combined classifi-ers	ROD	17	34	41	8	68.0	45.3	56.7	29.3	81.0	10.3	0.57	0.243
Generalization to the prediction of having at least 1 DSM-IV-TR diagnosis at the T1 examination (mood, anxiety, substance abuse disor-ders)													
Clinical classifiers	CHR	**25**	**47**	**24**	**6**	**80.7**	**65.7**	**73.2**	**51.0**	**88.5**	**39.5**	**0.77**	**0.027**
Clinical classifiers	ROD	20	38	25	17	54.1	60.3	57.2	44.4	69.1	13.5	0.53	0.281
sMRI classifiers	CHR	22	33	37	9	71.0	47.1	59.1	37.3	78.6	15.9	0.65	0.138
sMRI classifiers	ROD	19	32	31	18	51.4	50.8	51.1	38.0	64.0	2.0	0.50	0.425
Combined classifi-ers	CHR	25	38	32	6	80.7	54.3	67.5	43.9	86.4	30.2	0.72	0.054
Combined classifi-ers	ROD	24	29	34	13	64.9	46.0	55.4	41.4	69.1	10.4	0.53	0.243

Conclusion

- Combined model outperforms in most cases

- Machine learning can be used for the prediction and prevention of social functioning impairments

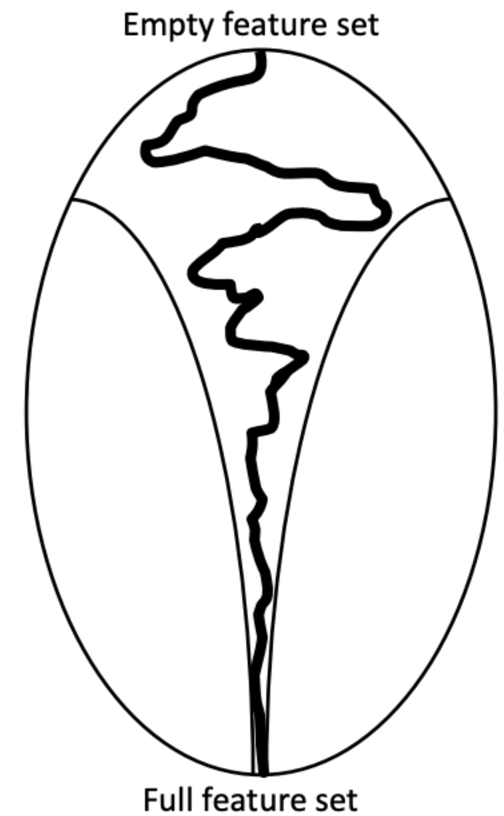
Further study..

- Inclusion of environmental and clinical variables
- Add value of different data combinations
- More diverse patient populations

Thank you 😊

Sequential forward search

1. Start with the empty set $Y_0 = \{\emptyset\}$
2. Select the next best feature $x^+ = \underset{x \notin Y_k}{\arg\max}\, J(Y_k + x)$
3. Update $Y_{k+1} = Y_k + x^+;\ k = k + 1$
4. Go to 2



Sequential backward search

1. Start with the full set $Y_0 = X$
2. Remove the worst feature $x^- = \underset{x \in Y_k}{\arg\max}\, J(Y_k - x)$
3. Update $Y_{k+1} = Y_k - x^-;\ k = k + 1$
4. Go to 2