The Impact of FLARE

An Integrated Investigation of Vascular Cognitive Impairment (VCI) in Europe (2008-2010)

Blossom Stephan

Lecturer

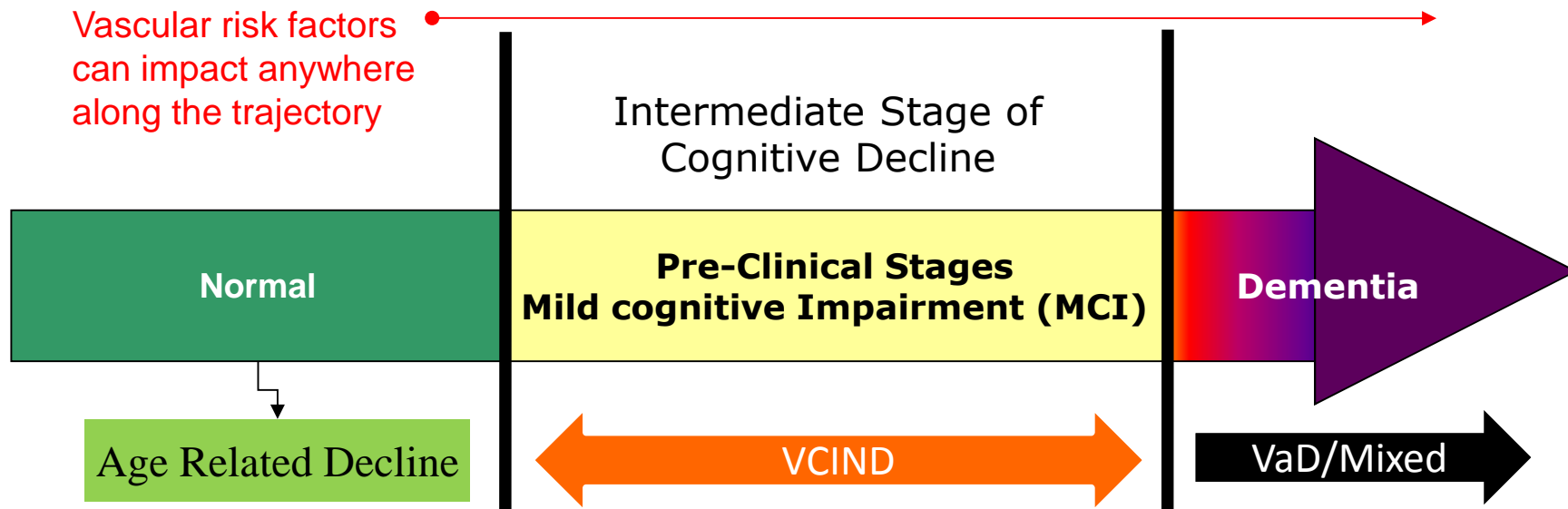Newcastle University

11 September 2012, Brussels

Overview

1. Background to the FLARE project
2. Research outcomes
3. Where to next
4. The contribution of FLARE to my career

Background: What is VCI?

- Group of cognitive disorders that share a presumed vascular cause
  - Vascular Disease Factors (e.g., stroke & hypertension)
  - Lifestyle Factors (e.g., tobacco use & physical inactivity)

Vascular risk factors can impact anywhere along the trajectory

Intermediate Stage of Cognitive Decline

Normal

**Pre-Clinical Stages
Mild cognitive Impairment (MCI)**

Dementia

Age Related Decline

VCIND

VaD/Mixed

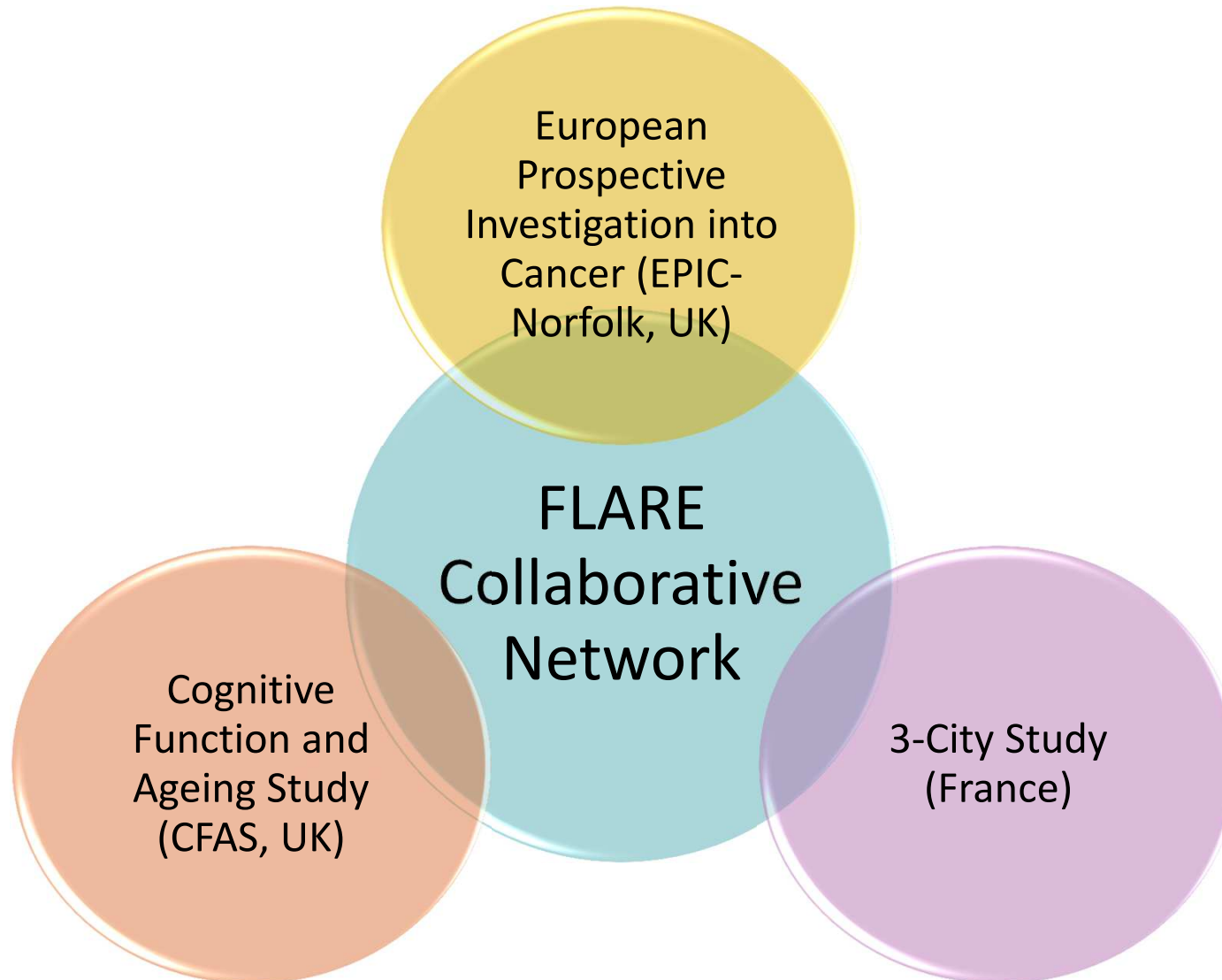Stephan et al., Alzheimer's Research & Therapy, 2009

Research Objectives

- Explore the interrelationships between vascular factors, cognitive decline and dementia using a population based approach

- Develop a predictive model (incorporating vascular markers) for identifying individuals at high risk of future dementia

Data Resources

European Prospective Investigation into Cancer (EPIC-Norfolk, UK)

FLARE Collaborative Network

Cognitive Function and Ageing Study (CFAS, UK)

3-City Study (France)

Data Resources

CFAS, UK
- N=13,004
- 65+ years
- Cognition, health, physical function, blood biomarkers & neuropathology

3C-Study, France
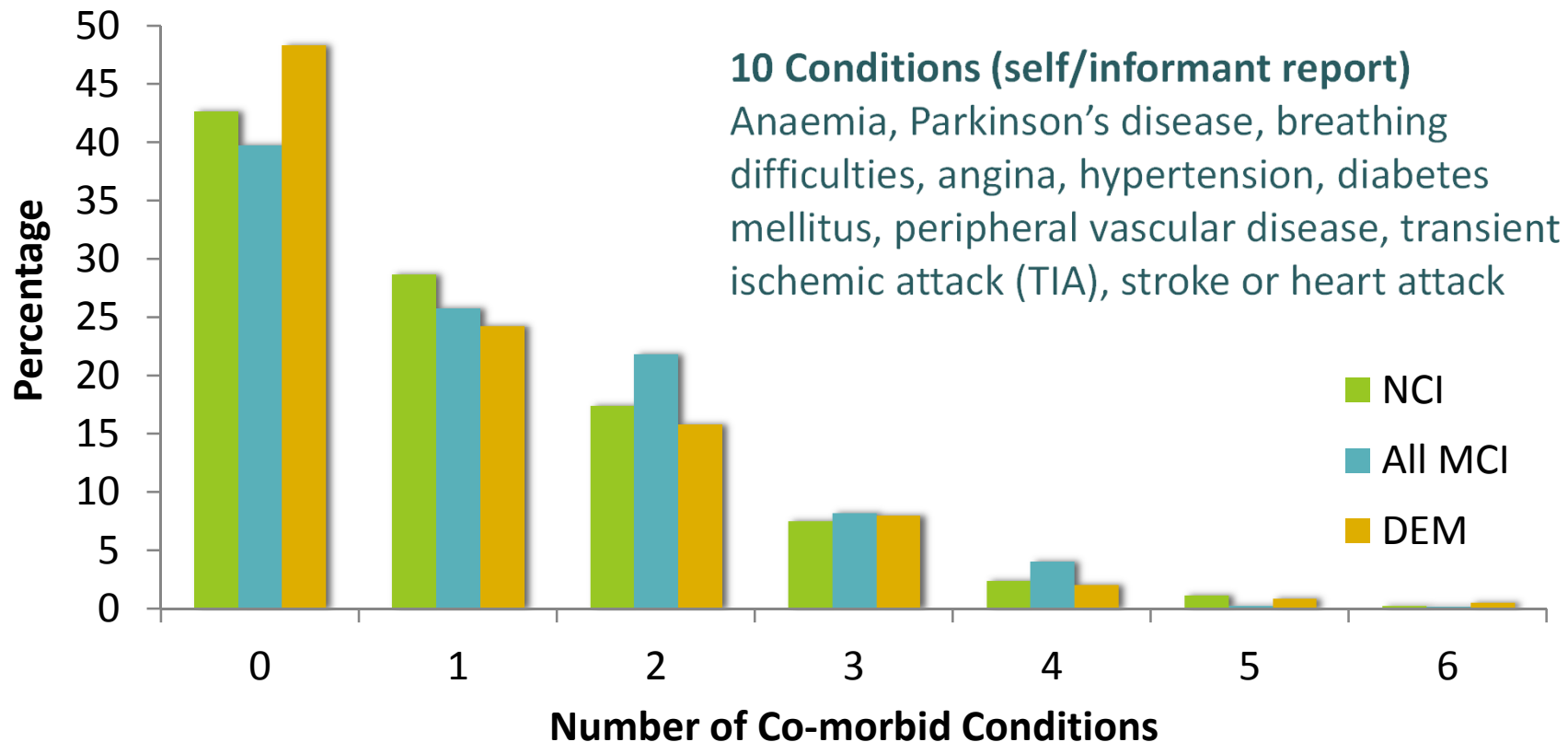- N=3,442
- 65+ years
- Cognition, vascular related disease, MRI & blood biomarkers

FLARE Collaborative Network

Cognitive Function and Ageing Study (CFAS, UK)

3-City Study (France)
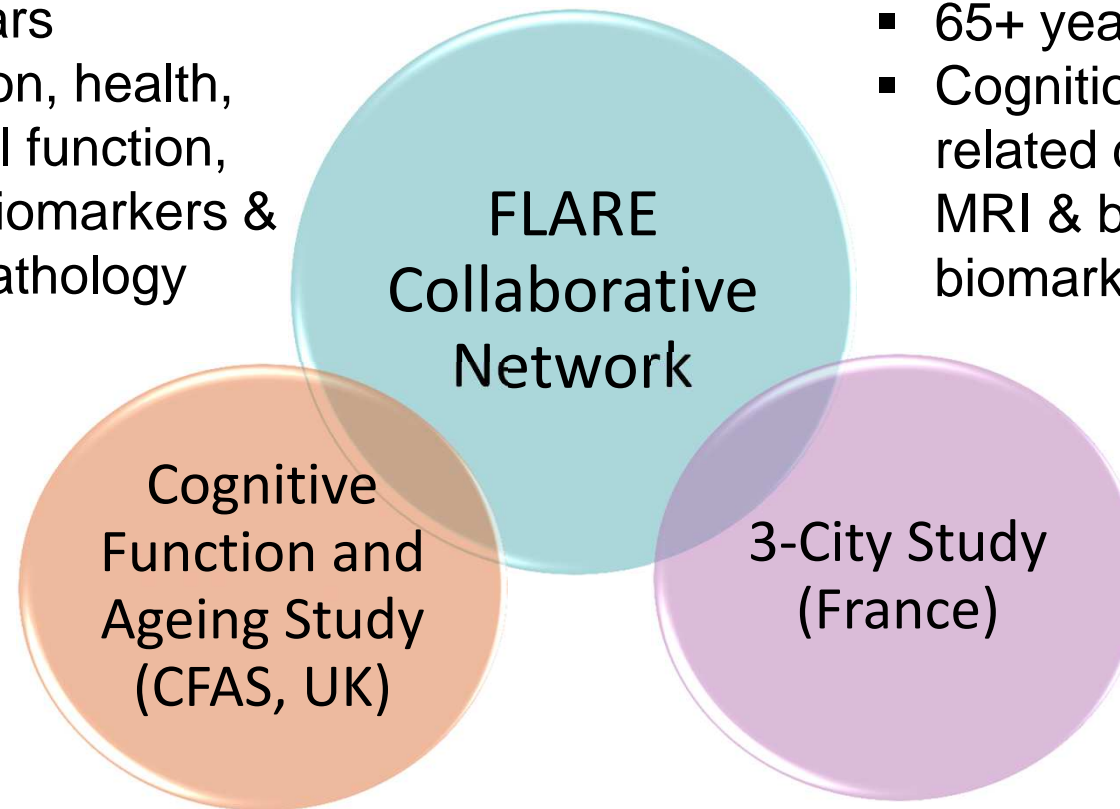
Health Co-morbidity in Individuals with Mild Cognitive Impairment (MCI)

- High incidence of disease co-morbidity in all groups
  - Most MCI cases satisfy criteria for VCIND

10 Conditions (self/informant report)
Anaemia, Parkinson's disease, breathing difficulties, angina, hypertension, diabetes mellitus, peripheral vascular disease, transient ischemic attack (TIA), stroke or heart attack

Percentage (y-axis) vs Number of Co-morbid Conditions (x-axis)

Legend:
- NCI
- All MCI
- DEM

Risk Factors for Progression

- Does disease co-morbidity increase risk of dementia (2-years follow-up) in MCI?

Risk Factor	Unadjusted OR	Adjusted* OR
Anaemia	13.5 (2.6-71.3)	10.6 (2.3-48.7)

*Adjusted for age, sex and education (years)

- Overall, medical co-morbidity does not appear to help distinguish individuals with and without progressive MCI

Stephan et al., Age and Aging, 2011

Risk Models for Mass Prediction

Mobility Research Project

- Focus on the whole non-demented population

- **Research Question** Can we develop a simple tool that can identify those individuals at high risk of future dementia?

Potential Predictors
4 Year Incident Dementia

Easily Obtainable

Demographics
(e.g., age, gender)

Lifestyle
(e.g., smoking and alcohol use)

Cognition
(e.g., memory and non-memory)

Functional/Motor Status

Moderately Easily Obtainable

Psychiatric Co-morbidity
(e.g., depression)

Vascular Health
(e.g., stroke, obesity, CHD)

Medication History
(e.g., psychotropic or statins)

Difficult to Obtain

MRI and Ultrasound
(e.g., WMLs, atrophy, IMT)

Blood/Serum (e.g., glycaemia, cholesterol)

Genetics
(e.g., APOE e4)

The Model

- **Simple Risk Model** Age, cognition, functional performance, motor performance and psychotropic medication use

    - 3 risk categories: low (2.2% incident cases), moderate (18.3% incident cases) and high (56.3% incident cases)
    - Area Under the Curve (AUC)=0.81 [95%CI: 0.78-0.84]

- Discriminative accuracy was not improved with the addition of MRI, blood or genetic risk markers

Stephan et al., in preparation

Conclusions

- Relatively simple measures can be used to identify individuals at high risk of dementia with reasonable accuracy

- Identification of high-risk individuals is important to better focus prevention and early intervention efforts

Where to Next ...

- New projects for funding and extending collaborations

  - **3-City Study** Develop a risk model where all components are modifiable (Research mobility July 2012)

  - **EPIC-Norfolk** Undertake an MRI programme to determine the association between brain structural changes, health status and cognitive impairment

  - **Research Sabbatical** to the National Institutes of Health in the USA in October 2012 (identified through the French team)

Contribution of FLARE to my Career

- Research progression

  - Publications, conferences and new research projects

- Training and professional development

  - In-depth research and focus on my own topic

  - Project leadership (at home and abroad)

- Inter-disciplinary exchange of ideas through the FLARE Fellow community

- Senior Researcher post (2011) and permanent academic position (Lecturer, 2012)

  - Permanent residency in the UK and British citizenship

Newcastle University

Acknowledgements

- Thank you to collaborating studies and researchers:

  - MRC CFAS (Bond, Brayne, Matthews, McKeith)
  - EPIC-Norfolk (Hayat, Khaw)
  - 3-City Study (Dufouil, Kurth)