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What are the causes of individual differences between children in terms of aggressive behavior and associated behavioural problems?

Submission date
06/08/2019

Recruitment status
No longer recruiting

Registration date
01/10/2019

Overall study status
Completed

Last Edited
01/10/2019

Condition category
Mental and Behavioural Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Childhood aggression and its resulting social impairment inflict a huge personal and financial burden on affected children, their relatives, peers and society as a whole. The prevalence of clinical aggression in children ranges from 2-16%, and early-onset childhood aggression continues into adolescence and adulthood in a substantial proportion of children. There are large differences between children in aggression levels and this study asks “what are the causes of individual differences between in children for aggressive behaviour and associated behavioural problems?”. We look at genetic, epigenetic and metabolomics markers, in different cohorts that collected these data in birth cohorts and population-based registries. We combine information from cohorts in a series of meta-analyses.

Who can participate?
Children below age 18 years for whom information on aggression and attention problems is available and who have been genotyped on a genome-wide SNP (Single nucleotide polymorphism) arrays; participants of any age with information on aggressive and attention problems and genome-wide epigenetic data; children for whom information on aggressive and attention problems is available and for whom urine samples for metabolomics were collected.

What does the study involve?
Estimating the associations between the phenotypes (aggression and attention problems) and the biomarker data. Primary analyses are carried out by each cohort and results are combined in meta-analyses.
What are the possible benefits and risks of participating? This project generates information on associations of behaviour with biomarkers. There are no individual-level risks or benefits to participants.

Where is the study run from?
The cohort studies run in their own countries (USA, UK, Europe, Australia and New Zealand). The meta-analyses is carried out in the Netherlands.

When is the study starting and how long is it expected to run for?
The cohort studies run in their own countries and typically are longitudinal projects. The meta-analyses will be finished and submitted for publication in 2019.

Who is funding the study?
FP7-EU 602768

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
ACTION: Aggression in Children: Unraveling gene-environment interplay to inform Treatment and InterventiON strategies

Acronym
ACTION

Study objectives
Improve the understanding of the genetic and non-genetic etiology of aggression in children to inform the development of novel prevention and treatment strategies by unraveling in large twin and genotyped cohorts the causes of variation in aggression, disentangling (epi)genetic and environmental effects and their interplay with a focus on critical developmental periods, gender, and comorbid disorders; by investigating metabolomic profiles of aggressive behavior to establish direction of causation for existing and new biomarkers and gain insight regarding the predictive power of pediatric aggression for adult outcome variables.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Meta-analysis of existing cohort studies does not require ethical approval (confirmed by Central Ethics Committee on Research Involving Human Subjects of the VU University Medical Centre; BS7 Kamer H-565l; +31 (0)20 44 45585; metc@vumc.nl), ref: 2014.252

Study design
Epidemiological meta-analysis

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Childhood behavioral problems, with a focus on aggression and attention problems

Interventions
The researchers are doing a series of large meta-analyses, which either take cross-sectional or longitudinal data and test associations of trait outcomes (aggression and attention problems) with SNP data, epigenetics and metabolomics markers. in this work there is no follow-up (though the data mainly derive from ongoing population-based cohorts).

Data were drawn from the following cohorts:
Amsterdam Born Children and their Development Study
Avon Longitudinal Study of Parents and Children
Brain dEvelopment and Air polluTion ultrafine particles in scHool childrEn
Child and Adolescent Twin Study in Sweden
Christchurch Health and Development Study
Collaborative Studies on the Genetics of Alcoholism
Copenhagen Prospective Studies on Asthma in Childhood 2010
Dunedin Multidisciplinary Health and Development Study
Environmental Risk Longitudinal Twin Study
Finnish Twin Cohort
Generation R Study
German Infant study on the influence of Nutrition Intervention PLUS environmental and genetic influences on allergy development / The influence of Life-style factors on the development of the Immune System and Allergies in East and West Germany
Great Smoky Mountains Study

Institute for Behavioral Genetics
Infancia y Medio Ambiente
Impact of Neurodevelopmental disorders and School performance: genes and environment
Minnesota Center for Twin and Family Research
Norwegian Mother and Child Cohort Study
Michigan State University Twin Register
Mater University of Queensland Study of Pregnancy
Northern Finland Birth Cohort 1986
Netherlands Twin Register
Queensland Institute of Medical Research
Western Australian Pregnancy Cohort (Raine) Study
Swedisch Twin study of CHild and Adolescent Development
Twin Early Development Study
TRacking Adolescents' Individual Lives Survey
Virginia Twin Study of Adolescent Behavioral Development
Young Finns Study

Intervention Type
Other

Primary outcome(s)
Measures of association (from regression analyses) for biomarker-outcome analyses.
For each set of biomarkers (metabolomics, SNP and epigenetic data) an appropriate level of statistical significance is specified. Outcome data on problem behaviors were collected by birth and child cohorts by standardized surveys.

The most commonly employed instruments to assess childhood aggressive and attention problems came from the Achenbach System of Empirically based Assessment (ASEBA; Achenbach et al. 2017) and the Strengths and Difficulties Questionnaire (SDQ; Goodman 2001). These two instruments accounted for > 70% of the phenotype data.
-Achenbach TM, Ivanova MY, Rescorla LA (2017) Empirically based assessment and taxonomy of psychopathology for ages 1½–90+ years: Developmental, multi-informant, and multicultural findings. Compr Psychiatry 79:4–18. doi: 10.1016/J.COMPPSYCH.2017.03.006
- Goodman R (2001) Psychometric Properties of the Strengths and Difficulties Questionnaire. J Am Acad Child Adolesc Psychiatry 40:1337–1345. doi: 10.1097/00004583-200111000-00015

Key secondary outcome(s))
Based on primary analyses, gene-based and network tests were carried out.

Completion date
01/06/2019

Eligibility

Key inclusion criteria
Biomarker- outcome associations are tested in child (2-18 years) cohorts and for epigenetics also in adults. Inclusions into the original population-based cohort studies were voluntary.

Healthy volunteers allowed
No

Age group
All

Sex
All

Key exclusion criteria
For genetic studies, to avoid population stratification, ancestries that are different from EU are excluded

Date of first enrolment
01/06/2014

Date of final enrolment
01/06/2019

Locations

Countries of recruitment
United Kingdom

Australia

Denmark

Finland

Germany

Netherlands

New Zealand

Norway

Sweden

Switzerland

United States of America

Study participating centre
Vrije Universiteit
Van der Boechorststraat 7
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Sponsor information

Organisation
Vrije Universiteit - FGB

ROR
https://ror.org/008xxew50

Funder(s)

Funder type
Government

Funder Name
Seventh Framework Programme

Alternative Name(s)
Seventh framework programme of the European Community for research and technological development and demonstration activities (2007-2013), FP7

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Individual participant data (IPD) sharing plan
Over 30 cohorts are included in this effort, which each have their own repositories. The association results from all cohorts are uploaded to a central repository in the Netherlands. The full set of meta-analysis association results will be made available upon publication of the papers.

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes