PET based classification for clinical diagnosis

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Clinical Problem

Elderly subjects

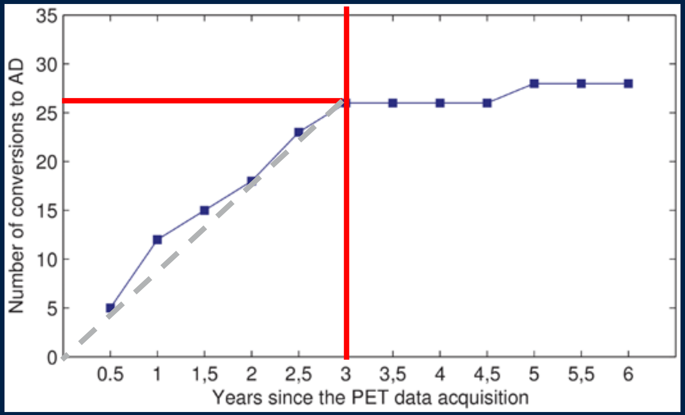
- showing ‘Mild Cognitive Impairment’ (MCI)
- some evolve to Alzheimer’s Disease (AD)
- some remain MCI

Question:

Can we predict which ones are “early AD”?

Segovia, 2014, *PLoS ONE*

Study Data



Population (n=46)

- all diagnosed with MCI
- monitoring over 6 years
- Groups:
  - 26 AD-converters (within 3 years),
  - 20 stable-MCI

Data

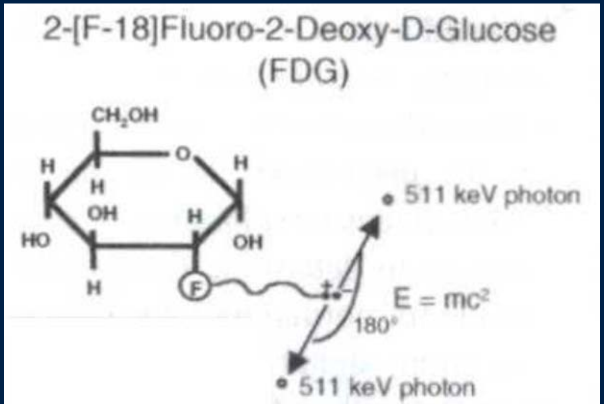
- 1 FDG-PET image at 1st visit
- Age + MMSE + 5 neuropsychological scores

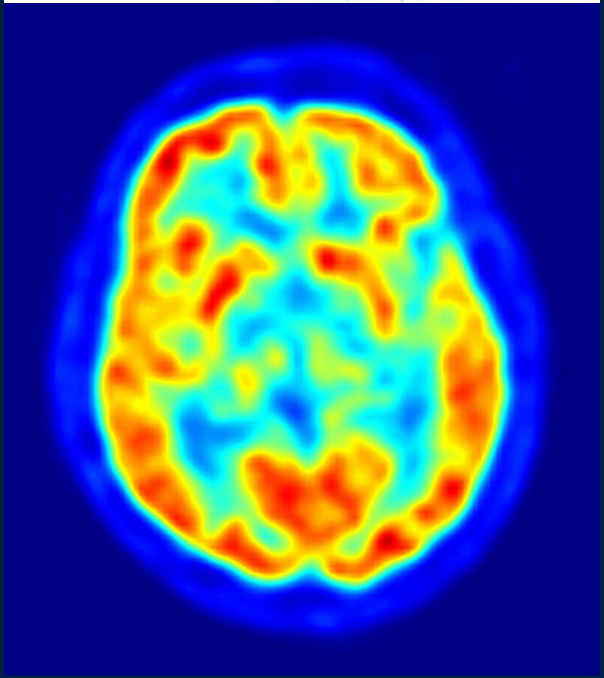
Folstein, 1975, *JoPR*
Adam, 2007, JoCEN
Artero, 2006, DGCD

FDG-PET IMAGING

^{18}F-FDG :

- glucose analogue
- fixes itself in cells consuming glucose
- radioactive decay with ~110 min half-life





FDG-PET image :

= resting state energy metabolism

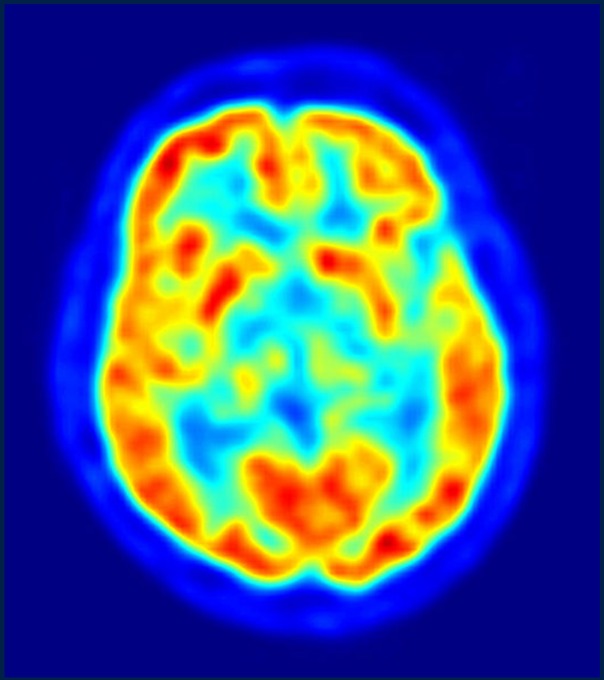
FDG-PET IMAGING ISSUES

Intensity scaling ?

- (semi-)quantitative values, e.g. “Standard Uptake Value” (SUV) → no scaling
- otherwise → scaling by
  - whole brain global signal, or
  - ROI signal, e.g. cerebellum

Partial volume effect correction?

- need structural MRI



Dukart, 2010, *NI*

FDG-PET IMAGING ISSUES

Spatial normalization based on:

- structural MRI (after coregistration),

  → need TPM matched for population age!
- PET images

  → need specific PET template for radiotracer, population age, scanner, reconstruction algorithm,…

→ Try to have both PET and sMRI data!

TECHNICAL ISSUES

Combination of imaging data and clinical scores

aka. feature combination

Dimension reduction of imaging data

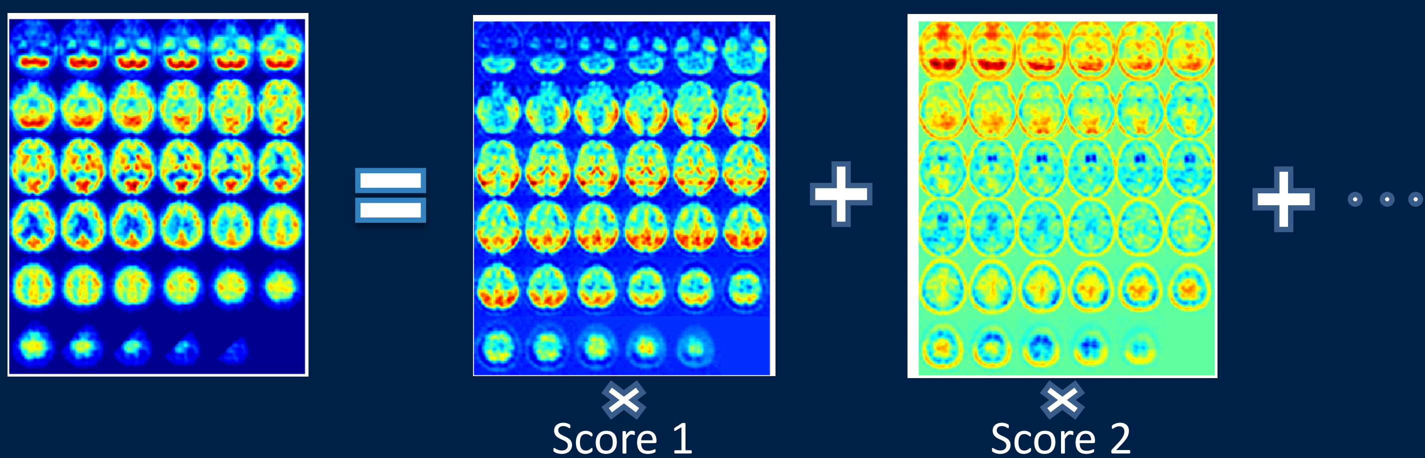
aka. feature extraction from images

Dimensionality Reduction

Principal Component Analysis (PCA)

→ Split images into orthogonal components

→ First components contains most of variance



Scores:

→ = projection of the images on the components

→ Summarize the image

Jolliffe, 2002

Dimensionality Reduction

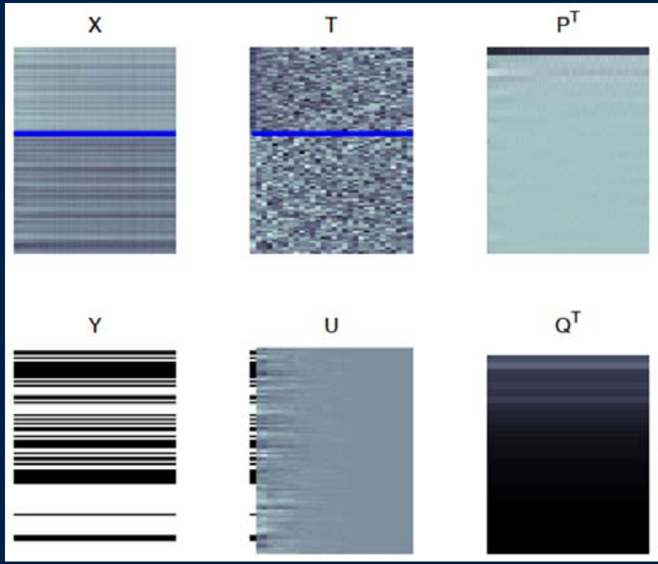
Partial Least Square (PLS)

→ "similar" to PCA but include label information

images→ $X = TP^t + E$

labels → $Y = UQ^t + F$

with P and Q orthogonal



Project images X onto p components of P

→ T summarizes images by p components score

Varmuza, 2009

Dimensionality Reduction

Independent Component Analysis (ICA)

- "Similar" to PCA but uses statistical independence criteria

$$X = AS \implies S = WX$$

and estimate $W = A^{-1}$ such that sources S are independent.

- ICA scores → Projection of the data on the independent components.
- Looking at A, we can choose components with the highest weight.

Illán, 2011, IS

DIMENSIONALITY REDUCTION

Selection of N components, e.g.:

- for PCA, use % of explained variance
- for PLS/ICA, use “Fisher Discriminant Ratio”

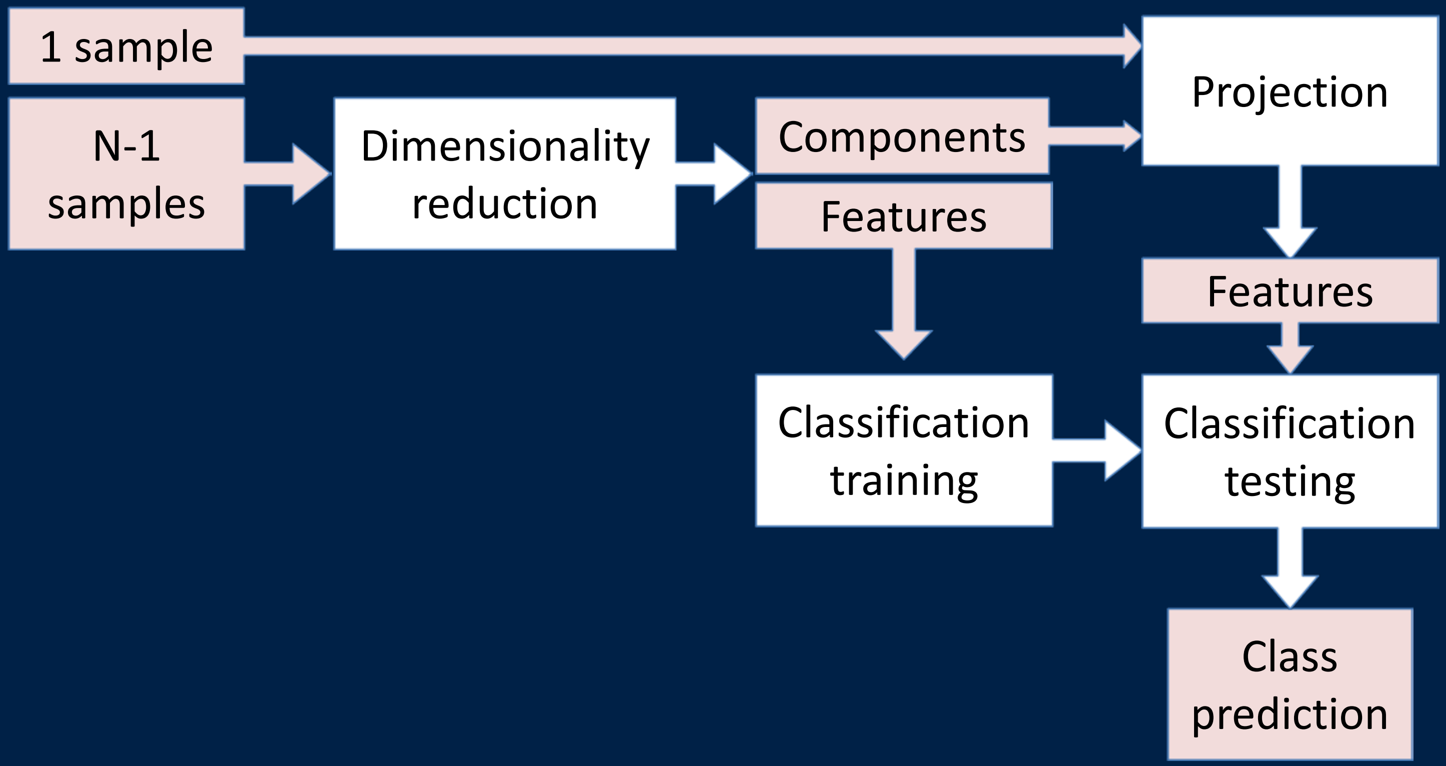
→ The fewer components

→ The fewer scores

→ The larger the dimensionality reduction

Webb, 2002

Dim. Reduction & Classification



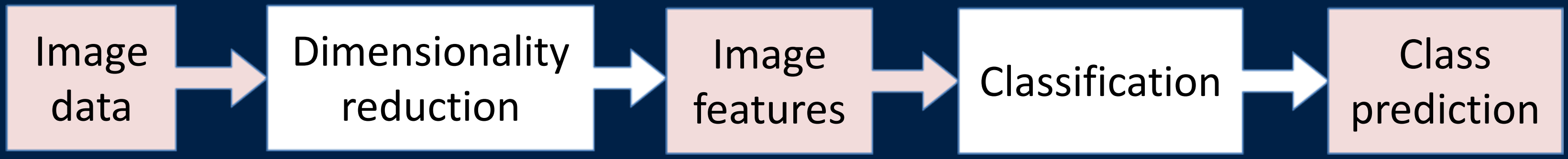
Note:

here SVM used for classification

Vapnik, 1998

Feature Combination

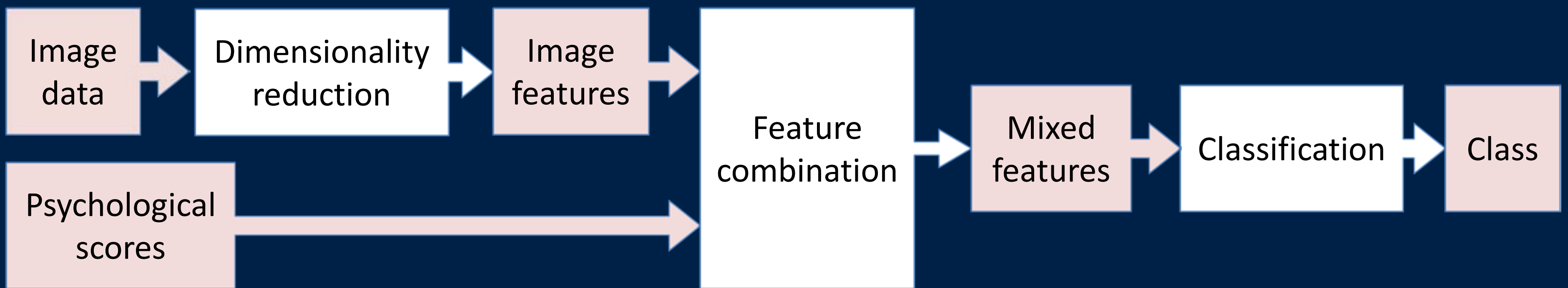
Classical approach



- Image only & no ‘clinical score’.
- (Usually image dimensionality reduction not required)

Feature Combination

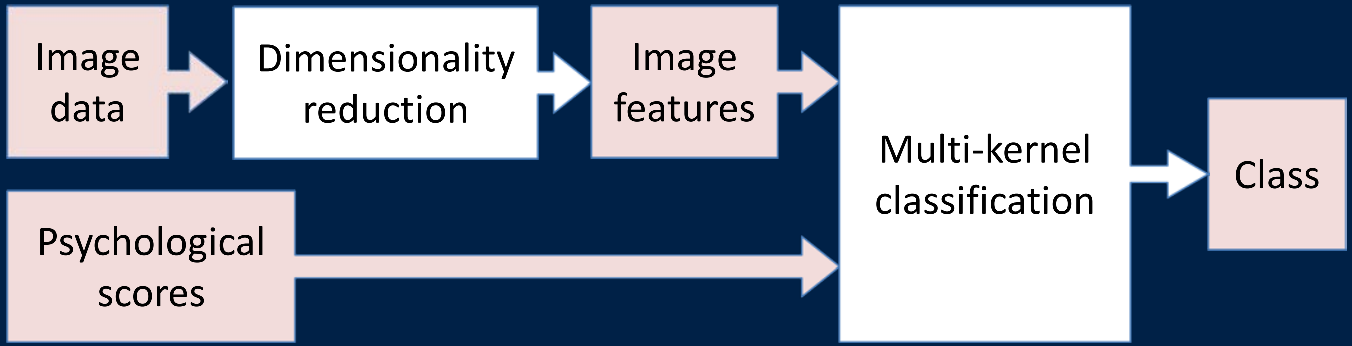
Early integration



- straightforward solution
- requires
  - image dimensionality reduction
  - feature scaling

Feature Combination

Intermediate integration

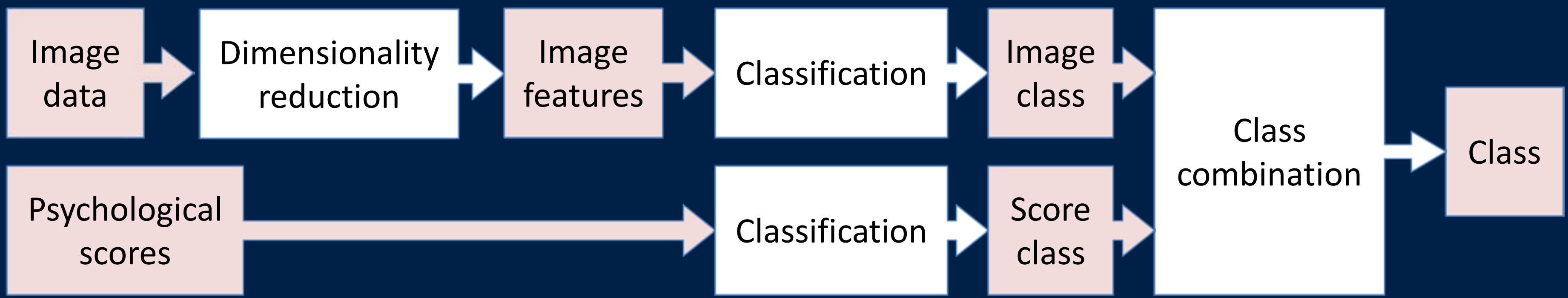


- keeps feature sets separated
- requires
  - Multi kernel learning

Gönen, 2011, *JMLR*

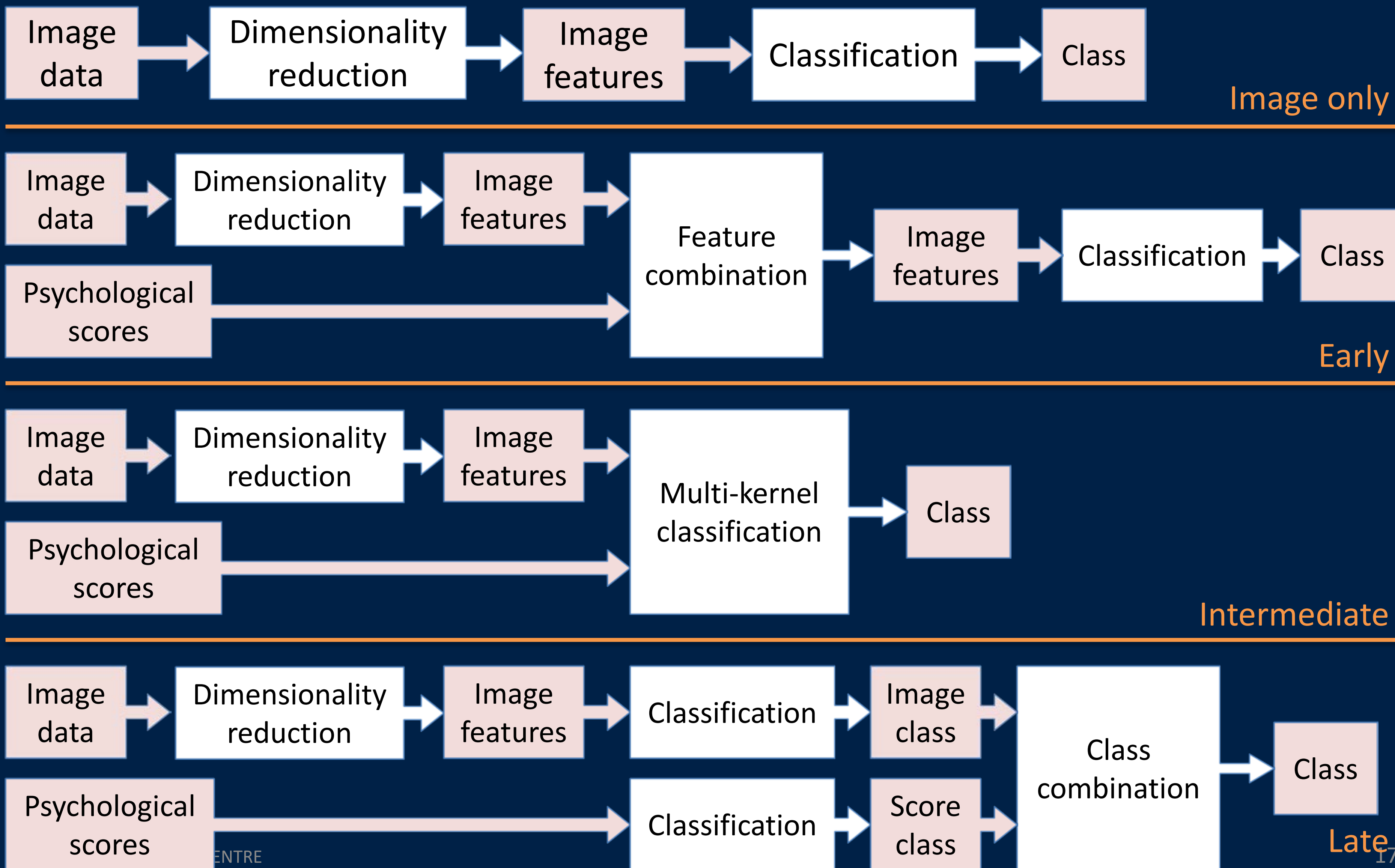
Feature Combination

Late integration



- keeps feature sets separated
- requires
  - classification per feature set
  - class combination

Feature Combination



RESULTS

Comping procedures based on accuracy, sensitivity/specificity, and AUC

- Only images

  PLS > PCA > ICA > ‘no reduction’

- With scores:

  Ψ-scores + MMSE + age > Ψ-scores alone

- Integration

  intermediate ≈ late > early

CONCLUSION & COMMENTS

Consider using

- image dimensionality reduction
- feature combination

BUT

- No "one size fit all" solution
- Probabilistic classification and/or confidence measure

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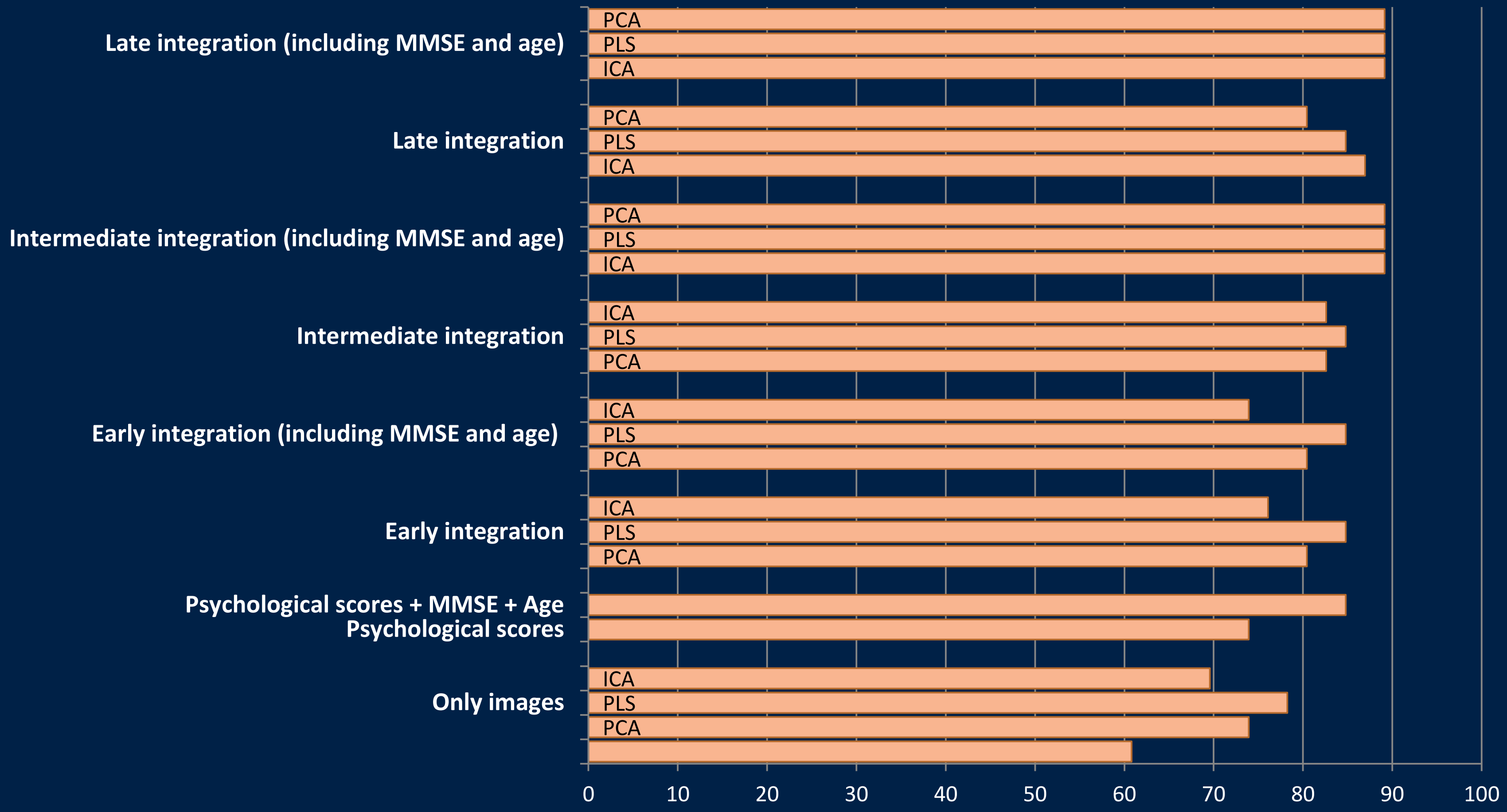
ACKNOWLEDGEMENTS

Fermin Segovia, Eric Salmon, Christine Bastin & the CRC team

Sponsors:

- University of Liège,
- the FRS-FNRS,
- the SAO-FRA
- the Inter University Attraction Pole P7/11

RESULTS



Late integration (including MMSE and age)
PCA
PLS
ICA
Late integration
PCA
PLS
ICA
Intermediate integration (including MMSE and age)
PCA
PLS
ICA
Intermediate integration
ICA
PLS
PCA
Early integration (including MMSE and age)
ICA
PLS
PCA
Early integration
ICA
PLS
PCA
Psychological scores + MMSE + Age
Psychological scores
Only images
ICA
PLS
PCA
0
10
20
30
40
50
60
70
80
90
100