

## INTEGRATIVE NEUROSCIENCE THROUGH HIGH-PERFORMANCE NEUROIMAGING

The McGill Centre for Integrative Neuroscience (MCIN) constitutes the neuroinformatics component of the recently launched Ludmer Centre for Neuroinformatics and Mental Health. The MCIN, led by Dr. Alan Evans, conducts computationally-intensive brain research using innovative mathematical and statistical approaches to integrate clinical, psychological... ..

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# Major unresolved questions in brain imaging across the lifespan

Alan C. Evans, PhD  
Montreal Neurological Institute/McGill University

Development of Brain Image Banks and  
Age-Specific Normative Human Brain Atlases

Edinburgh, U.K.  
August 28<sup>st</sup>, 2014

# Discussion points

Minimum image and metadata needed to define normality?

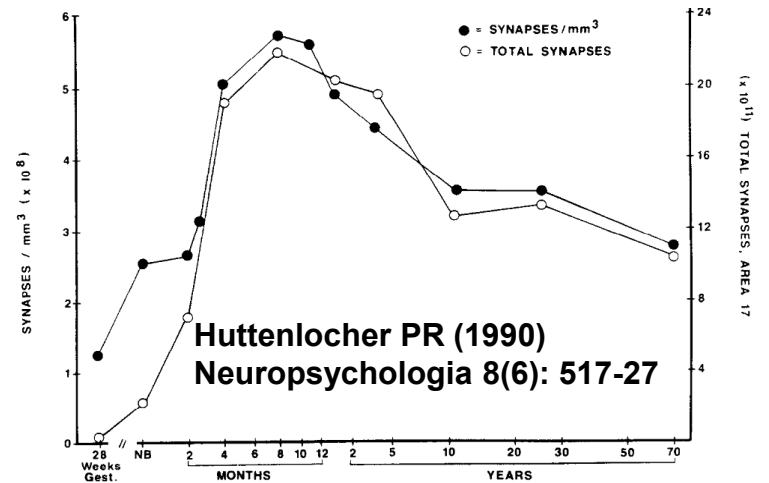
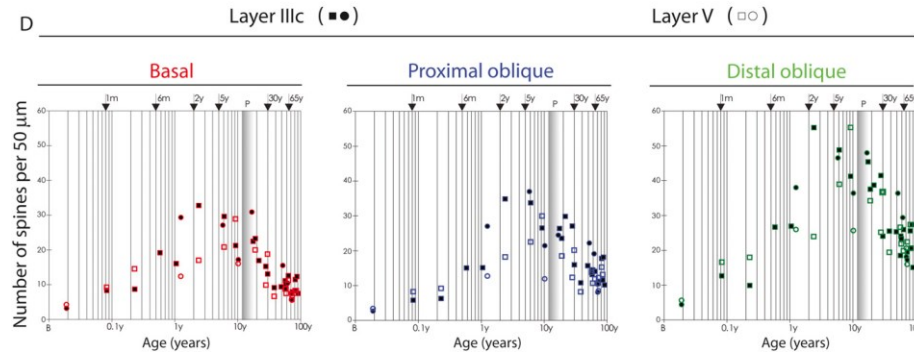
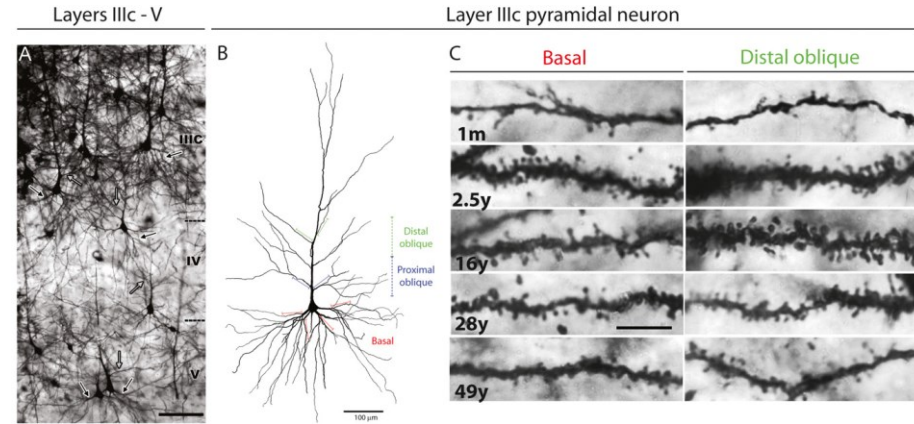
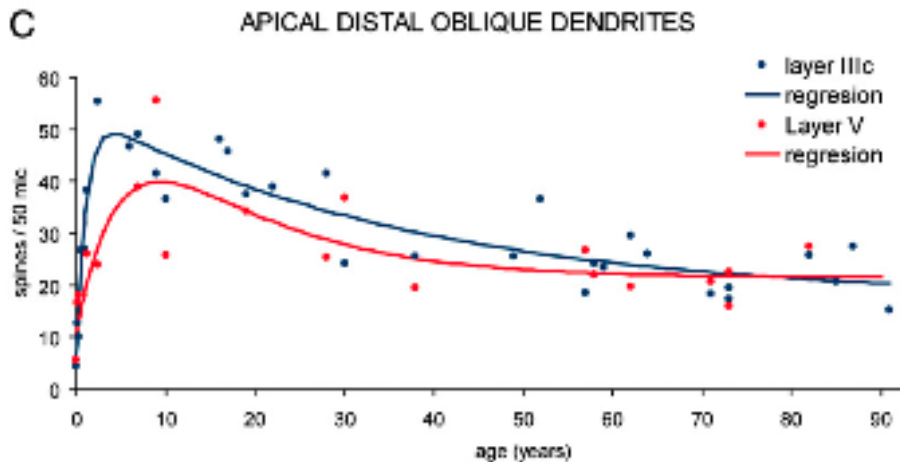
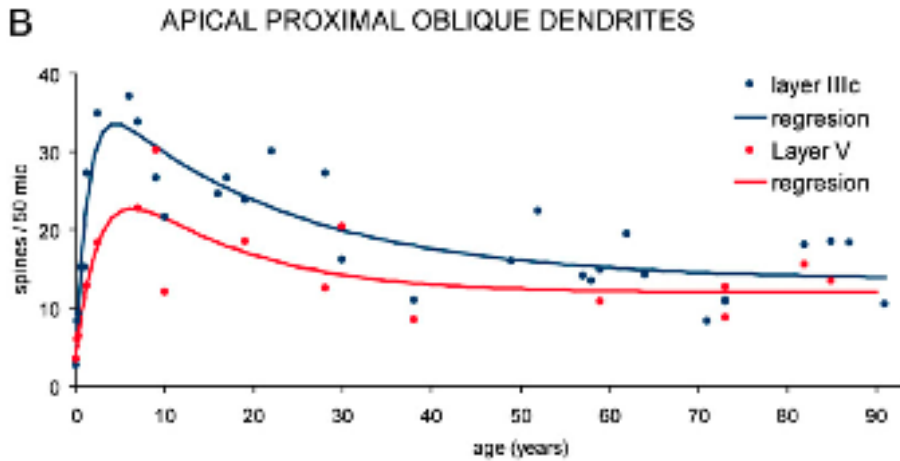
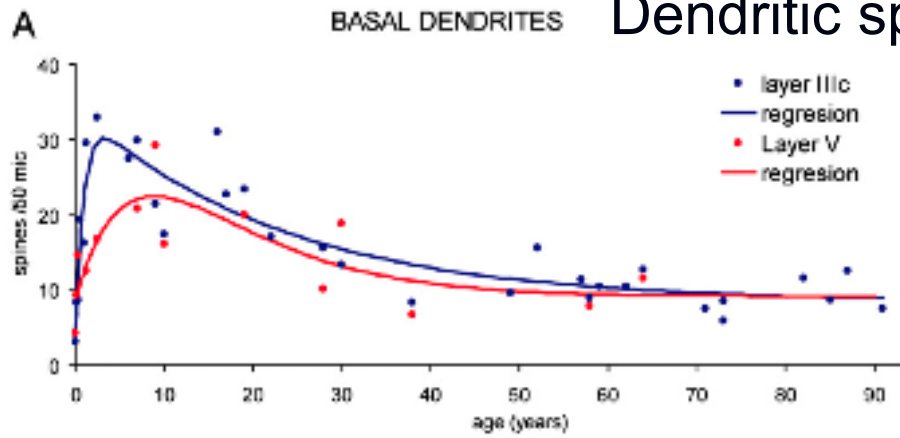
What can be done with existing data re. normality across lifespan ?

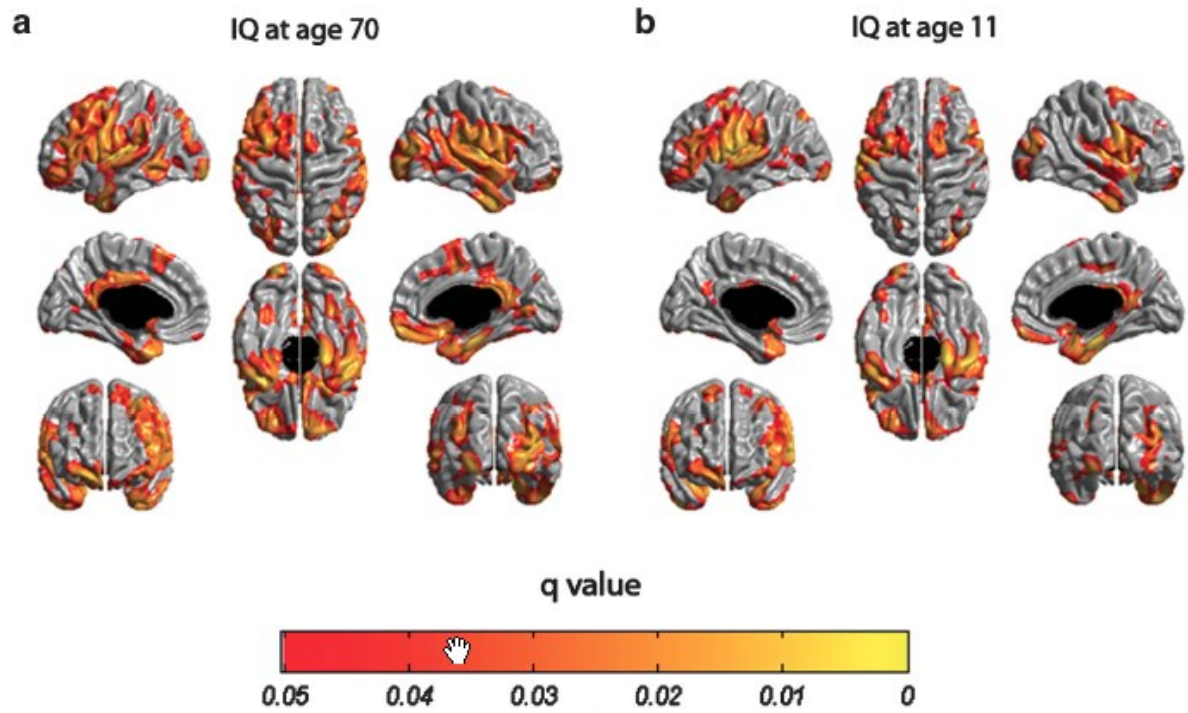
What are the likely gaps ?

Is it realistic to combine image data from all stages of life ?

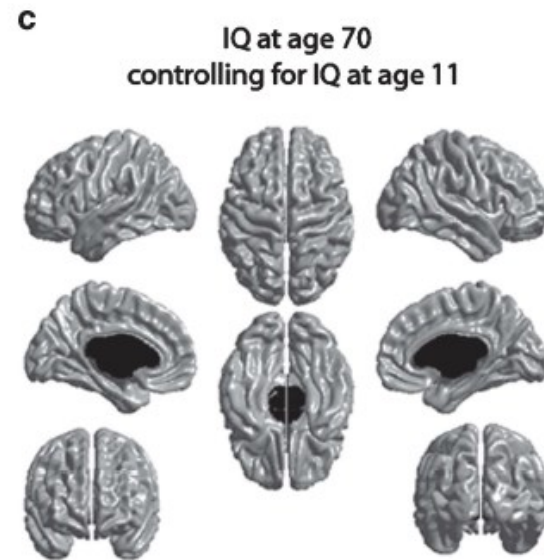
# Dendritic spine density vs age (prefrontal cortex)

Petanjek et al. (2011) PNAS 108 (32): 13281-6





Childhood IQ accounts for two-thirds of association between IQ at 70 and cortical thickness at 73



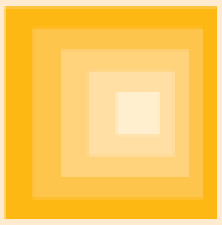




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HUMAN  
**Connectome**  
PROJECT



PARKINSON'S  
PROGRESSION  
MARKERS  
INITIATIVE

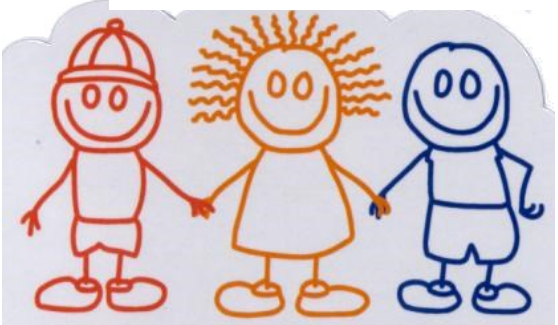
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OASIS



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Human Brain Project

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49

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"This groundbreaking and highly influential series ... remains a formidable achievement."  
—Stephen Aspinall, *Sight & Sound*

"A truly impressive, innovative reality-TV social document!"  
—Lisa Schwarzbaum, *Rolling Stone*

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"An extraordinary, bold series"  
(The Guardian)

In 1964 a group of seven-year-old children were interviewed for the documentary "Seven Up"

Michael Apted has been back to film them every seven years...

**THE UP SERIES**

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"On my list of the ten greatest films of all time."  
—ROGER EBERT

A FIRST RUN FEATURES RELEASE DVD

"Give me the child until he is seven and I will give you the man."

Starting in 1964 with *Seven Up*, renowned director Michael Apted has explored this Jesuit maxim. The original concept was to interview 14 children from diverse backgrounds from all over England, asking them about their lives and their dreams for the future. Every seven years, Apted has been back to talk to the same subjects, examining the progression of their lives.

From cab driver Tony to East End schoolmates Jackie, Lynn, and Susan and the heart-breaking Neil, we see, as they enter their 50's, how close these subjects are to realizing their ambitions.

An extraordinary look at the structure of life in the 20th century, *The Up Series* is, according to Roger Ebert, "an inspired, almost noble use of the film medium. Apted penetrates to the central mystery of life."

"Amazing! The spectacle, as in time-lapse photography, of human beings taking shape before our eyes." —Molly Haskell, *Vogue*

"One of the towering achievements in the history of documentary film. Endlessly rewarding and sometimes heartbreaking." —Desmond Ryan, *Philadelphia Inquirer*

In 1964 Michael Apted interviewed a group of seven year old children for the documentary "Seven Up".

He's been back to film them every seven years...

**THE UP SERIES**

THE DEFINITIVE COLLECTION OF ALL THE ORIGINAL UP SERIES FILMS  
SEVEN UP \* 7 PLUS SEVEN \* 21 UP \* 28 UP \* 35 UP \* 42 UP \* 49 UP

"On my list of ten greatest films of all times" - Roger Ebert

We need a decades-long longitudinal study



# Challenges to multi-site studies

## **Acquisition**

- Different scanner manufacturers
- Different field strengths
- Different protocol parameters
- Different acquisition procedures

## **Analysis**

- Slice registration/normalization
- Intensity non-uniformity
- Geometric distortion

## **Political (“herding cats”)**

- Different MRI research cultures
- Different psychology research cultures (clinical/experimental)
- Competition for data access/publication
- Communication problems (conference calls, e-mail poisoning)
- Subject confidentiality
- Different IRB regulations
- Bureaucracy (government, university, corporate)

# Unresolved questions in brain imaging across lifespan

- X-sectional (**large N**, **multisite**) vs. longitudinal (**true 4D**, **impractical**)
- Image (**3D**, **longitudinal**) vs Post-mortem (**res/specificity**, **x-sectional**)
- Acquisition protocol incompatibilities among contributing datasets
- Prospective acquisition protocol (coil, pulse sequence, field strength)
- Scanner stability across time (hardware/software upgrade, drift)
- Temporal changes in tissue contrast differ across pulse sequences
- Evolutionary changes in pulse sequence (e.g. DTI vs. HARDI)
- Compatibility: Raw data vs Derived data
- Demographic representation (age, gender, ethnicity, SES)
- Definition of “normal” (neurological, psychiatric, behavioural)
- Regulatory issues: IRB, confidentiality, ethics, levels of user access
- Scientific issues: Data ownership/sharing/publication
- Database issues: curation, federation: ontology, formats
- Ontology, “controlled vocabulary” incompatibilities (NeuroLex, CDE)







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## Welcome to **NeuroLex**, the Neuroscience Lexicon.

A dynamic lexicon of **33,383** neuroscience terms, including 752 neurons and 1290 parts of the nervous system supported by The Neuroscience Information Framework and the International Neuroinformatics Coordinating Facility

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- Behavioral Activity
- Behavioral Paradigms
- Brain Regions
- Cells
- Neurons
- Diseases
- Imaging protocols
- Molecules
- Nervous System Function
- Subcellular Parts
- Resource Types
- Qualities

### TABLES

- Behavioral Activity
- Behavioral Paradigms
- Brain Regions
- Overlapping Brain Regions
- Brain parcels
- Cell Types
- Diseases
- Molecules
- Nervous System Function
- Neurons
- Neurons by Neurotransmitter
- Organisms
- Resources and Information Entities
- Subcellular Parts
- Techniques
- Qualities
- Tissue banks
- Problem neural structures
- DICOM standard terms

### NIF NAVIGATOR

#### DATA TYPE →

- Animals (1607452)
- Annotation (22495494)
- Antibodies (2247176)
- Atlas (267687887)
- Biospecimen (638)
- Brain Activation Foci (3241980)
- Cell line (292624)
- Clinical Trials (349804)
- Connectivity (64204)
- Dataset (27562736)
- Disease (71422803)
- Drugs (38334733)
- Expression (5578686935)
- Gene (1395537)
- Grants (2940718)
- Images (489750)
- Interactions (747514)
- MRI (2831)
- Microarray (578219126)
- Models (1214650)
- Molecule (76)
- Multimedia (81553)
- Orthology (9895886)
- Pathways (801442)
- People (367)
- Phenotype (2129852)
- Plasmids (30432)
- Protocols (292)
- Software (2026)

#### NIF REGISTRY (12823)

#### LITERATURE (23672833)



The NeuroLex project, supported by the Neuroscience Information Framework project, is a dynamic lexicon of neuroscience terms. Unlike an encyclopedia, a lexicon provides the meaning of a term, and not all there is to know about it.

The NeuroLex is being constructed to help improve the way that neuroscientists communicate about their data, so that information systems like the NIF can find data more easily and provide more powerful means of integrating data that occur across distributed resources. One of the big roadblocks to data integration in neuroscience is the inconsistent use of terminology in databases and other resources like the literature. When we use the same terms to mean different things, we cannot easily ask questions that span across multiple resources. For example, if three databases have information about what genes are expressed in cortex, but they all use different definitions of cerebral cortex, then we cannot compare them easily.

As part of the NIF, we provide a simple search interface to many different sources of neuroscience information and data. To make this search more effective, we are constructing ontologies to help organize neuroscience concepts into category hierarchies, e.g., neuron is a cell. These

#### Contribution Scores

##### Last 30 days (Top 10)

Score	Pages	Changes	Username
675	645	863	Aarnaud (Talk   contribs)
46	39	51	Memartone (Talk   contribs)
39	39	39	Jugama (Talk   contribs)

► Brain region overview

**Page** | Discussion

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The list below is automatically generated by a query that extracts the definitions from classes that are children of the class "Regional part of brain". There are 905 classes here. This list is also available as CSV.

- A list of only brain regions in NeuroLex with definitions is available here.

A	I CONT.	P CONT.
<ul style="list-style-type: none"> <li>• Abducens nerve fibers</li> <li>• Abducens nerve root</li> <li>• Abducens nucleus</li> <li>• Accessory abducens nucleus</li> <li>• Accessory basal amygdaloid nucleus</li> <li>• Accessory cuneate nucleus</li> <li>• Accessory medullary lamina</li> <li>• Accessory nerve fiber bundle</li> <li>• Adenohypophysis</li> <li>• Aggregate regional part of brain</li> <li>• Alar central lobule</li> <li>• Allocortex</li> <li>• Alveus</li> <li>• Amiculum of dentate nucleus</li> <li>• Amygdala</li> <li>• Amygdala of Macaque</li> <li>• Amygdala of PHT00</li> <li>• Angular gyrus</li> <li>• Annectant gyrus</li> <li>• Ansa lenticularis</li> <li>• Ansoparamedian fissure</li> <li>• Antenna lobe of Manduca</li> <li>• Anterior Paravermal Cortex</li> <li>• Anterior amygdaloid area</li> <li>• Anterior cingulate cortex</li> <li>• Anterior cingulate gyrus</li> <li>• Anterior column of fornix</li> <li>• Anterior commissure anterior part</li> <li>• Anterior commissure</li> <li>• Anterior horn of lateral ventricle</li> <li>• Anterior hypothalamic region</li> <li>• Anterior limb of internal capsule</li> <li>• Anterior lobe of the cerebellum</li> </ul>	<ul style="list-style-type: none"> <li>• Inferior horn of the lateral ventricle</li> <li>• Inferior occipital gyrus</li> <li>• Inferior occipital sulcus</li> <li>• Inferior olivary complex</li> <li>• Inferior parietal cortex</li> <li>• Inferior pulvinar nucleus</li> <li>• Inferior rostral gyrus</li> <li>• Inferior temporal gyrus</li> <li>• Inferior transverse frontopolar gyrus</li> <li>• Inferior vestibular nucleus</li> <li>• Infracerbellar nucleus</li> <li>• Infundibular stem</li> <li>• Insula</li> <li>• Interanterodorsal nucleus of the thalamus</li> <li>• Intercalated amygdaloid nuclei</li> <li>• Intergeniculate leaflet of the lateral geniculate complex</li> <li>• Intermediate acoustic stria</li> <li>• Intermediate hypothalamic region</li> <li>• Intermediate oculomotor nucleus</li> <li>• Intermediate orbital gyrus</li> <li>• Intermediate part of hypophysis</li> <li>• Intermediate periventricular nucleus</li> <li>• Intermediodorsal nucleus of the thalamus</li> <li>• Internal arcuate fiber bundle</li> <li>• Internal capsule</li> <li>• Internal medullary lamina of thalamus</li> <li>• Interpeduncular nucleus</li> <li>• Interpolar part of spinal trigeminal nucleus</li> <li>• Interpositus Nucleus</li> <li>• Interstitial nucleus of Cajal</li> <li>• Interstitial nucleus of the posterior limb of the anterior commissure</li> <li>• Interthalamic adhesion</li> </ul>	<ul style="list-style-type: none"> <li>• Periamygdaloid area</li> <li>• Periamygdaloid cortex</li> <li>• Periaqueductal gray</li> <li>• Pericalcarine cortex</li> <li>• Pericentral nucleus of inferior colliculus</li> <li>• Periolivary nucleus</li> <li>• Peripeduncular nucleus</li> <li>• Perirhinal cortex</li> <li>• Peritrigeminal nucleus</li> <li>• Pineal body</li> <li>• Piriform cortex layer 1a</li> <li>• Piriform cortex layer 1b</li> <li>• Planum polare</li> <li>• Pons</li> <li>• Pontine nuclear complex</li> <li>• Pontine raphe nucleus</li> <li>• Pontine reticular formation</li> <li>• Pontine tegmentum</li> <li>• Pontobulbar nucleus</li> <li>• Postcentral gyrus</li> <li>• Postcommissural fornix</li> <li>• Posterior calcarine sulcus</li> <li>• Posterior cingulate cortex</li> <li>• Posterior cingulate gyrus</li> <li>• Posterior column of fornix</li> <li>• Posterior horn lateral ventricle</li> <li>• Posterior hypothalamic region</li> <li>• Posterior limb of internal capsule</li> <li>• Posterior lobe of the cerebellum</li> <li>• Posterior median eminence</li> <li>• Posterior nuclear complex</li> <li>• Posterior nucleus of hypothalamus</li> <li>• Posterior nucleus of thalamus</li> </ul>

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**NIF REGISTRY (0)**

**LITERATURE (0)**



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# European Population Imaging Infrastructure



*The mission of population imaging is to help develop and implement strategies to prevent or effectively treat disease through creation of a world class imaging research infrastructure within or in close vicinity to large population studies in the Netherlands and Europe. By shifting the focus from curative to preventive medicine, it will in the short-term improve people's quality of life and in the long-term reduce the costs for the healthcare sector.*

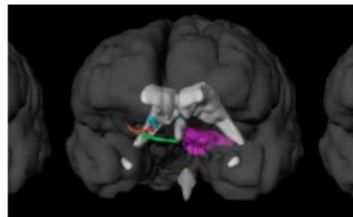
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## EIBIR SUMMER SCHOOL on Neurology Imaging

28 January 2013

August 26-30, 2013, Dubrovnik / HR  
GOAL: The EIBIR Summer School on Neurology Imaging is a multidisciplinary summer school, uniting 50 young researchers coming from a variety of backgrounds. The high scientific level and the relaxed atmosphere invite a close and fruitful interaction between everybody



## The Perspectief Program "Population Imaging Genetics (ImaGene)" has been granted

30 November 2012

Objective of the Program: The objective of the Program is to develop and evaluate novel methods to fully exploit imaging and genetics data from population studies in an integrated manner, for (early) disease detection, diagnosis, prognosis, therapy planning and therapy



## Medical Delta dient aanvraag in bij EFRO voor versterking Population Imaging

30 November 2012

Medical Delta heeft een aanvraag ingediend bij het Europees Fonds voor Regionale Ontwikkeling van de Europese Commissie (EFRO) om haar positie op het gebied van Population Imaging verder te versterken. Population Imaging is het systematisch maken en analyseren



## Boudewijn Lelieveldt has been appointed professor

30 October 2012

On 19 October, Boudewijn Lelieveldt (EEMCS) delivered his inaugural address as a professor of Biomedical Imaging at TU Delft and LUMC. In his address, Lelieveldt stated that medical science can often make excellent use of technologies from other fields. For example, knowledge from automatic facial recognition can also be used for

# Large Cohort Studies



## UK

### ABC and LBC

**Aberdeen and Lothian Birth Cohorts – Scottish Brain Image Bank**

Study website: [www.abdn.ac.uk/aberdeen-birth-cohort/](http://www.abdn.ac.uk/aberdeen-birth-cohort/)

Organization website: [www.abdn.ac.uk](http://www.abdn.ac.uk)

Study population size: ABC: **653** participants, LBC: **729** participants

Study population: **healthy participants**, 65-75 years old

Imaging modality 1: **MRI** – Brain MRI

Key publications:

- Leaper SA, et al. Neuropsychologic correlates of brain white matter lesions depicted on MR images: 1921 Aberdeen Birth Cohort. *Radiology*, 2001.
- Staff RT, et al. What provides cerebral reserve? *Brain*, 2004.
- Murray AD, et al. Brain white matter hyperintensities: relative importance of vascular risk factors in nondemented elderly people. *Radiology*, 2005.
- Staff RT, et al. Brain volume and survival from age 78 to 85: the contribution of Alzheimer-type magnetic resonance imaging findings. *J Am Geriatr Soc*, 2010.

### Spinal MR study

Study website: n.a.

Organization website: [www2.warwick.ac.uk](http://www2.warwick.ac.uk)

Study population size: **25000** participants

Study population: **patients referred for back pain**

Imaging modality 1: **MRI** - Spinal MR

Key publications: not yet available.

### UK Biobank

Study website: [www.ukbiobank.ac.uk](http://www.ukbiobank.ac.uk)

Organization website: [www.ctsu.ac.uk](http://www.ctsu.ac.uk)

Study population size: **500000** participants

Study population: **healthy participants**, 40-69 years old

Imaging modality 1: **MRI** – Cardiac and abdominal MR

Imaging modality 2: **Ultrasound** – Carotid

Key publications:

- Allen N, et al. UK Biobank: Current status and what it means for epidemiology. *Health Policy and Technology*, 2012.
- UK Biobank. UK Biobank: rationale, design and development of a large-scale prospective resource. <http://www.ukbiobank.ac.uk/resources/>
- Murray AD, et al. The UK Biobank sample handling and storage protocol for the collection, processing and archiving

## France

### 3C Study

**The Three-City Study**

Study website: [www.three-city-study.com/the-three-city-study.php](http://www.three-city-study.com/the-three-city-study.php)

Organization website: [www.upmc.fr](http://www.upmc.fr)

Study population size: **9294** participants

Study population: **healthy population**, aged 65 years and older

Imaging modality 1: **ultrasound** - Carotid-IMT

Imaging modality 2: **MRI** – Brain MRI

Key publications:

- The 3C Study Group. Vascular factors and risk of dementia. Design of the Three-City Study and baseline characteristics of the study population. *Neuroepidemiology*, 2003.
- Elbaz A, Ripert M, et al. Common carotid artery intima-media thickness, carotid plaques, and walking speed. *Stroke*, 2005.
- Ritchie K, Carrière I, et al. The neuroprotective effect of caffeine: a prospective population study (The Three City Study). *Neurology*, 2007.
- Godin O, Dufouil C, et al. White matter lesions as a predictor of depression in the elderly- The 3C-Dijon study. *Biological Psychiatry*, 2008.
- Maillard P, Delcroix N, et al. An automated procedure for the assessment of white matter hyperintensities on multispectral (T1, T2, PD) MRI and its between-centre reproducibility evaluation on two large community databases. *Neuroradiology*, 2008.
- Delsette S, Bis JC, et al. Genome-wide association studies of MRI-defined brain infarcts: meta-analysis from the CHARGE Consortium. *Stroke*, 2010.
- Stewart R, Godin O, et al. Longitudinal neuroimaging correlates of subjective memory impairment: 4-year prospective community study. *Br J Psychiatry*, 2011.

### EVA Study

**The Epidemiology of Vascular Aging Study**

Study website: n.a.

Organization website: n.a.

Study population size: **1389** participants

Study population: **healthy population**, aged 59 – 71 years old

Imaging modality 1: **ultrasound** – carotid-IMT

Imaging modality 2: **MRI** – Brain MRI

Key publications:

- Bonithon-Kopp C, Touboul PJ, et al. Relation of Intima-Media Thickness to Atherosclerotic Plaques in Carotid Arteries
- The Vascular Aging (EVA) Study. *Arterioscler Thromb Vasc Biol*, 1996.
- Dufouil C, Ducimetière P, et al. Sex differences in the association between alcohol consumption and cognitive performance. EVA Study Group. *Epidemiology of Vascular Aging*. *Am J Epidemiol*, 1997.
- Tzourio C, Dufouil C, et al. Cognitive decline in individuals with high blood pressure: a longitudinal study in the elderly. EVA Study Group. *Epidemiology of Vascular Aging*. *Neurology*, 1999.
- Dufouil C, de Kersant-Gilly A, et al. Longitudinal study of blood pressure and white matter hyperintensities: the EVA MRI Cohort. *Neurology*, 2001.
- Pico F, Dufouil C, et al. Longitudinal study of carotid atherosclerosis and white matter hyperintensities: the EVA-MRI cohort. *Cerebrovasc Dis*. 2002.

## Netherlands

### BIG project

**The Nijmegen Brain Imaging Genetics (BIG) project**

Study website: [www.cognomics.nl/big](http://www.cognomics.nl/big)

Organization website: [www.ru.nl](http://www.ru.nl)

Study population size: **2500** participants

Study population: **healthy population**, aged 45 and older

Imaging modality 1: **MRI** – Brain

Key publications:

- Bralten J, Arias-Vásquez A, et al. Association of the Alzheimer's gene SORL1 with hippocampal volume in young, healthy adults. *American Journal of Psychiatry*, 2011.
- Hoogman M, Rijpkema M, et al. Current self-reported symptoms of attention deficit/hyperactivity disorder are associated with total brain volume in healthy adults. *PLoS One*, 2012.

### Generation R Study

Study website: [www.generationr.nl](http://www.generationr.nl)

Organization website: [www.arasumc.nl](http://www.arasumc.nl)

Study population size: **10000** participants.

Study population: **healthy children**, from birth and on.

Imaging modality 1: **ultrasound** - Fetal, abdominal, thoracic

Imaging modality 2: **MRI** - brain, subgroup.

Key publications (see also: [www.generationr.nl/researchers/phd-theses-and-publications.html](http://www.generationr.nl/researchers/phd-theses-and-publications.html)):

- Jaddoe VW, van Duijn CM, et al. The Generation R Study: design and cohort update 2012. *Eur J Epidemiol*. 2012.
- Tiemeyer H, Velders FP, et al. The Generation R Study: A review of design, findings to date, and a study of the 5-HTTLPR by environmental interaction from fetal life onward. *J Am Acad Child Adolesc Psychiatry*, 2012.

### Maastricht Study

Study website: [www.demaastrichtstudie.nl](http://www.demaastrichtstudie.nl)

Organization website: [www.maastrichtuniversity.nl](http://www.maastrichtuniversity.nl)

Study population size: **10000** participants (expected); study started in 2010, imaging started end 2012).

Study population: **5000** with **diabetes mellitus type 2**, **5000** **healthy** participants, aged 40-75 years.

Imaging modality 1: **ultrasound** - Abdominal fat, cardiac

Imaging modality 2: **plain radiographs** - Knee

Imaging modality 3: **DEXA** - Body composition

Imaging modality 5: **CT** - Coronary calcium scoring, Coronary CTA (*future plans*)

Imaging modality 5: **MRI** – Brain, body fat quantification, carotids

Key publications: not yet available.

### NELSON Study

**Nederlands-Leuvens Longkanker Screenings Onderzoek**

Study website: [www.nelsonproject.nl](http://www.nelsonproject.nl)