The EU-AIMS Longitudinal European Autism Project:

Examples of novel approaches to biomarker discovery

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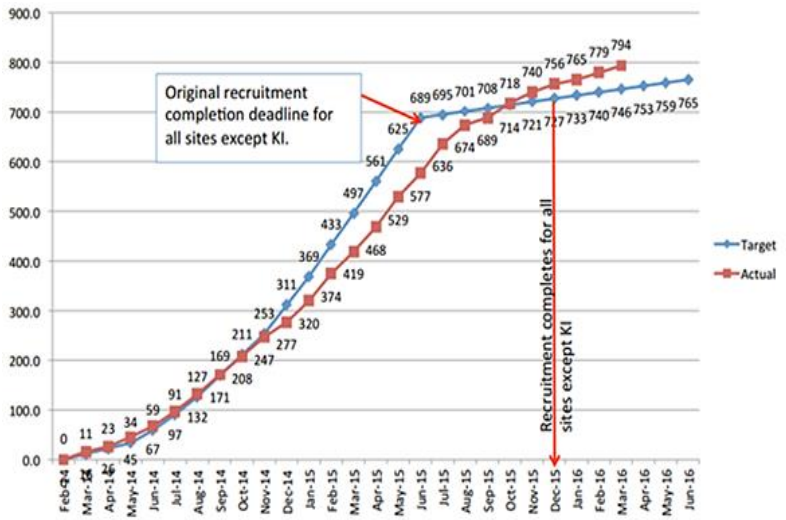
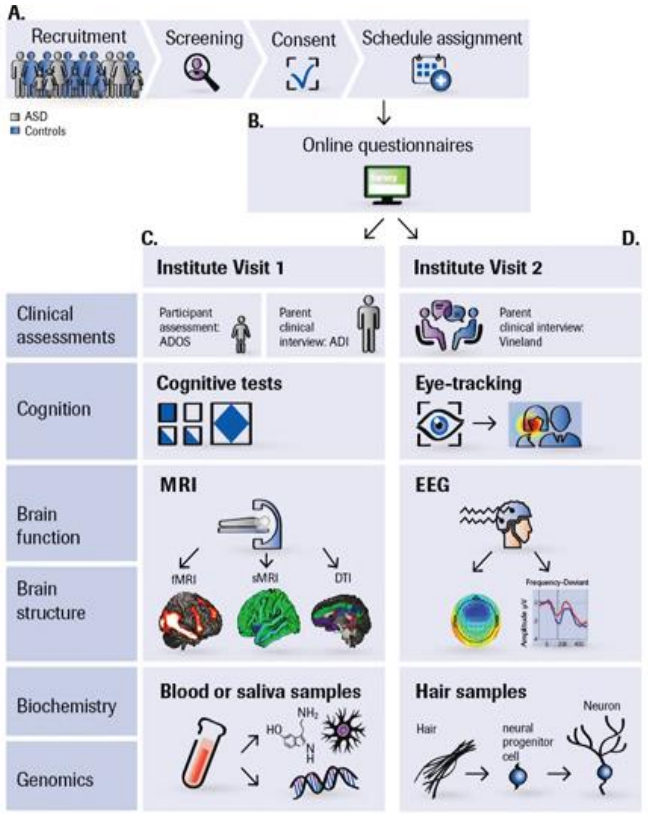
Longitudinal European Autism Project (LEAP)

Recruitment and protocol

GCP standardized





First study in Autism research that has received QA from EMA on biomarker methodologies and 5 letters of support

Clinical sites: London, Cambridge, Stockholm, Utrecht, Nijmegen, Mannheim, Rome

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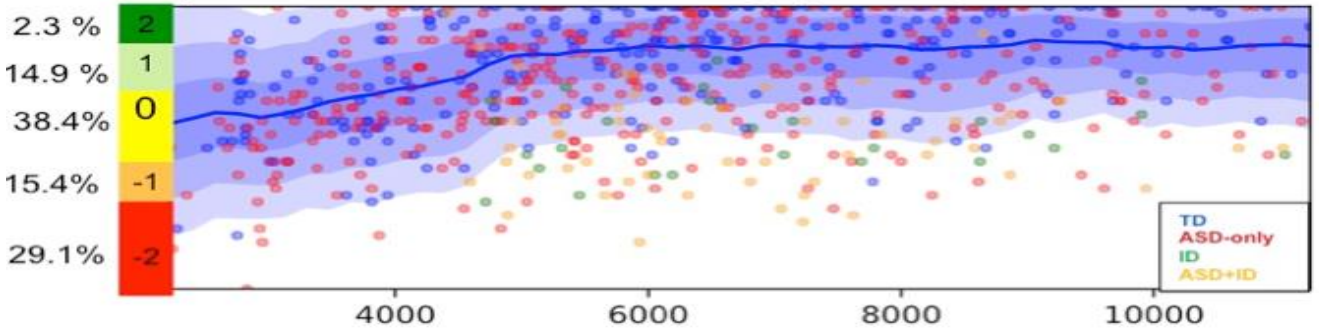
Loth et al., 2017, *Nat Rev Drug Discovery*, Charman et al *Mol Autism* 2107, Loth et al *Mol Autism, 2017*

Guillaume Dumas

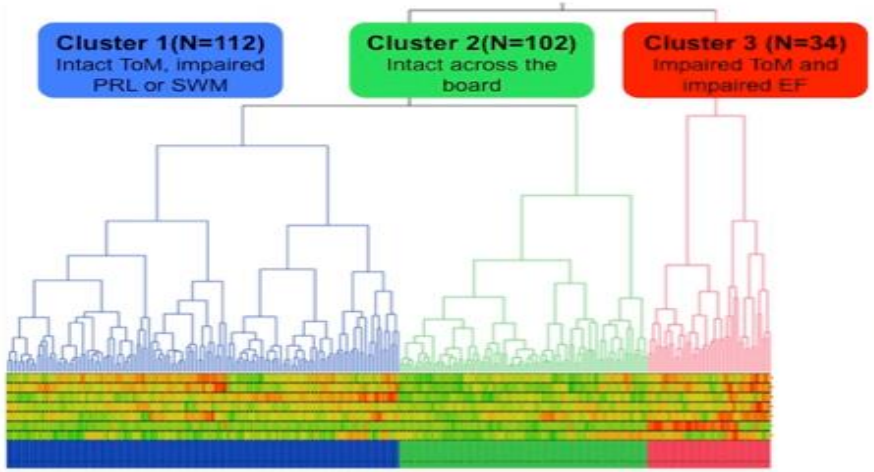
A. Between-group differences on each cognitive task

	Social cognition					Domain general		
	False belief	Animated Shapes	RMET	Social attention	Biological motion	SWM	Reversal Learning	Block Design
								
p *d*	**.0009** *d*=.27	ns	**1.5x10^{-9}** *d*=.54	**Face .001** *d*=.34	**4.7x10^{-5}** *d*=.39	**4.5x 10^{-8}** *d*=.43	**4.3x 10^{-5}** *d*=.35	.001# *d*=.23

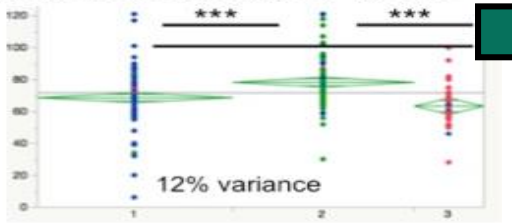
B. Non-parametric normative modelling against age: SWM

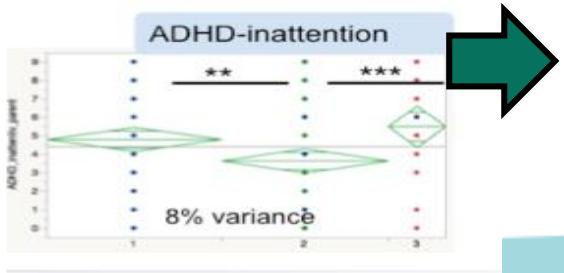


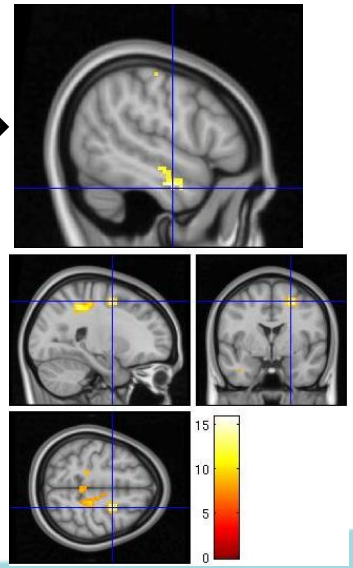
C. Hierarchical Clustering



D. Subgroup differences in VABS/ ADHD

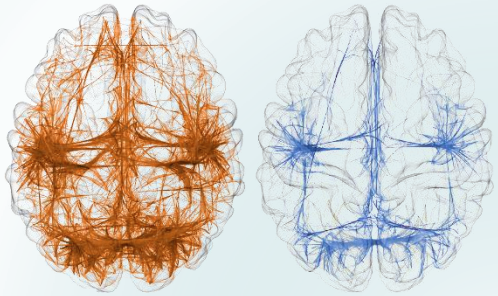






Autism and Functional Connectivity

Motivation

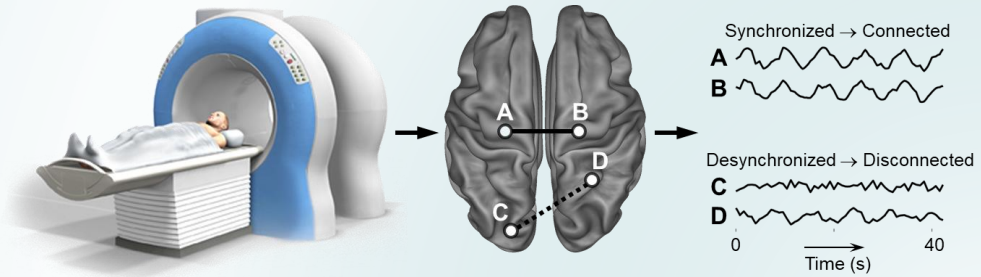


Brain connectivity of
people with autism is different

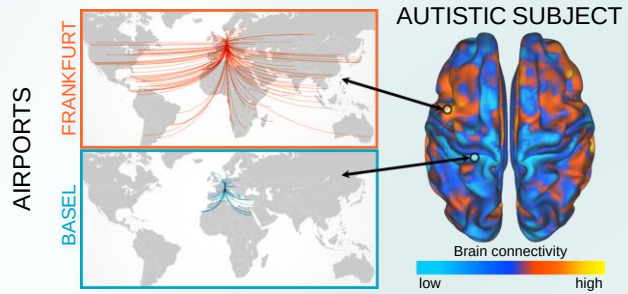
Literature evidence
is largely conflicting

Tackling the reproducibility problem:
Value of EU-AIMS and other large datasets

Methodology



Concept of functional connectivity
as measured using rs-fMRI



Assessing connectivity: Airports analogy

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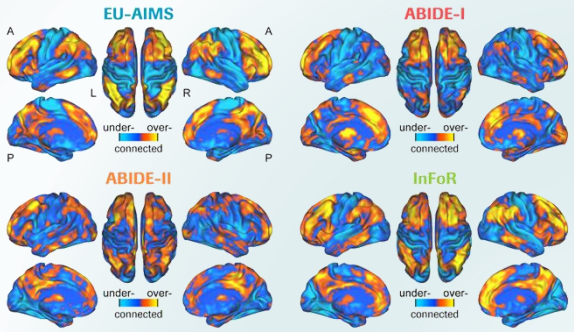
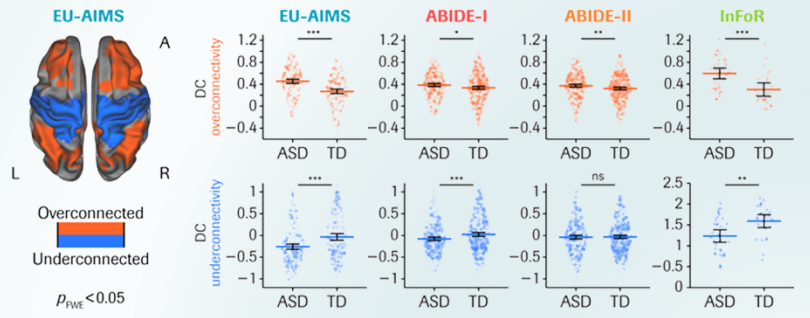
First Reproduced Connectivity Phenotype

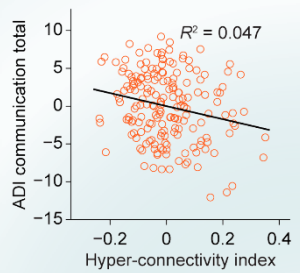
Results



Connectivity patterns are alike across the different datasets



Connectivity differences were quantified and reproduced in all cohorts



Correlates with core symptoms

Conclusions

- Identified **reproducible** differences in functional connectivity between typically developing controls and autistic subjects
- The results are currently used in Roche programs developing medicines for autism

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