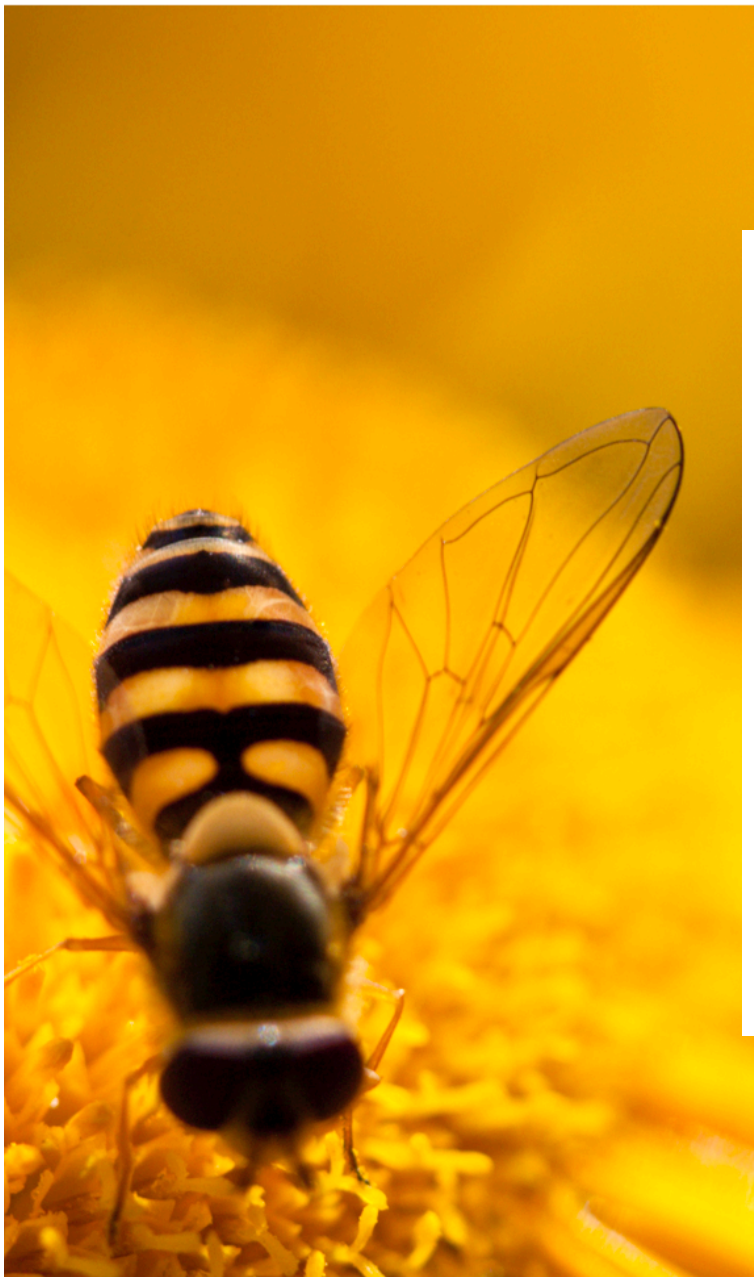

Gravitation

Consortium on Individual Development (CID)

Annual Report

2014-2015

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Nederlandse Organisatie voor Wetenschappelijk Onderzoek

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Gravitation Consortium on Individual Development (CID)

Annual report 2014-2015

Written by Chantal Kemner (project leader), René Kahn (WP1), Marinus van IJzendoorn (WP2), Wim Meeus (WP3), Marjan Joëls (WP4), Jacobine Buizer-Voskamp (project manager), Maartje Aukes (coordinator Education), and Mariska Phielix (financial manager).

Sent to the Supervisory Board at October 5, 2015

Organization

Steering Committee

Prof. dr. C. Kemner (Program Chair), Prof. dr. D.I. Boomsma, Prof. dr. P.M. Valkenburg, Prof. dr. M. Joëls, Prof. dr. R.S. Kahn, Prof. dr. M.H. van IJzendoorn, Prof. dr. W.H.J. Meeus

PI's

Prof. dr. M.J. Bakermans-Kranenburg, Prof. dr. J. van Berkum, Prof. dr. J.J. Bolhuis, Prof. dr. D.I. Boomsma, Prof. dr. E.A.M. Crone, Prof. dr. M. Dekovic, Prof. dr. S. Durston, Prof. dr. R.C.M.E. Engels, Prof. dr. H.J.A. Hoijtink, Prof. dr. H.E. Hulshoff Pol, Prof. dr. M.H. van IJzendoorn, Prof. dr. M. Joëls, Prof. dr. C. Kemner, Prof. dr. R.S. Kahn, Prof. dr. W.H.J. Meeus, Prof. dr. A.J. Oldehinkel, Prof. dr. J. Ormel, Prof. dr. P.M. Valkenburg, Prof. dr. F.C. Verhulst, Prof. dr. W.A.M. Vollebergh

Work Package Leaders

Prof. dr. R.S. Kahn (WP1)
Prof. dr. M.H. van IJzendoorn (WP2)
Prof. dr. W.H.J. Meeus (WP3)
Prof. dr. M. Joëls (WP4)

Cohort Representatives

Prof. dr. C. Kemner (YOUth cohort, Utrecht)
Prof. dr. M.H. van IJzendoorn (L-CID Intervention cohort, Leiden)
Prof. dr. D.I. Boomsma (NTR, Amsterdam)
Prof. dr. F.C. Verhulst (Generation-R, Rotterdam)
Prof. dr. A.J. Oldehinkel (TRAILS, Groningen)
Prof. dr. W.H.J. Meeus (RADAR, Utrecht)
Prof. dr. M. Joëls (Animal cohort, Utrecht)

Scientific Advisory Board

Prof. dr. J. Belsky (Davis)
Prof. dr. N. Martin (Queensland)
Prof. dr. M.J. Meaney (Montreal)
Prof. dr. B.J. Casey (New York)
Prof. dr. M.H. Johnson (London)
Prof. dr. L. Steinberg (Philadelphia)
G.C.M.L. Page-Christiaens, PhD (Netherlands; ethical advisor)

Supervisory Board

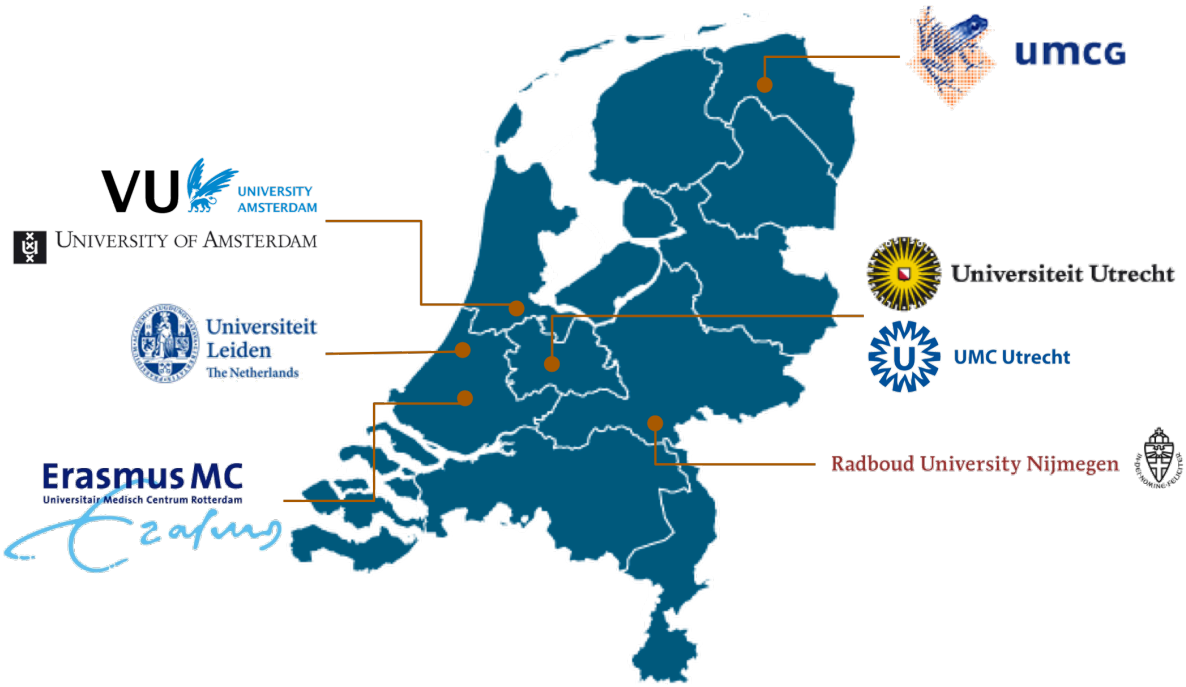
Prof. dr. W. Raub, Utrecht University
Prof. dr. F. Miedema, University Medical Center Utrecht
Prof. dr. E.J.C. de Geus, VU University of Amsterdam
Prof. dr. E.J. Fischer (a.i.), University of Amsterdam
Prof. dr. J.T. Swaab, Leiden University
Prof. dr. F. Kuipers, University Medical Center Groningen
Prof. dr. D. Wigboldus, Radboud University Nijmegen
Prof. dr. V.W.V. Jaddoe, Erasmus University Medical Center Rotterdam

Program Support Office

Drs. M. Phielix (Financial Manager)
Dr. J.E. Buizer-Voskamp (Project Manager)
Dr. M.F. Aukes (Coordinator Education)
Drs. E.J.T.R. van Ravenswaaij (Secretariat)

Consortium on Individual Development (CID)

Consortium Partners



Introduction

Most children develop well and find their way into society without many problems, but not all children manage to do so. We know that this difference is related to a combination of the child's disposition and the environment in which he or she is raised. The Consortium on Individual Development (CID) aims to understand and predict how the interplay of child characteristics and environmental factors results in individual differences in the development of social competence and behavioral control of the child and to understand the role of brain development herein.

CID brings together top researchers from several disciplines, with unique and relevant expertise involved in developmental research and has received a grant from the Dutch Science Foundation (NWO). The grant is part of the Gravity program, funded by the Ministry of Education, Culture and Science (OCW). The grant allows CID to follow large samples of children in their development during a decade, integrating approaches from many different disciplines. CID joins one of the four strategic themes by which the Utrecht University profiles itself: Dynamics of Youth (DoY). Characteristic for the Utrecht approach is cooperation of all faculties in the Dynamics of Youth strategic theme: Sciences, Humanities, Medicine, Social and Behavioral Sciences, Law, Economics and Governance, and Veterinary Medicine.

CID consists of four work packages (WP's). Because the focus of the project is on development from birth to adolescence, the core of all work packages consists of large-scale longitudinal cohort studies. Two new children cohorts will be implemented: a longitudinal cohort YOUth (based in Utrecht, WP1) and an intervention cohort L-CID (based in Leiden, WP2). In addition, four existing cohorts are involved: TRAILS (Groningen), Generation-R (Rotterdam), RADAR (Utrecht), and NTR (Amsterdam) (together WP3). WP4 provides a supportive basis using animal and mathematical models of development (Utrecht).

WP0 – General Management CID

Description of the organizational structure. Are there changes compared to the original proposal? Are there changes foreseen in the coming years and what will be the consequences? Including an organogram.

WP0, general management	Program Chair: Prof. dr. C. Kemner

The Consortium on Individual Development (CID) set off in May 2013. A Consortium Agreement (CA) was formulated, specifying the governance structure, the aim of collaboration, the relationship among the parties, the management of the consortium and the rights and obligations of the parties concerning - the carrying out of - the research projects and project budgets.

Organizational structure

Conform the CA, the organizational structure of the consortium is transparent and comprises of:

- A Program Chair (C. Kemner);
- A Program Support Office (Project manager, Financial Office (FO), Coordinator Education, secretariat);
- A Steering Committee
- Work Package leaders
- Cohort representatives
- A Scientific Advisory Board (including one ethical advisor);
- A Supervisory board.

The Program Chair organizes and chairs the meetings of the Steering Committee. She implements the Steering Committee's policy with respect to scientific direction, coherence and cooperation between the WPs.

The Program Support Office assists and facilitates the work of the Steering Committee and the Program Chair for executing the decisions of the Steering Committee as well as the day-to-day management of the program. The Program Support Office comprises of: Drs. M. Phielix (Financial Manager), Dr. J.E. Buizer-Voskamp (Project Manager), Dr. M.F. Aukes (Coordinator Education), and Drs. E.J.T.R. van Ravenswaaij (Secretariat).

The Steering Committee (SC) is composed of the program chair, the four work package leaders and two additional members who were co-applicants. The Steering Committee ensures the general management of the research program and ensures the coherence and cooperation between the different WP's. The SC monitors the scientific progress within each WP and decides on ethical issues, financial, administrative, and contractual matters. The members are: Prof. dr. C. Kemner (Program Chair), Prof. dr. D.I. Boomsma, Prof. dr. P.M. Valkenburg, Prof. dr. M. Joëls, Prof. dr. R.S. Kahn (replaces Prof. dr. S. Durston), Prof. dr. M.H. van IJzendoorn, and Prof. dr. W.H.J. Meeus.

The research program is subdivided in four work packages (WPs), each led by a work package leader. The WP leader implements the policy of the Steering Committee with respect to scientific direction, coherence, and cooperation between the WPs for their own WP. The WP leader monitors the scientific progress and is responsible for the management of the scientific staff (PhD-students/postdoc) that is related/assigned to their WP. The WP leaders are: Prof. dr. R.S. Kahn (WP1), Prof. dr. M.H. van IJzendoorn (WP2), Prof. dr. W.H.J. Meeus (WP3), and Prof. dr. M. Joëls (WP4).

Two new cohorts will be implemented in the research program: a longitudinal cohort (YOUth, based in Utrecht) and an intervention cohort (L-CID, based in Leiden). In addition, four other existing cohorts are

involved: TRAILS (Groningen), Generation-R (Rotterdam), RADAR (Utrecht, and NTR (Amsterdam). Furthermore, an animal cohort is implemented (based in Utrecht). For each cohort a CID representative is appointed as responsible for the organization of measurements that are needed to achieve the scientific goal of the WP they are related to. The cohort representative is responsible for the organization of the financial management of their cohort. The Cohort Representatives are: Prof. dr. C. Kemner (YOUth cohort, Utrecht), Prof. dr. M.H. van IJzendoorn (L-CID Intervention cohort, Leiden), Prof. dr. D.I. Boomsma (NTR, Amsterdam), Prof. dr. F.C. Verhulst (Generation-R, Rotterdam), Prof. dr. A.J. Oldehinkel (TRAILS, Groningen), Prof. dr. W.H.J. Meeus (RADAR, Utrecht), and Prof. dr. M. Joëls (Animal cohort, Utrecht).

The Scientific Advisory Board (SAB) is an advisory board to the research program in general and advises the Steering Committee. The members are: Prof. dr. J. Belsky (Davis), Prof. dr. N. Martin (Queensland), Prof. dr. M.J. Meaney (Montreal), Prof. dr. B.J. Casey (New York), Prof. dr. M.H. Johnson (London), Prof. dr. L. Steinberg (Philadelphia), and G.C.M.L. Page-Christiaens, PhD (Netherlands; ethical advisor). The SAB has had two meetings until now: on October 10, 2013 and on April 9, 2015.

The Supervisory Board (SB) is consisted of deans or division leaders of all consortium partners. It is the consortium's supervisory and ultimate decision-making body. The members are: Prof. dr. W. Raub (Utrecht University), Prof. dr. F. Miedema (University Medical Center Utrecht), Prof. dr. E.J.C. de Geus (VU University Amsterdam), Prof. dr. E.J. Fischer (a.i. University of Amsterdam), Prof. dr. J.T. Swaab (Leiden University), Prof. dr. F. Kuipers (University Medical Center Groningen), Prof. dr. D. Wigboldus (Radboud University Nijmegen), and Prof. dr. V.W.V. Jaddoe (Erasmus University Medical Center Rotterdam). The SB has had one meeting and one upcoming: on April 8, 2014 and on October 12, 2015.

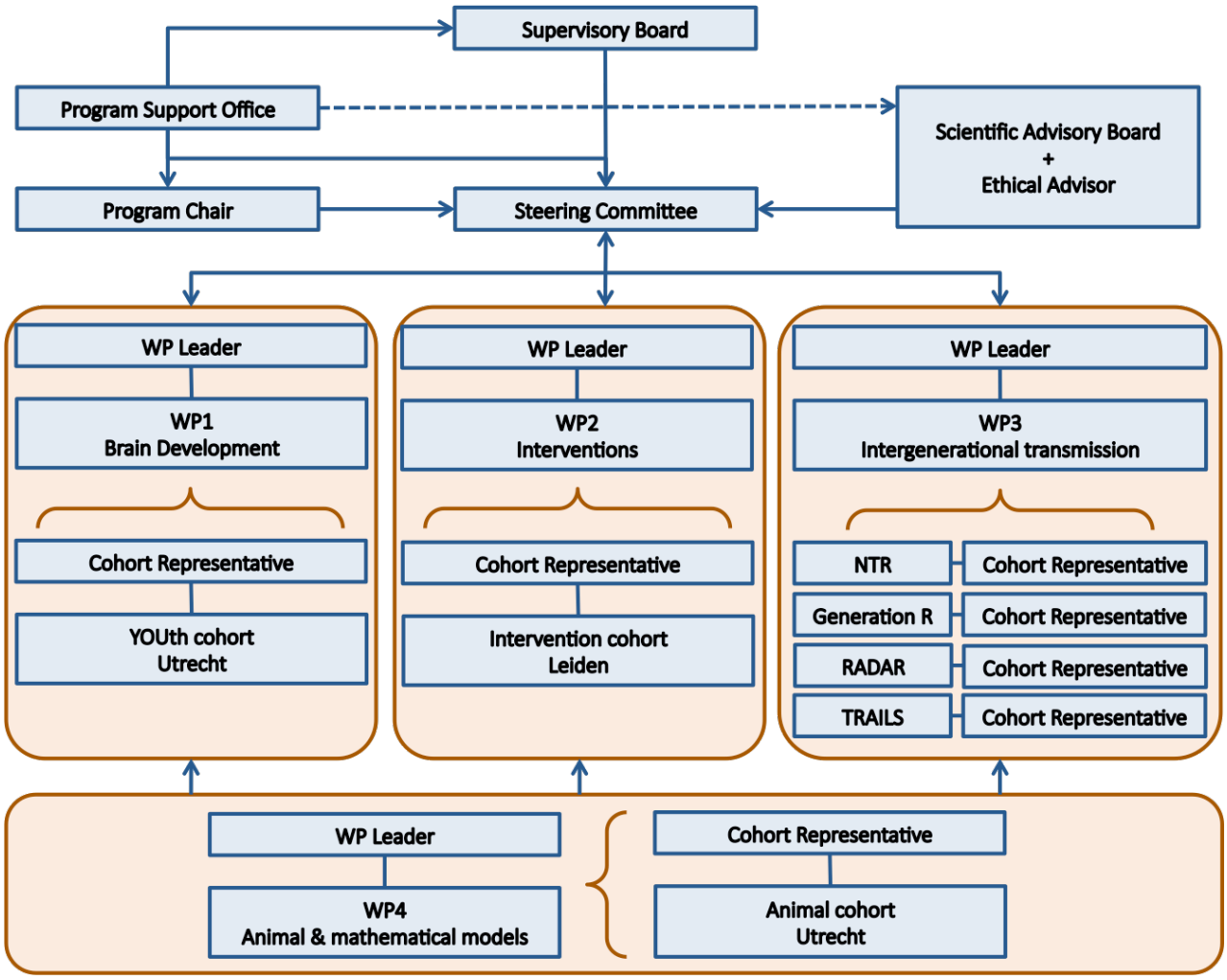
Conform the CA, structures for meetings, documentation, administration, and finance were set up in view of monitoring by NWO after 5 years. The Financial Office (manager and controller) set up a financial structure (control sheet, forms) and visited financial staff of all parties to explain procedures and structures. Each PI may use a maximum of 50% of their budget in the first 5 years: main applicants: 810.000 euro = 405.000 euro; other PI's: 540.000 euro = 270.000 euro. PI budgets are used for appointments of PhD-students and postdocs and need to be accepted by the Work package leader and the Steering Committee. Projects require the cooperation between minimally 2 PI's. Cohort representatives receive a fixed amount for the cohorts quarterly. PhD-students and postdoc staff on the cohort budget also have to be justified in an application to the steering committee.

CID Community

Network formation is one of the goals of the consortium. On September 15th 2015, CID counted 76 members: 20 Principle Investigators (PI's), 23 PhD-students, 22 postdocs and 11 senior scientists (assistant professor to professor) from eight different institutes. Twenty-eight researchers (15 PhD-students and 13 postdocs) are financed through CID budget (Appendix 1); others work in CID while being financed from cohort budgets or in another ways (Appendix 2).

Of the 20 PI's 55% is female. Of all CID appointed PhD-students and postdocs 82% is female (Appendix 1). Of all other CID researchers 85% is female (Appendix 2).

Organogram



Changes compared to original proposal

Because of health reasons, Prof. dr. Kahn took over the role of WP leader from Prof. dr. Durston from the start of the project.

In 2015, an ethical advisor is appointed and she takes place in the SAB as an extra member.
The ethical advisor advises the Steering Committee on various topics, including human and animal research, data protection, Biobank and database specialties. The ethical advisor is responsible for monitoring the proper application of the ethical rules and providing advice to consortium partners on ethical issues.
Instead of composing an Ethical Advisory Board of at least four experts (according to the CA), the Steering Committee and Supervisory Board agreed on appointing one ethical advisor as extra member of the Scientific Advisory Board. For the appointment, the different fields of expertise were taken into account. The Steering Committee decided on the appointment of the ethical advisor.
There are no changes foreseen in the coming years.

Activities and plans

Activities 2014-2015:

- 25 June 2014, Utrecht: we organized a 'Community kick-off lunch', following a CID tutorial, to make an inventory of the needs and suggestions in the community;
- 9 April 2015, Utrecht: Scientific Advisory Board meeting, with SAB members and Steering Committee;
- 10 April 2015, Utrecht: Second CID symposium with presentations by international experts (SAB members and PI) and poster presentations by PhD-students and postdocs;
- 31 August 2015, Utrecht: visit by Jet Bussemaker, minister of Education, Culture and Science and Jos Engelen, chairman of the governing board of NWO to meet with four program leaders of gravitation programs coordinated by Utrecht University, with a visit to the Child Research Center Utrecht (KinderKennisCentrum Utrecht), part of WP1;
- Every six months: CID meeting with all PI's, PhD-students, postdocs and others interested. Meetings were held on 17 December 2014, 18 March 2015 and 30 September 2015 in Utrecht. The meetings give CID researchers the opportunity to meet each other, to present their work and learn about each other activities. Every six months, the meeting is scheduled along with the PI-meeting and the Steering Committee meeting for convenience and to maximize turnout. Every meeting is completed with an informal reception;
- Every two months: Steering committee meeting.

Education and Talent management:

- As planned, we designed a curricular environment in which our Ma and PhD-students can obtain the right mix of deep disciplinary expertise *and* wider interdisciplinary outlook, needed for conducting world-leading child development research in the future. A list of specialized courses at Master/PhD level organized by the participating Graduate Programs for PhD-students and postdocs working in CID is available for download on the CID website (www.individualdevelopment.nl).
- Regular lectures/symposia: The students of the Graduate Program are regularly invited to attend a lecture given by one of the researchers, which addresses a specific topic from the research program in further depth. Examples are:
    - Keynote Lectures in the course 'Current Issues in Clinical Neuroscience' in the field of 'Translational Approaches in Developmental Disorders and Schizophrenia' from May 28 to June 3rd 2015 by BCRM, Utrecht.
    - The Symposium 'Using Big Data - Approaching complexity in neuroscience' on May 29th 2015 in RUG, by BCN Groningen.
    - The Symposium 'Emotions and the social brain in adolescence' on June 3rd 2015 in Leiden.
    - Keynote lectures during our own CID symposium.
- Summer Schools: During the course of the research program, Summer Schools rotate over the participating institutes. At Summer Schools, experts offer workshops on specific research skills, complemented by plenary keynote lectures. The topics partly capitalize on local research expertise, thereby also fostering cross-fertilization within the consortium. Students have the opportunity to present their research via mini-presentations.
  In 2015 Summer Schools were organized by:
    - The Faculty of Social and Behavioral Sciences of Utrecht University: 'Neurocognitive methods for infant and toddler research' from August 17th – 21st. All CID researchers were invited to join for a reduced fee.
    - The department methods and Statistics of Utrecht University: six Summer Schools on a range of methodological and statistical topics.
    - The Netherlands Graduate School of Linguistics: a Summer and a Winter school.

PR and branding:

- Maintenance of the CID website (www.individualdevelopment.nl), containing information and news about CID. It was developed for researchers working within the CID, but is open for

everyone. A member area with login contains items specifically for PI's working within the consortium. At the moment we are working on improving the website.
- At the moment we are working on the development of a CID logo and a new CID image for PR and branding purposes.

Plans 2015-2016:
- Extending the CID meetings every six months with the following activities: Factsheets will be distributed with the latest news from CID: publications, activities, poster presentations, oral presentations etc., combined with a 'Face page' introducing new staff. Preceding the meetings, a coffee session will be organized to inform the PhD-students and postdocs on community and educational activities.
- Organize a summer school each year and rotate the organization and location around the participating universities/university medical centers;
- Journal club / Opinion article assignment: A journal opinion article assignment was initiated to stimulate the multidisciplinary cooperation between CID PhD-students and postdocs. The CID PhD-students and postdocs may add to the existing studies by jointly publishing opinion articles. In small groups (2-4 persons) we ask researchers to participate in ongoing discourse in scientific communities or media. This may be done either by writing a journal club article, an opinion article in a scientific journal, or an opinion article in the (inter) national media.
  A first group started June 2015. At CID meetings, the end product is presented to the CID community and a new project will be started. In this way, we jointly a) train the PhD-students and postdocs within a multidisciplinary team to tackle scientific questions, b) stage our interdisciplinary strengths nationally and internationally and 3) increase our scientific output;
- Set up 'Tour de Consortium': Once a year we will organize a (lab) tour at one of the participating institutes, planning to start end of 2015. All CID members are invited for a (lab) tour around the institute showing the labs, facilities and methods/tools. A workshop or master class will be given by one of the principle investigators.
- We explore the possibilities of distributing a – digital – newsletter, containing news on the four work packages, recent publications, new staff short reviews of activities, and lists of upcoming activities organized by the consortium or its participating universities. Furthermore, we want to set up a closed LinkedIn group for the CID community. The digital newsletter could be spread via this LinkedIn group as well.

The following section is a description of the start and progression of the different research lines following the aims as described in the original NWO proposal. The progress per work package is specified and the future plans are described. Are there changes according to the original proposal and if yes, what was the motivation and what are the consequences. What is the added value of the Gravity subsidy for the different work packages?
We indicate per work package how the embedding and cooperation is organized nationally and internationally and we briefly indicate how we involve knowledge users in the research and how knowledge users benefit from the consortium.

WP1 – Brain development

Progression and future plans

WP1	WP-leader: Prof. dr. R.S. Kahn Cohort representative: Prof. dr. C. Kemner

Aim/objectives: The neurobiological developmental trajectory of newborns, children and adolescents is not well known. Particularly, the assessment of the extent to which genetic and environmental factors influence brain development and how these effects in turn influence behavior is only just emerging. WP1 focuses on brain development in relation to behavior, specifically on social competence and behavioral control and addresses questions regarding their interrelationships, how associations might develop as a function of age, sex genetic influences and environmental exposures.

Method/Cohorts: Two independent but related cohorts are studied within the YOUth research project. The first cohort is a birth cohort consisting of ~3,000 babies who are recruited through their pregnant mothers. Another cohort consists of a similar number of 8-10 year olds who will be recruited from the general population. Genetic and environmental data will be obtained and functional and structural neuroimaging will be acquired every three years.

Projects: In WP1 four PhD-students and four postdocs are employed via CID: Sanne Geeraerts (October 2014 – April 2019), Roy Hessels (January 2014 – December 2016), Fraukje Coopmans (June 2014 – June 2018), Dienke Bos (March 2015 – March 2017), Karin Fikkers (September 2015 – September 2019), Jalmar Teeuw (July 2015 – June 2019), Hannah de Mulder (January 2014 – May 2017), and Margot Peeters (January 2015 – December 2018). See appendix 1 for an overview of project titles and appendix 4 for progress reports.

Update progress: The large-scale longitudinal cohort study with repeated measurements (YOUth cohort) is being set up. YOUth follows children from before birth until the age of 18. Participants can enter at two moments: (1) When the mother is 20 weeks pregnant of the baby, and (2) when the child is at an age of 8, 9 or 10 years old. Subsequently the participants will be followed over an extended period of time. The YOUth cohort is conducted at the Child Research Center Utrecht (KinderKennisCentrum (KKC) Utrecht). After birth, the children visit the KKC at the ages of:

- 4-6 months and 9-11 months old (together referred to as '*rondom 0*');
- 2,3 or 4 years old ('*rondom 3'*);
- 5, 6 or 7 years old ('*rondom '6*);
- 8, 9 or 10 years old ('*rondom 9*', the second entry moment);
- 11, 12 or 13 years old ('*rondom 12*');
- 14, 15, and 16 years old ('*rondom 15*').

At each visit behavioral development and brain development is measured using EEG, Event-Related Potential (ERP), (f)MRI (from the age of 8), eye-tracking, behavioral development tasks, and computer tasks. Parent-child interaction and IQ (for both child and parents) are measured as well. Both parents (at the first visit) and children 8 years or older (at each visit) are asked to donate a blood sample. Furthermore, parents and children are asked to donate a buccal swap at each visit. Pregnant mothers are asked to donate a hair sample at 30 weeks of pregnancy and children that have at least 3 cm of hair are

also asked to donate a hair sample at each visit. Children aged 8 years or older are also asked to donate a spitting sample for steroid measurements. Finally, parents, children and teachers are asked to fill in several questionnaires at each wave.

The two enrolment moments were submitted to the IRB of the University Medical Center Utrecht as two separate protocols, but were handled simultaneously. We agreed with the IRB to first submit two framework protocols that described the general idea of YOUth, including follow-up and inclusion pregnant women. Subsequently, for each wave an amendment describing the specifics of each wave will be submitted to the IRB for approval.
In March and April 2015 the two framework protocols were approved (14-616/NL51465.041.14 and 14-617/NL51521.041.14). Subsequently, the amendments for '*rondom 9*' and '*rondom 0*' were submitted and '*rondom 9*' was recently approved.
At the end of May 2015 we started to include pregnant women. To date we included 49 women, with a response rate of 38%.

In the mean time, three pilot studies were conducted. One for the measurements of children aged approximately 5 months. This pilot included 70 babies. The second pilot included babies aged 10 months old. In this pilot approximately 70 babies were measured twice within 2 weeks, to calculate test-retest reliability. Finally, a pilot study on 135 children aged 8 to 16 years old was conducted. The data of these three pilot studies are currently being analyzed.

Plans: No adjustments. Start 8 years cohort in early 2016. Add MRI babies/pregnant women. Follow up 5 months/10 months.

Embedding and cooperation

There is extensive cooperation of P'Is in WP1 with other PI's, both within the WP and with the other WPs. Cooperation within WP1 includes projects on the effects of media violence exposure on aggression, development of infant self regulation and the role of attention herein, and a project on the role of narrative in behavioral development. Cooperation with WP2 involves two projects on the development of brain connectivity, and with WP3 there are several projects on adolescent development, including projects on the role of relationships, uncertainty dynamics and risk behavior. Additionally, there is a project on intergenerational transmission of skills. Finally, there are three projects in cooperation with WP4, two involving the use of advanced statistical methods in understanding development, and one on language development.

Knowledge utilization

At this point, it is somewhat premature to reach knowledge users because the YOUth cohort has just started up and data are not yet analyzed.
However, in 2014 there have been a few initiatives in the field of education for external parties and training. For example, the Brain Center Utrecht and the KKC organized a seminar for directors of primary schools, teachers, internal counselors and care teams on behavioral problems in children (October 29, 2014).
Furthermore, on October 16, 2014 the opening of the KKC took place by the mayor of Utrecht and the president of the executive board of Utrecht University, where local and national press together with external partners were invited.

WP2 – Interventions

Progression and future plans

WP2	WP-leader: Prof. dr. M.H. van IJzendoorn Cohort representative: Prof. dr. M.H. van IJzendoorn

Aim/objectives: Children are not equally vulnerable to adverse rearing environments, and they do not equally profit from supportive environments. Differential susceptibility theory proposes that vulnerable children who suffer most from bad environments also are more susceptible to positive changes in the child rearing and in the wider social environment. Central questions are: Who is most susceptible to the environment, and what are the neurobiological mechanisms of environmental influences on children's social competence and behavioral control? These questions are addressed experimentally in four longitudinal randomized controlled trials (L-CID), using cognitive and behavioral interventions.

Method/Cohorts: The four intervention studies within L-CID constitute an experimental cohort-sequential design. This implies a number of pre- and post-tests to examine the intervention effects with the added advantage that also the control groups of the four studies are partly overlapping in such a way that they can be combined in one series of quasi-longitudinal analyses from the first pre-test in the youngest L-CID cohort to the last post-test in the oldest L-CID cohort.
The four longitudinal experiments cover (1) infancy, (2) early childhood, (3) pre-adolescence, and (4) early adolescence respectively, and constitute four main projects. In the first half of the 10-years period covered by the grant, L-CID cohort 2 (starting at 3 years of age) and L-CID cohort 3 (starting at 7 years of age) will be focused upon, whereas in the second half L-CID cohort 1 and 4 will begin.

Projects: In WP2 four PhD-students are employed via CID: Michele Achterberg (September 2014 – September 2019), Rani Damsteegt (May 2013 – March 2018), Mara van der Meulen (January 2015 – January 2020), and Claudia Vrijhof (November 2013 – November 2017). See appendix 1 for an overview of project titles and appendix 4 for progress reports.

Update progress: Based on the discussions in the Scientific Advisory Board (SAB) and in the team of researchers it was decided to recruit families with same gender MZ and DZ twins as subjects for the studies. The advantages are: (i) more efficient recruitment/data collection/implementation of the intervention, (ii) potential for genetic modeling of intervention effects, and (iii) observing differential intervention effects between siblings within the same family at the behavioral, (epi-)genetic, hormonal and neural level of functioning. A working group has specified the overall design for the four intervention studies in L-CID and decided on the main behavioral and biological measures to be included.

Several pilots have been conducted. First is a pilot study on the association between behavior problems and tympanic membrane temperature (TMT) asymmetry (N=92). Second, the Video-feedback Intervention to promote Positive Parenting (VIPP) to be used in the Randomized Controlled Trials (RCTs) has been revised to include only 1 booster session. Piloting internet provision instead of home visits (meant to enhance efficiency) was deemed not to be feasible by pilot parents as well as interveners because of technical problems with two-way transfer of video-taped interactions for which strict confidentiality requirements had to be met. We adapted the VIPP for use with twins and successfully piloted the adapted protocol with three families. Third, two paradigms to assess the two central outcomes, namely prosocial behavior (Prosocial Cyberball, PCB) and aggressive behavior (Social Network Aggression Task, SNAT), have been developed and tested (N=136). PCB and SNAT were adapted to be used in the MRI scanner and have been adapted for a younger age group. In addition, pilots have been conducted on the Motionlogger (an actigraph to measure physical activity and sleep characteristics); on measurements of chaos in the home environment and the neighborhood; and on the use of the LENA (Language Environment Analysis), a small apparatus that records and analyzes speech/language and other auditory components in the home environment; and a digital ambulatory assessment app specifically developed for the current studies. After some adaptations these measures were found to be feasible and informative.

Study protocols for the early childhood (L-CID cohort 2) and pre-adolescence (L-CID cohort 3) RCTs have been submitted to the IRB of the institute of Education and Child Studies and the institute of Psychology, revised and submitted to the METC of LUMC (obligatory for studies with a neurobiological component), and to the national ethics committee CCMO. Both protocols have been positively evaluated. Both L-CID cohorts have been registered in the Netherlands Trial Register (NTR5312).

Recruitment and data collection: Recruitment for the first pre-test of the early childhood cohort has been finished with a high success rate: 239 families with twins (478 children) have been recruited and assessments of the first wave have been finished. Data collection for the second wave is in progress. Recruitment for L-CID cohort 3 started in the summer, and as of September 1, 2015, the first 44 children have participated in the fMRI lab visit, with great enthusiasm. Another 66 children have been scheduled already. Imaging and other lab tests are conducted in a newly built MRI facility at Leiden University Medical Centre, with two dedicated lab rooms, and a mock scanner nearby.

6 PhD-students, 2 research assistants, 2 postdocs, and a secretarial assistant have been involved in data collection and processing for the two cohort studies within L-CID since 2014.

Plans: Protocols for the two remaining cohorts 1 and 4 of L-CID will be prepared, and these studies will be implemented after piloting measures that are unique for these cohorts compared to L-CID cohort 2 and 3.

Embedding and cooperation

L-CID is most closely collaborating on the national level with Generation-R (Work Package 3, Henning Tiemeier, Frank Verhulst) and with Work Package 4 (animal models, Marian Joëls). Several co-supervised PhD projects cement this cooperation, and have already led to co-publications (see list of publications).

Cooperation with Work Package 3: Generation-R. Because we planned to include cortisol assessments in the L-CID cohorts and were searching for non-invasive but reliable assessments, we decided to analyze the psychometrics of hair cortisol collected in about 4,000 children in Generation-R. Another example is the collection of cyberball data in about 5,000 children and the development of an emotional reactivity observational system. Structural MRIs in almost 200 Generation-R children were analyzed in relation to parental sensitivity (a major variable in L-CID which is the focus of our intervention efforts with VIPP) and in relation to anti-social and prosocial behavior. A last example is the application of Genome-wide Complex Trait Analysis (GCTA) on attention and aggression issues with a combined dataset of Generation-R and NTR (Boomsma) to get a lower bound estimate of SNP heritability. Similarly, GCTA is applied to prosociality.

Cooperation with Work package 4: The first project involving a PhD-student from Work Package 4 (Jiska Kentrop) and a postdoc from Leiden University (UD, Rixt van der Veen) is on the influence of maternal deprivation and complex living conditions on behavioral inhibition and attention in adolescent Wistar rats. We found that animals that were raised in large, complex cages, together with 10 conspecifics, showed improved attention, but impaired behavioral inhibition in the 5-choice serial reaction time task. The early life challenge of 24h maternal deprivation on postnatal day 3 led to a decline in bodyweight during adolescence, but did not by itself influence responses in the 5-choice task in adulthood, nor did it moderate the effects of complex housing. Our data suggest that a complex rearing environment leads to a faster adaptation to changes in the environment, but at the cost of lower behavioral inhibition. A second study on prosocial behavior in rats is in progress, and a third study on differential susceptibility of mice to experimental manipulation of the environment (for better and for worse) dependent on their genotype is being planned and a PhD-student recruited.

Internationally, L-CID cooperates with Gusto, a large cohort study in Singapore (Michael Meaney), ALSPAC in the UK (Beate St Pourcain), Imperial College London (Ramchandani); MPEWS in Melbourne, Australia (Galbally), and with a network of researchers who were involved in a Jacobs Foundation meeting on prosocial development (including among others Andrew Fuligni, Ron Dahl, Jennifer Pfeifer, Eva Telzer, Nim Tottenham, and Sarah-Jayne Blakemore).

Knowledge utilization

At this point it is somewhat premature to try and reach knowledge users with findings of WP2. Some pilot results have been publicized in popular media and at popular meetings, but in the second half of the funding period we plan to actively distribute L-CID findings to practitioners and professionals working with children.

WP3 – Intergenerational transmission

Progression and future plans

WP3	WP-leader:	Prof. dr. W.H.J. Meeus
	Cohort representatives:	
	NTR:	Prof. dr. D.I. Boomsma
	Generation-R:	Prof. dr. F.C. Verhulst
	TRAILS:	Prof. dr. A.J. Oldehinkel
	RADAR:	Prof. dr. W.H.J. Meeus

Aim/objectives: WP3 will study how characteristics of (grand)parents (Generation 1 (G1)) impact the development of adolescents and adults (Generation 2 (G2)) and – through them – the development of their children (Generation 3 (G3)). To do so, WP3 adopts a multi-generation design and establishes the extent to which genetic and non-genetic transmission between generations causes differences between children and adolescents in developmental outcomes.

Method/Cohorts: WP3 uses existing cohorts that collected G1 and G2 data (Generation-R, NTR, RADAR, TRAILS) and will set up additional data-collection among Generation 3.
WP3 implements the research in the four strongest cohort studies on child development in the Netherlands: Generation-R, the Netherlands Twin Register (NTR), Research on Adolescent Development and Relationships (RADAR), and the Tracking Adolescents' Individual Lives Survey (TRAILS).

Projects: In WP3 three PhD-students and four postdocs are employed via CID: For Generation-R Alexander Neuman (Aug 2014 – Aug 2018); for NTR Eveline de Zeeuw (December 2014 – December 2017) and Sabine Veldkamp (May 2015 – May 2019); for RADAR Andrik Becht (September 2014 – September 2018) and Stefanie Nelemans (September 2014 – September 2017); for TRAILS Annelene Bloemen (December 2014 – December 2017; not financed by CID), Tina Kretschmer (October 2013 – December 2017), and Odilia Laceulle (October 2013 – Augustus 2015); her project will be continued by Anoek Sluiter-Oerlemans (September 2015 – February 2018). See appendix 1 for an overview of project titles and appendix 4 for progress reports.

Update progress:
Generation-R
The epigenetic measurements have been commissioned and are currently ongoing; these are funded in part by the Gravity subsidy and will be analyzed by personnel funded by this program.
Currently, we are working on the construction of a general psychiatric vulnerability factor, estimation of its Single Nucleotide Polymorphism (SNP) heritability, and have begun Genome Wide Association Study (GWAS) analyses of parent-rated problem scores and this vulnerability factor.
In parallel, the assessment of life events is ongoing, and large parts of the data have been cleaned and structured.

NTR
The aim of the project 'Longitudinal development and intergeneration transmission of psychopathology versus wellbeing' is to understand the genetic versus cultural mechanisms and contrast the findings for psychopathology to those for wellbeing by collecting intergenerational data in four designs:

(1) Parents of young twins who are twins themselves,
(2) Young twins who become parents themselves,

(3) Adult twins with adult offspring, and
(4) Grandparents of twins.

The Netherlands Twin Register (NTR) asked parents of young twins whether they themselves were also part of a twin pair. When this was the case they and their co-twins were asked to fill out surveys about themselves. These twin pairs, of which one of the twins is the mother or father of a twin pair, and their twin children have been identified in the different data sets (Y(oung)NTR and A(dult)NTR). Measures that are available for both the parents and children are psychopathology, well-being, education, physical activity and physical characteristics. Preparations have been made to start the data collection in children of twins of the YNTR. All twins in the cohorts 1986-1990 that have offspring themselves have been identified. These twins will be approached in the upcoming months to invite them to fill out a survey about the development of their own children. Extensive longitudinal data on, amongst others, psychopathology and well-being are available for this sample of parents, and the to-be-collected survey for the children will include measures on psychopathology, well-being, behavioral control, temperament and the home environment.

RADAR

Wave 8 of data-collection took place in fall 2014 and spring 2015. 1,152 target parents participated along with 567 intimate partners. Attrition between w1 and w8 is about 15%. Data-collection of Generation 3 participants is underway in close collaboration with TRAILS, see there. Planned publications on anxiety development and identity formation were realized.

TRAILS

As intended and in close collaboration with the RADAR study group, we made preparations to enrich the TRAILS study with measures of a third generation, involving questionnaires and/or observational measures during pregnancy and at 3, 24, and 48 months of age. Parental measures include personality, psychopathology, life events, and difficulties; offspring measures early movements, milestones, temperament, cognitive control, social competence, and psychopathology. The actual data collection started in April 2015 with the screening of the cohort regarding pregnancies; the upcoming period will additionally be devoted to the inclusion of children who were already born in the past years (> 80). According to plan and intention, we investigated interpersonal environments of the TRAILS participants Generation 2, and assessed the quality of relationships with parents in adolescence, as well as quality of relationship with intimate partner in emerging adulthood. Also in line with the plan, we started investigating developmental models of psychological distress. The main aim was to use longitudinal and transactional models to disentangle the complex interplay between individuals and their environments in the prediction of psychological distress (i.e., psychopathology). Two publications explicitly focus on this topic by examining how respectively pathways by which individual characteristics (temperament, self-regulation) and environmental characteristics (perceived affection, negative social interactions) contribute to subsequent developmental outcomes (stress exposure, internalizing and externalizing problems). Two other publications focus more generally on the structure and psychopathology and correlates between psychopathology and personality.
These studies were conducted in collaboration with other CID-PIs (Deković, Meeus, Verhulst, Vollebergh).

Apart from the data collection and scientific staff made possible by the Gravitation subsidy, the consortium had clear added value by facilitating collaboration and harmonization, notably between RADAR and TRAILS, and offering inspiring meetings to PhD-students and postdocs.

Plans: The four studies plan to look for additional funding, as the current budget is very tight for their large-scale investigations, especially given the large scale new data collection in children of generation 3.

Embedding and cooperation

The four studies participated in Investment Grant NWO Large. They also take part, in different combinations, in international consortia: the EAGLE consortium for genetic analyses of child behavior (GWAS) (Gen-R, TRAILS), the PACE consortium for epigenetic analyses (Gen-R) and the ACTION consortium for the study of conduct disorder problems (Generation-R), the GWA consortium on literacy, named GenLang (NTR), and the International Cannabis Consortium (all 4 studies).

NTR, RADAR and TRAILS have had several conference calls to gain insight into the overlapping measures of the various cohorts. NTR, RADAR and TRAILS discussed the collection of data in children of active participants.

Knowledge utilization

Study findings are communicated through Twitter (NTR and TRAILS), study websites (Generation-R, NTR, TRAILS), and newsletters for respondents (NTR, RADAR, TRAILS). TRAILS has a Facebook page. Many study results attract attention from the (inter) national press. A recent example: the TRAILS dissertation on alcohol use and brain development on the front page of national newspaper De Volkskrant (3-12-2014).

WP4 – Animal and mathematical models

Progression and future plans

WP4	WP-leader: Prof. dr. M. Joëls Cohort representative: Prof. dr. M. Joëls

Aim/objectives: WP4 provides modeling tools that form a supportive basis for WPs 1 to 3. The main aim is to run animal/modeling 'experiments' in parallel with the human cohorts.

Method: The specific goals of WP1-3 will be pursued in parallel in existing rodent and avian models. This allows optimal alignment between WP1-3 and WP4, as well as a level of control over gene x environment (GxE) and detail on neural function that cannot be achieved in humans. Furthermore, a theoretical framework derived from animal studies, among other things, will be used as the basis for confirmatory statistical models for the analysis of experimental and longitudinal data form the human cohorts. Prof. dr. Joëls is PI for the rodent models, Prof. dr. Bolhuis is PI for the avian models and Prof. dr. Hoijtink is PI for the statistical models.

Projects: In WP4 four PhD-students and five postdocs are employed via CID: For rodent models Manila Loi (September 2013 – September 2015), Jiska Kentrop (July 2014 – July 2018), Rixt van der Veen (October 2013 – August 2014; currently junior staff member in the group of Marinus van IJzendoorn/Marian Bakermans-Kranenburg), and Angela Sarabdjitsingh (November 2013 – February 2018); for bird models Gabriel Beckers (October 2014 – October 2017), Sita ter Haar (March 2015 – January 2016), and Carien Mol (October 2015 – June 2018); for statistical models Mariëlle Zondervan (July 2014 – June 2018), Sofia Kanatsou (August 2015 – April 2016) and Yasin Altinisik (February 2015 – February 2019; not financed by CID). See appendix 1 for an overview of project titles and appendix 4 for progress reports.

Update progress:

Use of rodent models

Several animal models for early life adversity (based on disturbed mother-infant interactions) have been implemented, against a precisely controlled genetic background, targeting genes involved in the stress system. We set up lines with MR overexpression, MR knockout, GR knockout and combinations thereof. In these animals we can test to what extent genetic predisposition exacerbates or protects against adverse early life conditions.

A second question addressed concerns the extent to which the consequences of early life adversity on the developing rodent brain can be normalized during the sensitive peri-pubertal period, through

environmental or pharmacological interventions. In case the latter was possible, we next tested if epigenetic programming is a critical step in this normalizing process.
In all studies, special attention was paid to male-female differences.
Experimental endpoints encompassed:

- Impulsive behavior and selective/sustained attention in the 5-choice serial reaction time task
- Social play and social interaction behavior
- Reward-based decision making
- Contextual memory formation
- Sensory-motor development, social behavior and behavioral flexibility

Use of avian models
This sub-project has two research lines: (1) Gene-environment interactions in the development of social behavior in birds, and (2) How do developmental factors affect each other in the development of song and social preferences in birds?
Regarding research line 1, unfortunately planned collaboration with Dr. Brian McCabe (Univ. of Cambridge, UK) cannot be executed, due to closure of the Cambridge lab. We hope to be able to start a planned collaborative project on the neurogenetics of birdsong learning with Prof. dr. Claudio Mello (Portland, USA).
Regarding research line 2, further technical advancements of high-density multi-electrode recording setup now enable us to measure auditory evoked and event-related action and local field potential activity in a sleep-like state with sub millisecond precision over long recording episodes (hours). The data collection stage of a first experiment has almost been completed. Preliminary results show sensitivity of neural systems, particularly secondary auditory cortices, to vocal sequence structure (Gabriël Beckers).
Song recordings at different stages of development will be analyzed. One of the goals is to find precursors for good or bad vocal learning. We can use such precursors to distinguish 'good' from 'bad' learners early in development and study if there are gene expression differences in their brains based on learning level (Sita ter Haar). We further completed a first experiment studying song recognition in zebra finches by exposing them to manipulated songs in phonotaxis preference tests (Carien Mol).

Use of statistical models
We develop inferential procedures that are relevant for CID research in cooperation with CID researchers. In the past year the following projects have been initialized:

- Using data and expert knowledge to estimate a model parameter.
- Developing statistical tools for replication studies in the context of cumulative stress and match/mismatch theories (in cooperation with CID-PI's Tineke Oldehinkel and Marian Joëls).
- Developing statistical tools for theory based evaluation of contingency tables in the context of eye-tracking studies (in cooperation with CID-PI Chantal Kemner).

It is expected that in the coming year this projects will lead to four papers that will be submitted for publication to international peer reviewed journals.

Plans:
Use of rodent models
Two experimental series will be started in the coming year:

- Testing the influence of early life environment (and intervention) on prosocial behavior.
- Testing the influence of increased maternal care – in interaction with genetic background – on neuroendocrine development, social behavior and on nursing style in the next generation.

These studies will be carried out in close collaboration between Marian Joëls (PI WP4) and Marinus van IJzendoorn/Marian Bakermans-Kranenburg (PI's WP2), with support of junior PI's Rixt van der Veen en Angela Sarabdjitsingh.
Use of avian models
Dr. Beckers will focus on a neural analysis of perception of syntacticly structured auditory stimuli, as well as of sleep and its role in song learning. He will develop methods that will enable him to record

electrophysiological activity in awake birds.
Dr. Ter Haar will investigate the role of predispositions, hemispheric lateralization and sleep on vocal learning quality. Specifically, she will study the effect of sleep deprivation on vocal learning quality, measuring several neuronal and behavioral parameters. Using the same measures, she will test the effect of predispositions on learning quality and neural activity. In addition, Dr. Ter Haar will investigate the possibility of a joint project with Prof. dr. Mello on the neurogenetics of birdsong learning.
Ms. Mol will investigate birdsong production, perception and learning, and directly compare this to human language and speech acquisition. The latter will be done in collaboration with Prof. dr. Rene Kager (UU, linguistics).

Use of statistical models
One additional research project will be initialized in the coming year. In cooperation with CID-PI Jos van Berkum (WP1) statistical tools for theory based data evaluation will be applied (to data on the relation exposure to fiction and social competence).

Embedding and cooperation

- Rodents: Most of the studies on rodents were carried out in close collaboration between Marian Joëls (PI WP4) and Marinus van IJzendoorn/Marian Bakermans-Kranenburg (PI's WP2), with support of junior PI's Rixt van der Veen en Angela Sarabdjitsingh.
- Birds: We collaborate with prof. dr. Joëls and prof. dr. Kemner.
- Models: The projects on statistical models described above are nationally embedded through cooperation of WP4-PI Herbert Hoijtink with CID-PIs Tineke Oldehinkel, Marian Joëls, Chantal Kemner, and Jos van Berkum.

Overall, the projects are carried out in collaboration with PI's from all CID work packages. Collaborations outside of CID are extensive but not mentioned here.

Knowledge utilization

Use of rodent models (PI: M. Joëls)
PI's of WP4 have reached out to school teachers to supply the latest insights in behavioral problems in the school setting. The rodent work was featured several times on national radio and magazines. Pharmacological interventions, if successful, could be translated to the human situation. However, at this stage such a translation is not appropriate yet.

Use of bird models (PI: J. Bolhuis)
We study birdsong acquisition as a model for human speech and language acquisition. The first step towards knowledge utilization is interacting with linguists and with the general public. We accomplished this by organizing an Academy Colloquium on The Biology of Language. Johan Bolhuis and Martin Everaert (UU, linguistics) are editing a special issue of Neurosci. Biobehav. Rev. on the same topic. Noam Chomsky's talk at the Colloquium was put online on our Youtube channel BirdsongLanguage: https://www.youtube.com/user/BirdsongLanguage/videos
Prof. dr. Bolhuis has given a number of interviews for TV and radio and was recently interviewed by BBC Radio4 (http://www.bbc.co.uk/programmes/b05tz9jr).

Use of statistical models (PI: H. Hoijtink)
The knowledge we render is methodology and statistics for theory based data evaluation and replication studies. The users of this knowledge are the other CID PIs. As elaborated above, these are involved in our studies to ensure that the knowledge we render is relevant to them.

Interrelation between the four Work Packages

Work Package 1, rooted in the Utrecht YOUth cohort, focuses on longitudinal changes in brain structure and the way these changes relate to genetic and environmental factors, and how this brain development in turn mediates behavioral development.
Work Package 2 aims to dissect the reason why not all children are equally responsive to variations in the social environment. It is based on the Leiden L-CID cohort, where large-scale experimental-longitudinal interventions of parent and peer behavior allow for testing of which child characteristics shape the effect of (manipulated) environmental factors.
Work Package 3 focuses on the continuity of thriving (or failure to thrive) across three generations, and uses information available in large existing Dutch cohorts. The aim is to determine which factors are involved in the transmission of behavior between grandparents, parents, and children.
Work Package 4 complements the studies in work packages 1-3 with advanced mathematical modeling and animal research. Both behavioral rodent and avian models of social and adaptive behavior will be used, with the additional possibility of detailed analyses focusing on development of involved brain structures. Mathematical models allow better description of longitudinal effects and ensure better data quality.

Because the focus of the project is on development from birth to adolescence, the core of all Work Packages consists of large-scale longitudinal cohort studies, a method for which the Netherlands has a strong reputation. Data collection for the new cohorts YOUth and L-CID are organized in Utrecht and Leiden, the combined existing cohorts from WP3 are used for a series of three-generation studies. Combined we study how environmental factors and child characteristics affect the development of social competence and behavioral control, and the mechanisms through which this occurs. The studies are addressed in three separate but interrelated WPS, each linked to a specific (set of) cohort(s). WP4 provides a supportive basis using animal and mathematical models of development.
All WPs focus on the development of social competence and behavioral control, and will use partly the same measures to establish this. In all WPs there is a focus on specific child characteristics (including candidate genes, perinatal factors and temperament) and environmental factors (parent, peers and media), and their interactions.

Budgets and actuals

Table A – Allocation PI budgets and actuals

(€)	2013		2014		2015		Total		Total Budget	
	Allocated	Actual	Allocated	Actual	Allocated	Actual	Allocated	Actual	5 yr	10 yr
WP1 – Brain Development										
Berkum, Jos van			61.106	38.629	62.182	18.463	270.000	57.092	270.000	540.000
Deković, Maja			4.306	3.219	37.197	5.250	223.638	8.469	270.000	540.000
Durston, Sarah					75.254	12.824	160.904	12.824	405.000	810.000
Hulshoff Pol, Hilleke[a]					62.917		270.000		270.000	540.000
Kahn, René			25.903	26.532	68.386	14.341	268.983	40.873	270.000	540.000
Kemner, Chantal	3.750		68.147	68.926	52.280	16.704	187.934	85.630	405.000	810.000
Valkenburg, Patti[b]					15.967		216.905		405.000	810.000
Vollebergh, Wilma					33.961	10.436	146.645	10.436	270.000	540.000
Total WP1	**3.750**		**159.462**	**137.306**	**408.144**	**78.019**	**1.745.009**	**215.324**	**2.565.000**	**5.130.000**
WP2 - Intervention										
Bakermans-Kranenburg, Marian	21.332	19.443	40.550	33.734	42.639	11.217	204.297	64.394	270.000	540.000
Crone, Eveline			11.658	9.451	35.046	10.039	205.335	19.489	270.000	540.000
Engels, Rutger					32.975	9.853	205.335	9.853	270.000	540.000
Ijzendoorn, Marinus van	6.682	6.797	44.964	38.260	51.791	14.560	206.600	59.617	405.000	810.000
Total WP2	**28.014**	**26.240**	**97.173**	**81.445**	**162.451**	**45.669**	**821.567**	**153.354**	**1.215.000**	**2.430.000**
WP3 - Intergenerational										
Boomsma, Dorret			1.387	4.579	69.998	22.990	405.000	27.569	405.000	810.000
Meeus, Wim			40.440	14.160	105.084	32.736	382.146	46.895	405.000	810.000
Oldehinkel, Tineke	16.570	15.327	68.624	58.384	68.812	20.497	270.000	94.208	270.000	540.000
Ormel, Hans	11.811	8.516	45.662	43.316	52.224	16.243	270.000	68.075	270.000	540.000
Verhulst, Frank			75.349	17.814	61.887	14.249	270.000	32.063	270.000	540.000
Total WP3	**28.380**	**23.843**	**231.462**	**138.252**	**358.005**	**106.715**	**1.597.146**	**268.811**	**1.620.000**	**3.240.000**
WP4 - Animal										
Bolhuis, Johan			27.427	1.976	59.337	22.082	121.989	24.058	270.000	540.000
Hoijtink, Herbert			25.153	23.741	83.905	13.131	269.600	36.872	270.000	540.000
Joëls, Marian[c]	11.802		71.775		89.405		318.002		405.000	810.000
Total WP4	**11.802**	**0**	**124.355**	**25.717**	**232.647**	**35.213**	**709.591**	**60.930**	**945.000**	**1.890.000**
TOTAL	**71.945**	**50.083**	**612.451**	**382.720**	**1.161.247**	**265.616**	**4.873.312**	**698.419**	**6.345.000**	**12.690.000**

Please note that all actuals shown for Tables A, B and C are for the period including April 2015.

Please note that the allocated budgets are only shown for the years 2013-2015. There are projects that have a longer term (e.g. until 2019) and therefore more allocated budget than shown in the separate columns. Therefore, the cumulative of allocated budget for 2013-2015 can be less that the total allocated budget.

As the numbers of the table show, almost all PI's have allocated most of their 5-year budget, indicating that all Work Packages have taken off successfully.

[a] PhD-student started from 1 July 2015, so actuals could not be given.

[b] PhD-student started from 1 September 2015, so actuals could not be given.

[c] PI-budget Joëls will be corrected out of the UMCU. Therefore, no actuals could be given at this moment.

Table B – Cohort budgets and actuals

(€)	2013		2014		2015		Total Budget		
	Budget	Actual	Budget	Actual	Budget	Actual	5 yr	10 yr	Total Actual
WP0 – Project Management									
1. Project Management	104.400	93.273	156.600	48.446	156.600	32.379	779.850	1.559.700	174.098
2. General Project Costs	38.020	51.224	57.030	13.865	57.030	28.104	285.150	570.300	93.193
Total WP0	**142.420**	**144.496**	**213.630**	**62.312**	**213.630**	**60.483**	**1.065.000**	**2.130.000**	**267.291**
WP1 - Brain Development									
1. Direct Costs	119.520	52.970	352.062	210.556	352.062	127.095	1.673.919	3.347.838	390.621
2. Marketing & Communication	27.240	0	66.150	2.871	66.150	623	318.105	636.210	3.495
3. Recruitment	67.488	0	163.350	19.710	163.350	108	785.691	1.571.382	19.819
4. Accommodation	6.780	0	22.500	92	22.500	1.456	106.335	212.670	1.549
5. ICT costs	43.080	0	127.800	0	127.800	17.142	607.410	1.214.820	17.142
6. Equipment	217.080	0	0	186.918	0	2.377	108.540	217.080	189.295
Total WP1	**481.188**	**52.970**	**731.862**	**420.148**	**731.862**	**148.802**	**3.600.000**	**7.200.000**	**621.920**
WP2 - L-CID Intervention									
1. Intervention	234.000	21.587	351.000	162.702	351.000	45.409	1.755.000	3.510.000	229.697
Total WP2	**234.000**	**21.587**	**351.000**	**162.702**	**351.000**	**45.409**	**1.755.000**	**3.510.000**	**229.697**
WP3 - Intergenerational									
2. NTR	24.000	98	36.000	31.806	36.000	11.596	180.000	360.000	43.499
3. Radar[a]	24.000	0	36.000	0	36.000	0	180.000	360.000	0
1. Trails	24.000	0	36.000	21.412	36.000	16.277	180.000	360.000	37.690
4. Generation-R[b]	6.000	0	9.000	25.000	9.000	0	45.000	90.000	25.000
Total WP3	**78.000**	**98**	**117.000**	**78.218**	**117.000**	**27.873**	**585.000**	**1.170.000**	**106.189**
WP4 - Animal costs									
1. Animal costs[c]	60.000	14.285	90.000	70.028	90.000		450.000	900.000	84.313
Total WP4	**60.000**	**14.285**	**90.000**	**70.028**	**90.000**		**450.000**	**900.000**	**84.313**
TOTAL	**995.608**	**233.436**	**1.503.492**	**793.408**	**1.503.492**	**282.566**	**7.455.000**	**14.910.000**	**1.309.410**

[a] RADAR will have actualization of cohort budget in the course of 2015-2016.

[b] For Generation-R there was a prepayment, resulting in higher actuals than estimated for 2014. This is compensated in the years 2013 and 2015.

[c] Because of inaccuracies in the reporting of the UMCU, actuals could not be given for 2015. The Financial Office of CID is in contact with the UMCU.

Table C – Co-funding budgets and actuals

(€)	2013		2014		2015		Total	
	Budget	Actual	Budget	Actual	Budget	Actual	Budget	Actual
UMCU Contribution of strategic budget year 1 to 5[a]	360.000		360.000	0	360.000		1.800.000	0
UMCU Intended contribution strategic budget year 6 to 10[a]	0		0		0		1.800.000	
UMCU Free MRI Scans[a]	0		777.778		777.778		7.000.000	
UU Top area Youth (Topgebied Jeugd)	1.000.000	0	1.000.000	260.761	1.000.000	41.034	4.000.000	301.794
UU Contribution FSW for additional postdocs[b]	0	16.769	0	203.275	340.000	86.484	1.360.000	306.528
UMCG Additional PhDs infrastructure TRAILS and intended PhDs	200.000	22.600	200.000	132.238	200.000	49.110	800.000	203.948
UL Free MRI-scans	0	0	20.000	0	20.000	8.333	200.000	8.333
UL Additional PhDs	0	0	50.000	14.337	50.000	10.121	200.000	24.458
UvA Four additional PhDs[c]	0	0	0	0	0	0	200.000	0
TOTAL	**1.560.000**	**39.369**	**2.407.778**	**610.611**	**2.747.778**	**195.082**	**17.360.000**	**845.062**

[a] The UMCU did not report actuals for matching. The Financial Office of CID is in contact with the UMCU.

[b] UU (Faculty of Social and Behavioral Sciences) started with the appointment of postdocs as matching before 2013.

[c] UvA has no actuals for matching, conform budget.

Appendices

Appendices

Appendix 1 – CID appointed PhD-students and postdocs

CID appointed researchers	
WP1	
Dr. Dienke J. Bos *Connected and in control* Durston, Crone; UMC Utrecht	**Postdoc** Mar/15 - Mar/17
Fraukje Coopmans *Developmental trajectory of the human connectome in health and disease* Kahn, Crone; UMC Utrecht	**PhD-student** Jun/14 - Jun/18
Dr. Karin Fikkers *The effects of media violence exposure on aggression: A differential susceptibility perspective* Valkenburg, Dekovic, University of Amsterdam	**Postdoc** Sept/15 - Sept/19
Sanne B. Geeraerts *Development of infant self-regulation within the early caregiver relationship: A cascade model* Dekovic, Kemner; UU Faculty of Social and Behavioral Sciences	**PhD-student** Oct/14 - Apr/19
Roy S. Hessels *The effects of social stimulation/interaction on perceptual and social development* Kemner, Hoijtink; UU Faculty of Social and Behavioral Sciences	**PhD-student** Jan/14 - Dec/16
Jalmar Teeuw *Genetic and environmental influences on development of structural and functional brain connectivity* Hulshoff Pol, Boomsma; UMC Utrecht	**PhD-student** Jul/15 - Jun/19
Dr. Hannah de Mulder *The power of stories: exploring the effects of (self) narrative on the development of social competence and behavioral control* Van Berkum, Valkenburg; UU Faculty of Humanities	**Postdoc** Jan/14 - May/17
Dr. Margot Peeters *Behavioral control and reward sensitivity as predictors of adolescents' risk behaviors* Vollebergh, Oldehinkel; UU Faculty of Social and Behavioral Sciences	**Postdoc** Jan/15 - Dec/18
WP2	
Michele Achterberg *Social aggression regulation in childhood and emerging adolescence* Crone, Bakermans-Kranenburg; UL Faculty of Social and Behavioral Sciences	**PhD-student** Sep/14 - Sep/19
Rani Damsteegt *Intervention effects of video/feedback on parenting and social competence in preschoolers: The role of genetic polymorphisms, temperament and tympanic membrane temperature* Bakermans-Kranenburg, Crone; UL Faculty of Social and Behavioral Sciences	**PhD-student** May/13 - Mar/18
Mara van der Meulen *Social aggression regulation in childhood and emerging adolescence* Engels, Crone, Van IJzendoorn; UL Faculty of Social and Behavioral Sciences	**PhD-student** Jan/15 - Jan/20

Claudia I. Vrijhof *Intervention effects of video-feedback on social competence and behavior control in preschoolers: the mediating role of parenting and physiological regulation* Van IJzendoorn, Bakermans-Kranenburg, Crone; UL Faculty of Social and Behavioral Sciences	**PhD-student** Nov/13 - Nov/17
WP3	
Andrik Becht *Why some adolescents thrive and others don't: The role of uncertainty dynamics* Meeus, Vollebergh; UU Faculty of Social and Behavioral Sciences	**PhD-student** Sep/14 - Sep/18
Dr. Tina Kretschmer *Examining the complex interplay between relationship experiences and individual factors to understand adolescent development* Oldehinkel, Meeus, Dekovic; UMC Groningen	**Postdoc** Oct/13 - Dec/17
Dr. Odilia M. Laceulle *Investigating developmental models of psychological distress: transactional processes and explanatory models of individual differences* Ormel, Meeus, Van IJzendoorn; UMC Groningen <u>Project to be continued by:</u> **Dr. Anoek Sluiter-Oerlemans**	**Postdoc** Oct/13 - Aug/18 **Postdoc** Sep/15 - Feb/18
Dr. Stefanie A. Nelemans *Development of anxiety symptoms in adolescence and early adulthood: over/time links with biological, psychological, and social factors* Meeus, Oldehinkel; UU Faculty of Social and Behavioral Sciences	**Postdoc** Sep/14 - Sep/17
Alexander Neumann *The epigenetics of intergenerational transmission* Verhulst, Oldehinkel, van IJzendoorn; Rotterdam Erasmus MC	**PhD-student** Aug/14 - Aug/18
Sabine Veldkamp *Intergenerational transmission of reading and cognitive skills* Boomsma, Van Berkum; VU University Amsterdam	**PhD-student** May/15 - May/19
Eveline de Zeeuw *Longitudinal development and intergeneration transmission of psychopathology versus wellbeing* Boomsma, Oldehinkel; VU University Amsterdam	**Postdoc** Dec/14 - Dec/17
WP4	
Dr. Gabriël J.L. Beckers *A neurogenetic analysis of birdsong learning as a model for infant development* Bolhuis, Joëls; UU Faculty of Social and Behavioral Sciences	**Assistant professor** Oct/14 - Oct/17
Dr. Sita M. ter Haar *A neurogenetic analysis of birdsong learning as a model for infant development* Bolhuis, Joëls; UU Faculty of Social and Behavioral Sciences	**Postdoc** Mar/15 - Jan/16
Dr. Sofia Kanatsou *Environmental influences on brain development: rodent models* Hoijtink, Joëls; UU Faculty of Social and Behavioral Sciences	**Postdoc** Aug/15 - Apr/16
Jiska Kentrop Joëls, Bakermans-Kranenburg; UMC Utrecht, UL	**PhD-student** Jul/14 - Jul/18

Manila Loi *Intervention at puberty after early life adversity* Joëls, van IJzendoorn; UMC Utrecht	**PhD-student** Sep/13 - Sep/15
Carien Mol *Twitter evolution: Comparative linguistics of birdsong and child language acquisition* Bolhuis, Kemner; UU Faculty of Social and Behavioral Sciences	**PhD-student** Oct/15 – Jun/18
Angela Sarabdjitsingh *Environmental influences on brain development: rodent models* Joëls; UMC Utrecht	**Postdoc** Nov/13 - Feb/18
Dr. Rixt van der Veen *Development of behavioral tasks to monitor empathy and behavioral inhibition in rodents* Joëls, van IJzendoorn, Bakermans-Kranenburg; UL Faculty of Social and Behavioral Sciences	**Assistant professor** Oct/13 - Aug/14 *From Aug/14 still working on CID in WP2, but no longer financed through CID (see also Appendix 2)*
Mariëlle A.J. Zondervan-Zwijnenburg *Formalization and evaluation of prior knowledge based on prior/posterior predictive inference* Hoijtink, van Berkum; UU Faculty of Social and Behavioral Sciences	**PhD-student** Jul/14 - Jun/18

Appendix 2 – Other CID researchers

Other CID researchers[a]		
WP1		
Marieke E.W. Albers	UMC Utrecht	PhD-student
Dr. Carlijn van den Boomen	UU Faculty of Social and Behavioral Sciences	Postdoc
Dr. Rachel M. Brouwer	UMC Utrecht	Assistant professor
Dr. Janna Cousijn	UU Faculty of Social and Behavioral Sciences	Postdoc
Dr. Regina van den Eijnden	UU Faculty of Social and Behavioral Sciences	Associate professor
Branko van Hulst	UMC Utrecht	PhD-student
Dr. Caroline M.M. Junge	UU Faculty of Social and Behavioral Sciences	Postdoc
Dr. Marinka M.G. Koenis	UMC Utrecht	Postdoc
Dr. N. Charlotte Onland-Moret	UMC Utrecht	Associate professor
Rianne van Rooijen	UU Faculty of Social and Behavioral Sciences	PhD-student
Lara Wierenga	UMC Utrecht	PhD-student
WP2		
J. E. (Elisabeth) Bilo	UL Faculty of Social and Behavioral Sciences	PhD-student
Dr. Szilvia Biro	UL Faculty of Social and Behavioral Sciences	Assistant Professor
Dr. Bianca G. van den Bulk	UL Faculty of Social and Behavioral Sciences	Postdoc
Dr. Anna C.K. van Duijvenvoorde	UL Faculty of Social and Behavioral Sciences	Assistant Professor
Dr. Saskia Euser	UL Faculty of Social and Behavioral Sciences	Postdoc
Dr. Renske Huffmeijer	UL Faculty of Social and Behavioral Sciences	Assistant Professor
Dr. Nikolaus Steinbeis	UL Faculty of Social and Behavioral Sciences	Assistant Professor
Dr. Rixt van der Veen	UL Faculty of Social and Behavioral Sciences	Postdoc
Ilse C. van Wijk	UL Faculty of Social and Behavioral Sciences	PhD-student
WP3		
Prof. dr. Meike Bartels	VU University Amsterdam	Professor
Dr. Elsje van Bergen	VU University Amsterdam	Postdoc
Annelene Bloemen	UMC Groningen	PhD-student
Dr. Catharina A. Hartman	UMC Groningen	Assistant Professor
Dr. Esther Nederhof	UMC Groningen	Postdoc
Prof. Dr. Henning Tiemeier	Rotterdam Erasmus MC	Professor
WP4		
Yasin Altinisik	UU Faculty of Social and Behavioral Sciences	PhD-student
Dr. Rebecca Kuiper	UU Faculty of Social and Behavioral Sciences	Assistant professor

[a] Some of the above mentioned researchers are financed from CID cohort budget. All above-mentioned PhD-students and postdocs are not financed by CID, but directly from the government, from the government through a funding allocation agency or by contracts with third parties (e.g. some postdocs were appointed as matching as seen in Table C from the Budgets and Actuals).

Appendix 3 – CID publications and activities

To indicate the coherence and interaction between the different research lines, we provide a list of (joint) key publications and (joint) societal relevant activities from 2013 onwards.

Publications are counting as CID publications when:

- The first or second author is appointed by CID (from PI budget or cohort budget), or
- CID is mentioned in the acknowledgements

(JOINT) CID PUBLICATIONS

WP1 (16)	
Published (10)	
1	Cousijn J, Koolschijn PCMP, Zanolie K, Kleibeuker SW, Crone EA (2014): The relation between gray matter morphology and divergent thinking in adolescents and young adults. Plos One 9(12), e114619.
2	Schulte M, Cousijn J, Den Uyl T, Goudriaan AE, Van den Brink W, Veltman DJ, Schilt T, Wiers RW (2014): Recovery of neurocognitive functions following sustained abstinence after substance dependence and implications for treatment. Clinical Psychology Review, 34(2014): 531-550.
3	Cousijn J, Zanolie K, Munsters RJM, Kleibeuker SW, Crone EA (2014): The relation between resting state connectivity and creativity in adolescents before and after training. Plos One 9(9), e105780.
4	Cousijn J, Luijten M, Wiers RW (2014): Mechanisms underlying alcohol approach action tendencies: the role of emotional primes and drinking motives. Frontiers in Psychiatry, 5:44.
7	Hessels, R. S., Cornelissen, T. H. W., Kemner, C., & Hooge, I. T. C. (2014). Qualitative tests of remote eyetracker recovery and performance during head rotation. Behavior Research Methods. doi:10.3758/s13428-014-0507-6
5	Cousijn J (2015): Embracing comorbidity: a way towards understanding the role of motivational and control processes in cannabis use disorders. Frontiers in Psychology, 6:677.
6	Van den Boomen C, Jonkman LM, Jaspers-Vlamings PHJM, Cousijn J, Kemner C (2015): Developmental changes in ERP responses to spatial frequencies. Plos One, 10(3): e0122507.
7	Hessels, R. S., Andersson, R., Hooge, I. T. C., Nyström, M., & Kemner, C. (2015). Consequences of Eye Color, Positioning, and Head Movement for Eye-Tracking Data Quality in Infant Research. Infancy. doi:10.1111/infa.12093.
8	Geeraerts, S. B., Deutz, M. H. F., Deković, M., Bunte, T., Schoemaker, K., Espy, K. A., ... & Matthys, W. (2015). The Child Behavior Checklist Dysregulation Profile in Preschool Children: A Broad Dysregulation Syndrome. Journal of the American Academy of Child & Adolescent Psychiatry, 54, 595-602.
9	Deutz, M. H., Geeraerts, S. B., van Baar, A. L., Deković, M., & Prinzie, P. (2015). The Dysregulation Profile in middle childhood and adolescence across reporters: factor structure, measurement invariance, and links with self-harm and suicidal ideation. European Child & Adolescent Psychiatry, Online First publication
10	Liu, Liquan, and René Kager. (2015). "Bilingual exposure influences infant VOT perception". Infant Behavior and Development 38, 27-36.
In Press (3)	
11	Liu, Liquan, and René Kager. (2015). "Perception of a native vowel contrast by Dutch monolingual and bilingual infants: A bilingual perceptual lead". To appear in International Journal of Bilingualism.
12	Cousijn J, Van Benthem P, Van der Schee E, Spijkerman RZ (2015): Motivational and control mechanisms underlying adolescent cannabis use disorders: a prospective study. Developmental Cognitive Neuroscience, in press.
13	Liu, Liquan, and René Kager. (2015). "Understanding phonological acquisition through phonetic perception: the influence of exposure and acoustic salience". To appear in Phonological Studies.
Submitted and In Progress (3)	
14	De Mulder, H. N. M. & Watzema, A. (under review). Acquiring epistemic modal auxiliaries: The role of Theory of Mind.
15	Bergstra, M., De Mulder, H.N.M. & Coopmans, P.H.A. (in prep.) Do children go for the nice guys? The influence of speaker affect and certainty on selective word learning.

16	Van den Boomen, C., Munsters, N.M., & Kemner, C. (submitted). Processing facial expressions in the infant brain: the use of detailed and global information.

WP2 (17)	
Published (14)	
17	Windhorst, D.A., Mileva-Seitz, V.R., Linting, M., Hofman, A., Jaddoe, V.W.V., Verhulst F.C., Tiemeier, H., Van IJzendoorn, M.H., & Bakermans-Kranenburg, M.J. (2014). Differential susceptibility in a developmental perspective: DRD4 and maternal sensitivity predicting externalizing behavior. Developmental Psychobiology. DOI 10.1002/dev.21257
18	Damsteegt, R. C., Van IJzendoorn, M.H., Out, D., & Bakermans-Kranenburg, M. J. (2014). Tympanic membrane temperature in adopted children associated with sleep problems and pre-adoption living arrangements: an exploratory study. BMC Psychology, 2:51. doi:10.1186/s40359-014-0051-2.
19	Bakermans-Kranenburg, M.J. & Van IJzendoorn, M.H. (2015).The hidden efficacy of interventions: Gene x Environment experiments from a differential susceptibility perspective. Annual Review of Psychology, 66, 381-409.
20	Thijssen, S., Ringoot, A.P., Wildeboer, A., Bakermans-Kranenburg, M.J., El Marroun, H., Hofman, A., Jaddoe, V.W.V., Verhulst, F.C., Tiemeier, H., Van IJzendoorn, M.H., White, T. (2015) Brain morphology of childhood aggressive behavior: A multi-informant study in school-age children. Cognitive, Affective, & Behavioral Neuroscience. DOI 10.3758/s13415-015-0344-9
21	Irene Pappa, Iryna O. Fedko, Viara R. Mileva-Seitz, Jouke-Jan Hottenga, Marian J. Bakermans-Kranenburg, Meike Bartels, Catharina E.M. van Beijsterveldt, Vincent W.V. Jaddoe, Christel M. Middeldorp, Ralph C.A. Rippe, Fernando Rivadeneira, Henning Tiemeier, Frank C. Verhulst, Marinus H. van IJzendoorn, Dorret I. Boomsma (2015, in press). SNP heritability of Behavior Problems in Childhood: Genome-Wide Complex Trait Analysis. Journal of the American Academy of Child and Adolescent Psychiatry, 54, 737-744. DOI: http://dx.doi.org/10.1016/j.jaac.2015.06.004
22	Wildeboer, A., Thijssen, S., Van IJzendoorn, M. H., van der Ende, J., Jaddoe, V. W., Verhulst, F. C., et al. (2015). Early childhood aggression trajectories Associations with teacher-reported problem behaviour. *International Journal of Behavioral Development,* 39(3), 221-234.
23	Huffmeijer, R., Bakermans-Kranenburg, M. J., Alink, L. R. A., & Van IJzendoorn, M. H. (2014). Reliability of event-related potentials: The influence of number of trials and electrodes. *Physiology & Behavior, 130*, 13-22.
24	Pappa, I., Szekely, E., Mileva-Seitz, V. R., Luijk, M. P., Bakermans-Kranenburg, M. J., van, I. M. H., et al. (2015). Beyond the usual suspects: a multidimensional genetic exploration of infant attachment disorganization and security. *Attach Hum Dev, 17*(3), 288-301.
25	Riem, M. M. E., Alink, L. R. A., Out, D., Van Ijzendoorn, M. H., & Bakermans-Kranenburg, M. J. (2015). Beating the brain about abuse: Empirical and meta-analytic studies of the association between maltreatment and hippocampal volume across childhood and adolescence. *Development and Psychopathology, 27*(2), 507-520.
26	Sellaro, R., Steenbergen, L., Verkuil, B., van Ijzendoorn, M. H., & Colzato, L. S. (2015). Transcutaneous Vagus Nerve Stimulation (tVNS) does not increase prosocial behavior in Cyberball. *Frontiers in Psychology, 6*, article 499.
27	Thijssen, S., Wildeboer, A., Muetzel, R. L., Bakermans-Kranenburg, M. J., El Marroun, H., Hofman, A., et al. (2015). Cortical thickness and prosocial behavior in school-age children: A population-based MRI study. *Soc Neurosci*, 1-12.
28	Van IJzendoorn, M. H., & Bakermans-Kranenburg, M. J. (2014). Prosocial Development and Situational Morality Neurobiological, Parental, and Contextual Factors. In J. F. Leckman, C. Panter-Brick & R. Salah (Eds.), *Pathways to Peace: The Transformative Power of Children and Families* (Vol. 15). Cambridge: MIT Press.
29	Van IJzendoorn, M. H., & Bakermans-Kranenburg, M. J. (2014). Confined quest for continuity: the categorical versus continuous nature of attachment. *Monographs of the Society for Research in Child Development, 79*(3), 157-167.
30	Van IJzendoorn, M. H., & Bakermans-Kranenburg, M. J. (2015). Genetic differential susceptibility on trial: Meta-analytic support from randomized controlled experiments. *Development and Psychopathology, 27*(1), 151-162.
In Press (1)	
31	Mileva-Seitz, V. R., Bakermans-Kranenburg, M. J., & Van IJzendoorn, M. H. (In press). Genetic

	mechanisms of parenting. *Hormones and Behavior*.
Submitted and In Progress (2)	
32	Achterberg, M., van Duijvenvoorde, A.C., Bakermans-Kranenburg, M.J. & Crone, E.A. (2015). Control your anger! The neural basis of aggression regulation in response to social rejection. Submitted for publication.
33	Van der Meulen, M., Van IJzendoorn, M.H., & Crone, E.A. (2015). Neural correlates of prosocial behavior: Compensating social exclusion in a four-player Cyberball Game. Sumitted for publication.

WP3 (24)	
Published (9)	
34	Brummelman, E., Thomaes, S., Nelemans, S. A., Orobio de Castro, B., & Bushman, B. J. (2015). My child is God's gift to humanity: Development and validation of the Parental Overvaluation Scale (POS). *Journal of Personality and Social Psychology, 108,* 665-679. doi:10.1037/pspp0000012
35	Brummelman, E., Thomaes, S., Nelemans, S. A., Orobio de Castro, B., Overbeek, G., & Bushman, B. J. (2015). Origins of narcissism in children. *Proceedings of the National Academy of Sciences of the United States of America, 112,* 3659–3662. doi:10.1073/pnas.1420870112
36	Brummelman, E., Thomaes, S., Nelemans, S. A., Orobio de Castro, B., Overbeek, G., & Bushman, B. J. (2015). Reply to Kealy et al.: Theoretical precision in the study of narcissism and its origins [Letter to the editor]. *Proceedings of the National Academy of Sciences of the United States of America*, *112*, E2987. doi:10.1073/pnas.1507468112
37	Hawk, S. T., Ter Bogt, T., Van den Eijnden, R., & Nelemans, S. A. (2015). Too little power, too much information! Power, narcissism, and adolescents' disclosures on social networking sites. *Computers in Human Behavior, 52,* 72-80. doi:10.1016/j.chb.2015.05.014
38	Laceulle, O.M., Jeronimus, B.F., van Aken, M.A.G., & Ormel, J. (2015). Why not everybody gets their fair share of stress: Adolescent's perceived relationship affection mediates associations between temperament and stressful social events. *European Journal of Personality, 29: 125–137.*
39	Nelemans, S. A., Hale, W. W. III, Branje, S. J. T., Hawk, S. T., & Meeus, W. H. J. (2014). Maternal criticism and adolescent depressive and Generalized Anxiety Disorder symptoms: A 6-year longitudinal community study. *Journal of Abnormal Child Psychology, 42*, 755-766. doi:10.1007/s10802-013-9817-x
40	Nelemans, S. A., Hale, W. W. III, Branje, S. J. T., Raaijmakers, Q. A. W., Frijns, T., Van Lier, P. A. C., & Meeus, W. H. J. (2014). Heterogeneity in development of adolescent anxiety disorder symptoms in an 8-year longitudinal community study. *Development and Psychopathology, 26,* 181-202. doi:10.1017/S0954579413000503
41	Nelemans, S. A., Hale, W. W. III, Branje, S. J. T., Van Lier, P. A. C., Jansen, L. M. C., Platje, E., … Meeus, W. H. J. (2014). Persistent heightened cortisol awakening response and adolescent internalizing symptoms: A 3-year longitudinal community study. *Journal of Abnormal Child Psychology, 42*, 767-777. doi:10.1007/s10802-013-9820-2
42	Ormel, J., Laceulle, O.M., & Jeronimus, B.J. (2015). Why personality and psychopathology are correlated: developmental perspective is a first step but more is needed. *European Journal of Personality, 28,* 396-398.
In Press (10)	
43	Becht, A., Branje, S., Vollebergh, W., Maciejewski, D., Van Lier, P., Koot, H., Denissen, J., & Meeus, W. (in press). Assessment of identity during adolescence using daily diary methods: Measurement invariance across time and sex. *Psychological Assessment.*
44	Becht, A. I., Prinzie, P.., Dekovic, M., van den Akker, A. L., & Shiner, R. L. (in press). Child personality facets and overreactive parenting as predictors of aggression and rule-breaking trajectories from childhood to adolescence. *Development and Psychopathology.*
45	Hale, W. W. III, Crocetti, E., Nelemans, S. A., Van Lier, P. A. C., Koot, J. M., Meeus, W. H. J., & Branje, S. J. T. (in press). Mother and adolescent expressed emotion and adolescent internalizing and externalizing symptom development: A six-year longitudinal study. *European Child & Adolescent Psychiatry*.
46	Hawk, S., Becht, A. & Branje, S. (2015). "Snooping" as a distinct parental monitoring strategy: Comparisons with overt solicitation and control. *Journal of Research on Adolescence.*
47	Kretschmer, T., Sentse, M., Meeus, W., Verhulst, F., Veenstra, R., Oldehinkel, A. J. (in press). Configurations of adolescents' peer environments: Associations with parent-child relationship quality and parent problem behaviour. *Journal of Research on Adolescence.*
48	Kretschmer, T., Vollebergh, W., Oldehinkel, A. J. (in press) Parent-child positivity and romantic relationship in emerging adulthood – Congruence, compensation, and the role of social skills.

	International Journal of Behavioral Development.
49	Laceulle, O.M., Nederhof, E., van Aken, M.A.G. & Ormel, J. (in press) Adolescent personality: associations with basal, awakening and stress-induced cortisol responses. *Journal of Personality.*
50	Laceulle, O.M., Vollebergh, W.A.M., & Ormel, J. (in press). The Structure of Psychopathology in Adolescence: Replication of a General Psychopathology Factor in the TRAILS Study. *Clinical Psychological Science DOI: 10.1177/2167702614560750*
51	Maciejewski, D., van Lier, P., Branje, S., Meeus, W., & Koot, H. (in press). A five-year longitudinal study on mood variability across adolescence using daily diaries. *Child Development.*
52	Nelemans, S. A., Hale III, W. W., Raaijmakers, Q. A. W., Branje, S. J. T., Van Lier, P. A. C., & Meeus, W. H. J. (in press). Longitudinal associations between social anxiety symptoms and cannabis use throughout adolescence: The role of peer involvement. *European Child & Adolescent Psychiatry*. Advance online publication. doi:10.1007/s00787-015-0747-8
Submitted and In Progress[a] (5)	
53	De Zeeuw, E., Catharina E.M. van Beijsterveldt, Tina J. Glasner, Eco J.C. de Geus & Dorret I. Boomsma. Arithmetic, reading and writing performance has a strong genetic component: A study in primary school children. *Learning and Individual Differences* (in revision).
54	De Zeeuw, E., Catharina E.M. van Beijsterveldt, Erik A. Ehli, Eco J.C. de Geus & Dorret I. Boomsma. Attention Deficit-Hyperactivity Disorder symptoms and education: testing the causal hypothesis. Submitted.
55	Kan, K.J., Catharina E.M. van Beijsterveldt, Meike Bartels, and Dorret I. Boomsma. What molecular genetic studies do not capture, but twin studies (often) do: Context specific genetic variance. Submitted
56	Kretschmer T, Veenstra, R, Dekovich M, Oldehinkel AJ. Mean girls get the blues? Bullying development across adolescence, its antecedents, outcomes, and gender-specific patterns. (submitted for publication)
57	Laceulle, O.M., Vollebergh, W.A.M., Veenstra, R., & Ormel, J. (In progress). Sequences of Mal-adaption: Pre-adolescent Self-regulation, Adolescent Negative Social Interactions and Young Adult Psychopathology

WP4 (11)	
Published (11)	
58	Loi M, Mossink JC, Meerhoff GF, Den Blaauwen JL, Lucassen PJ, Joëls M (2015) Effects of early-life stress on cognitive function and hippocampal structure in female rodents. *Neuroscience*. 2015 Aug 20 (Epub)
59	Loi M, Koricka S, Lucassen PJ, Joëls M (2014) Age- and sex-dependent effects of early life stress on hippocampal neurogenesis. *Front Endocrinol* 5:13
60	Sarabdjitsingh RA, Zhou M, Yau JL, Webster SP, Walker BR, Seckl JR, Joëls M, Krugers HJ. Inhibiting 11β-hydroxysteroid dehydrogenase type 1 prevents stress effects on hippocampal synaptic plasticity and impairs contextual fear conditioning. *Neuropharmacology*. 2014 Jun;81:231-6.
61	Sarabdjitsingh RA, Joëls M. Rapid corticosteroid actions on synaptic plasticity in the mouse basolateral amygdala: relevance of recent stress history and β-adrenergic signaling. *Neurobiol Learn Mem*. 2014 Jul;112:168-75.
62	Sarabdjitsingh RA, Jezequel J, Pasricha N, Mikasova L, Kerkhofs A, Karst H, Groc L, Joëls M.Ultradian corticosterone pulses balance glutamatergic transmission and synaptic plasticity. *Proc Natl Acad Sci U S A*. 2014 Sep 30;111(39):14265-70.
63	Berwick, R.C., Friederici, A.D., Chomsky, N. & Bolhuis, J.J. (2013) Evolution, brain, and the nature of language. *Trends in Cognitive Sciences,* 17, 89-98.
64	Bolhuis, J.J., Tattersall, I., Chomsky, N. & Berwick, R.C. (2014) How could language have evolved? *PLoS Biology*, 12(8), e1001934.
65	Bolhuis, J.J. & Moorman, S. (2015) Birdsong memory and the brain: In search of the template. *Neuroscience & Biobehavioral Reviews*, 50, 41-55.
66	Bolhuis, J.J., Tattersall, I., Chomsky, N. & Berwick, R.C. (2015) Language: UG or not to be, that is the question. *PLoS Biology*, 13(2): e1002063.
67	Moorman, S., Gobes, S.M.H., van de Kamp, F.C., Zandbergen, M.A. & Bolhuis, J.J. (2015) Learning-related brain hemispheric dominance in sleeping songbirds. *Sci. Rep*., 5: 9041.
68	Bolhuis, J.J. (2015) Evolution cannot explain how minds work. *Behav. Proc*., 117, 82-91.

[a] For information only, not edited

(JOINT) CID SOCIETAL RELEVANT ACTIVITIES

ACTIVITIES FROM 2013 ONWARDS	
1	Refereed Book Chapter: Lorenzetti V, Cousijn J (in press): *Cannabis use disorders and brain morphology.* In V R Preedy (Eds.), Neuropathology of drug addictions and substance misuse Volume 1: Common substances of abuse - tobacco, alcohol, cannabinoids and opioids. London, UK: Elsevier Inc.
2	Refereed Book Chapter: Cousijn J, Filbey F (2015): *New approaches to treating cannabis dependence: from neuroscience to practice.* In S Feldstein Ewing, K Witkiewitz, F Filbey (Eds.), Neuroimaging and Psychosocial Addiction Treatment: An Integrative Guide for Researchers and Clinicians. Basingstone, Hampshire, UK: Palgrave MacMillan.
3	Refereed Book Chapter: Creemers HE, Cousijn J, Wiers RW (2015): *Cannabisafhankelijkheid.* In I Franken, P Muris, D Denys (Eds.), Psychopathologie: Oorzaken, diagnostiek en behandeling. Tijdstroom.
4	Adolescent Development Lab Talk, Utrecht. What to say when you talk to yourself: Effects of reappraisal strategies on behavioral control (November 7th 2013)
5	Seminar for directors of primary schools, teachers, internal counselors and care teams on behavioral problems in children. Brain Center Utrecht and KKC, October 29, 2014
6	Cousijn J. Cognitieve ontwikkeling van kinderen en adolescenten: gedragscontrole en verleidingen uit de omgeving. Studiemiddag UMC Utrecht Hersencentrum, Juni 2015
7	Geeraerts, S. B., Artikel in NVO Bulletin (vakblad voor orthopedagogen), jaargang 16, februari 2015: Thesisprijzen: digitale kinderboeken & Dysregulatie Profiel bij kleuters.
8	Crone, E.A. (2015, September). 3rd Annual Flux Congress, Leiden, the Netherlands
9	Van IJzendoorn, M.H. (2015, September). NIRS Workshop on Challenges and opportunities of fNIRS in developmental neuroscience, Leiden, the Netherlands
10	Van Bergen, E. (2015). *"Waarom is dyslexie familiair?"* Guest lecture for educational professionals, Nationale Dyslexie Conferentie [National Dyslexia Conference], Ede, the Netherlands, 8th April 2015.
11	"Translational approaches in developmental disorders and schizophrenia". Course for PhD-students (including 5 plenary lectures accessible to a broad audience). May 28 – June 3, 2015; Utrecht. Organizers: Marian Joëls and Mariken de Krom.
12	Royal Dutch Academy of Sciences (KNAW) Academy Colloquium 'The Biology of Language', plus Master class, Amsterdam, 10-13 Dec 2014.

Appendix 4 – Progress Reports CID PhD-students and postdocs

Progress reports

WP1

Dr. Dienke J. Bos, Postdoc, Mar/15 - Mar/17

Connected and in control: What puts the development of neural networks underlying behavioral control at risk?
Durston, Crone; UMC Utrecht

Aim: to investigate the neurobiological processes underlying (a)typical development of behavioral control networks in a large cohort of children.
Methods: Participants will be profiled on a broad, multimodal array of characteristics, including several MRI-based measures, neurocognition and psychophysiology. This project will consist of two phases. In the first phase, a pilot study using existing data will be conducted as a proof of concept before phase 2, where we will conduct a multimodal study of the development of behavioral control.
Progress up to now: The preprocessing of all data of the pilot study (phase one) has recently been completed. The data are ready to be analyzed, which will happen as soon as Dienke has returned from her maternity leave (1 January 2016).

Sanne B. Geeraerts, PhD-student, Oct/14 - Apr/19

Development of infant self-regulation within the early caregiver relationship: A cascade model
Dekovic, Kemner; UU Faculty of Social and Behavioral Sciences

Aim: Examining the processes through which the early development of infant self-regulation within the proximal caregiver relationship influences broad socio-emotional adaptation over time, as proposed by a developmental cascade model.
Methods: Meta-analysis, observational data, eye tracking and a longitudinal survey. We will use both existing data and newly collected data, also from YOUth baby cohort.
Progression up to now: At the moment I am working with existing data from the YOUth pilot study of the 10 month old infants. An observational coding scheme for coding parent-child interactions during this pilot study is in the making, as well as a proposal for a follow-up study on these children. Additionally, she is developing more detailed dissertation plan (including a plan for future articles).

Dr. Marinka M.G. Koenis, Postdoc,

IQ and cognitive test battery (CNP) subtest selection, and creation of MRI scan protocol
Hulshoff Pol; UMC Utrecht

Aim: Determine selection of subtests that provide enough reliable information in a short time and overlap with international child cohorts.
Method: Literature search as well as experience from other cohorts/labs on validation and use of short versions of full IQ test. For CNP, we looked at selection of CNP tests in other cohorts. Assist in development of scan protocol.
Progress: IQ: We considered using the WISC V (expected to come out in the Netherlands in 2016), but had to conclude that this was not feasible. In the pilot study the following 4 verbal tests of the WISC III were used: vocabulary, similarities, arithmetic, digit span; and the following 2 nonverbal tests: block design and coding. When the maximum time of 45 minutes was expected to be exceeded, digit span and coding were excluded. Because in that case nonverbal IQ will be based only on block design, we might want to exclude arithmetic instead of coding.
CNP: The following three tests will be used: Motor Speed, Emotion Recognition, Verbal Memory (immediate and delayed). These tests take about 11 minutes to complete. Pilot data showed good reliable results.

MRI: First multiband scan protocols have been tested. At the moment the protocol is being improved. With regard to different scanners: the cohort will not start on the MR8, but on the new scanner that is

expected to be running in January. Inter individual (n=15) tests scans are planned on the MR7, MR8 and the new scanner to check data consistency across scanners.

Dr. Hannah de Mulder, Postdoc, Jan/14 – May/17

The power of stories: exploring the effects of (self) narrative on the development of social competence and behavioral control
Van Berkum, Valkenburg; UU Faculty of Humanities

Subproject 1 title: From book smart to street smart: does exposure to fiction enhance social competence?
Subproject 2 title: What to say when you talk to yourself: the role of verbal reappraisal in behavioral control
Aims Subproject 1: To assesses the predicted positive impact of exposure to fictional narrative on the child's socio-emotional development, in his/her actual behavior (tendency to engage in pro-social behavior) and in relevant cognitive component skills (perspective taking, empathy and moral values).
Aims Subproject 2: To assess how the development of verbally mediated reappraisal, at the level of linguistic form and content, affects the development of the child's ability to regulate emotion and how general linguistic and narrative abilities mediate this relationship.
Methods Questionnaires and experimental tasks for use in the cohort; physiological (EEG, skin conductance, facial EMG) and behavioral tasks for additional testing outside of the cohort.
Progression up to now:
Subproject 1:
- Creation of fiction exposure questionnaire for use in the cohort (pilot data gathered from a large online study)
- Creation of additional measures to assess fiction exposure for use outside of cohort (data gathered for validation of Author Recognition Test for 8-17 year olds)
- Bayesian analysis plan created for analysis of data from the YOUth adolescent cohort (to be implemented once data collection has terminated)
- Intervention study considering effects of reading particular types of fiction on adults' social competence (currently still in data gathering phase, to be modified for use with adolescents at a later stage)

Subproject 2:
- Intervention study considering effects of particular reappraisal strategies on adults' ability to deal with verbal insults (currently still in data gathering phase, to be modified for use with adolescents at a later stage)
- Intervention study considering effects of particular reappraisal strategies on adults' ability to deal with social exclusion (currently still in data gathering phase, to be modified for use with adolescents at a later stage)

Dr. Margot Peeters, Postdoc, Jan/15 - Dec/18

Behavioral control and reward sensitivity as predictors of adolescents' substance use
Vollebergh, Oldehinkel; UU Faculty of Social and Behavioral Sciences

Former studies suggest that risk-taking behavior among adolescents is a result of different underlying motivational and cognitive processes, in particular a heightened sensitivity for reward on the one hand, and impaired behavioral control on the other. Most of this research includes fMRI studies that report on differences in brain activity, however, the translation of these neurocognitive results into actual behavior has less often been studied. In the present proposal, we intent to focus on the way these two processes interact with each other in impacting developmental trajectories of risk behavior in adolescence, hereby using both a variable-centered and a person-centered approach. In addition, we will look at peer status as possible interacting variable. We will use data from a large longitudinal national cohort study, TRAILS (total sample N = 2223; and data from a high risk focus cohort used in this study N = 715), in which a number of behavioral tests have been taken. The first results suggest that behavioral control at age 11 (assessed with self-report measures) predict initiation of alcohol use at age 16. No such effects are found for neurocognitive measures of behavioral control. In addition, alcohol use at age 16 is predicted by an interaction effect between behavioral control at age 11 and reward sensitivity at age 16, suggesting that lower levels of control in early adolescence combined with

higher sensitivity for reward in mid adolescence predict alcohol use.

WP2

Michele Achterberg, PhD-student, Sep/14 - Sep/19

Social aggression regulation in childhood and emerging adolescence
Crone, Bakermans-Kranenburg; UL Faculty of Social and Behavioral Sciences

Aim: The goal of this project is to study how the developing brain is shaped by the interplay of personal and environmental factors using a randomized controlled trial with longitudinal brain imaging. Specifically, my project focuses on the developmental differences in social rejection related aggression and aggression regulation.
Method: We developed a new social evaluation paradigm. During the experiment, participants view pictures of peers who responded to the participants' profile (accept, neutral or reject). Participants are requested to react to the peer feedback by pressing a button, producing a loud noise. Noise blast duration is used as an index of aggression.
Progression up to now: The paradigm was first tested in an adult sample (N=30, 15 males). Rejection led to more aggression (longer noise blast). Social evaluation, being accepted or rejected versus neutral responses, resulted in neural activation in a network of insula, medial prefrontal cortex and striatum. In addition, more activation in the right dorsal lateral PFC during rejection versus neutral feedback resulted in more aggression regulation (shorter noise blast). Next, we tested the paradigm in a pilot sample of 7 to 8 year old children (N=19, 10 males) with similar behavioral results (more aggression after rejection). On a neural level we found a comparable network of insula activation, but additionally the children showed heightened amygdala activation after rejection. Recently we started with the data collection of the longitudinal study: we have data collected of 44 participants and another 66 are scheduled for the upcoming weeks.

Rani Damsteegt, PhD-student, May/13 - Mar/18

Parenting and prosocial development in childhood
Bakermans-Kranenburg, Crone; UL Faculty of Social and Behavioral Sciences

Aim: The aim of this project is to examine the effects of an intervention focused on positive parenting and sensitive discipline on prosocial behavior of preschoolers.
Methods: Families with 3 or 4-year-old twins were invited to participate in our study. Two pretests will be conducted, after which families will be randomly assigned to an intervention or control group. Prosocial behavior will be measured annually with two tasks: the Owl task (an age-appropriate version of prosocial Cyberball) to measure non-costly prosocial behavior, and the Donating task to measure costly prosocial behavior. We will also annually administer the Strengths and Difficulties questionnaire, which includes a prosocial behavior scale.
Progress: Since September 2014 we have recruited 239 families with 3-4-year-old twins (total N = 478). We visited each family at home for the first pretest. We have recently started year 2 of the study, during which we invite families to the university for a lab visit. I am currently processing and analyzing the data of the home visits from year 1, in which I will focus specifically on parental sensitivity and its relation with prosocial behavior.
Presentations and papers:
Damsteegt, R. C., van IJzendoorn, M. H., Out, D., & Bakermans-Kranenburg, M. J. (2014). Tympanic membrane temperature in adopted children associated with sleep problems and pre-adoption living arrangements: an exploratory study. BMC Psychology, 2:51. doi:10.1186/s40359-014-0051-2.
Damsteegt, R. C. (2015, March). Owl task: Measuring prosocial behavior in early childhood. Presented at the CID meeting, Utrecht, the Netherlands.

Mara van der Meulen, PhD-student, Jan/15 - Jan/20

Prosocial development in childhood and emerging adolescence
Engels, Crone, van IJzendoorn; UL Faculty of Social and Behavioral Sciences
Aim: The goal of this project is to study how the developing brain is shaped by the interplay of personal

and environmental factors using a randomized controlled trial with longitudinal brain imaging. Specifically, my project focuses on developmental differences in compensating prosocial behavior.
Methods: We use a four-player Cyberball Game to investigate prosocial behavior. During the task, the participant is one of the four players in the game. Initially all players toss the ball to each other. In the second block two players no longer toss the ball to the third player, thereby giving the participant the opportunity to compensate for this exclusion. The percentage of tosses to the excluded player, compared to tosses to the other two players, is used as a measure for prosocial behavior.
Progression up to now: The paradigm was first tested in an adult sample (N = 23, all female). We found that participants showed prosocial compensating behavior towards the excluded player in the Cyberball Game. This behavior resulted in neural activity in the right temporo-parietal junction and bilateral insula. In addition, the observation of social exclusion of one of the players was associated with neural activity in bilateral insula.
Next, we tested the same paradigm in a pilot sample of 7-8 year old children (N = 16, 8 males). We found similar behavior results in this group: the participants showed prosocial compensating behavior towards the excluded player. Imaging data is currently being analyzed, and preliminary findings indicate that children do not show the same neural activity as adults when engaging in prosocial behavior.
In August we started with the data collection of the longitudinal study: we have data collected of 44 participants and another 66 are scheduled for the upcoming weeks.

Claudia I. Vrijhof, PhD-student, Nov/13 - Nov/17

Development of behavioral control in early childhood
Van IJzendoorn, Bakermans-Kranenburg, Crone; UL Faculty of Social and Behavioral Sciences

Aim: The aim of this project is to explore the effects of an intervention aimed at enhancing parental sensitivity and sensitive discipline on environmental chaos and the development of behavioral control in young children.
Methods: Caucasian families with 3 or 4-year-old twins were invited to participate in our study. Two pretests will be conducted, after which families will be randomly assigned to an intervention or control group. We will use various observational measures to measure behavioral control, such as a cheating game, an age-appropriate version of the stop-signal task, and the marshmallow task.
Progress: From September 2014 to September 2015, we recruited and visited 239 families with 3-4 year old twins (total N = 478). During the home visit, the cheating game and a stop-signal task were administered to measure children's level of behavioral control. Furthermore, we videotaped parent-child interactions and we coded the level of environmental chaos in the homes of the family. From Mei 2015 to September 2015, we successfully piloted the VIPP-SD for families with twins. We recently started with the data collection of year 2. Currently, we are coding and analyzing the data from the home visits of year one.

WP3

Annelene J.P. Bloemen, PhD-student, Dec/14 - Dec/17

Knowledgeable Youngsters – Youth, media and early modern knowledge societies
Oldehinkel, Hartman, UMC Groningen

Aim: It is our goal to investigate the various relations between the early modern youth and media, and the various degrees of dependence these relations reflect, in the acquisition of knowledge in Northern European countries, 1500-1800, following these lines of inquiries:
1. Theory and Practice of Curiosity and Inquisitiveness
- What models of learning aimed at various forms of (in)dependent knowledge acquisition were represented and developed?

2. Theory and Practice of Creative and Self-Willed Use of Media
- What reading, visualising, sensing etc. practices aimed at various forms of (in)dependent knowledge acquisition were developed?

3. Forms of Knowledge
- In what ways was knowledge variously construed and defined in the early modern period

and how do they resonate today?
Methods: We focus on Northern European countries to be able to chart transnational trends in knowledge cultures in neighbouring countries, prompted by cooperation and competition between for instance universities, artisans workshops and publishing houses. For now, we look at a variety of age groups (children, adolescents, young adults) to chart the full scope of changes in knowledge cultures.
Progression: We pursue our central questions from a number of disciplinary angels: labor history, intellectual history, religious history, the history of travel, the history of certain kinds of texts and objects and their uses, as well as number of fields that are often grouped under "history of science" such as history of mathematics and history of botany.

Andrik Becht, PhD-student, Sep/14 – Sep/18

Why some adolescents thrive and others don't: The role of uncertainty dynamics
Meeus, Vollebergh; UU Faculty of Social and Behavioral Sciences

Aim: There is massive evidence that uncertainty is a major risk factor in adolescent development. However, information on the development of uncertainty, the transmission of uncertainty in parent-adolescent relationships and how uncertainty predicts adaptive development is lacking. Aim of this CID-project is to overcome these limitations.
Methods: an intensive longitudinal design is used including 75 between day measures across five years to tap into certainty-uncertainty dynamics across adolescence.
Progression: First paper published (Becht ea 2015); investigated longitudinal measurement invariance and measurement invariance across sex of the daily diary reports on identity, which are used for further study in the CID project. Second paper in progress (to be submitted by the end of October) with title: 'Becoming certain about the self: Developmental profiles of certainty and uncertainty dynamics in identity formation across adolescence using daily diary reports'. This study investigates heterogeneity in development of certainty and uncertainty in identity formation across adolescence and concurrent development of psychosocial adjustment. A third paper in progress (currently statistical analyses are conducted). For this paper, we will investigate certainty-uncertainty dynamics in identity formation across adolescence. Specifically, we will investigate direction of effects (i.e., developmental order) between certainty and uncertainty across adolescence.

Dr. Tina Kretschmer, Postdoc, Oct/13 - Dec/17

Examining the complex interplay between relationship experiences and individual factors to understand adolescent development
Oldehinkel, Meeus, Dekovic; UMC Groningen

Aim: This project seeks to identify predictors of positive outcomes (educational and occupational success, prosocial behavior, self-competence, empathy) and problem development (internalizing and externalizing behavior). In detail, component #1 asked whether experiences in parent-child relationships are associated with experiences in relationships with peers and intimate partners and components #2 and #3 focus on the interplay between relationship experiences and individual factors in predicting positive and negative outcomes.
Method: Data from all waves of the Tracking Adolescents' Individual Lives Survey (TRAILS) are used, though the focus is on measures of social relationships with parents, peers, and romantic partners and measures of adjustment.
Progression: One article on the link between parent-child relationships/parent characteristics and peer experiences has been published in the Journal of Research on Adolescence (doi: 10.1111/jora.12206, co-authors Sentse, Meeus, Verhulst, Oldehinkel). Another article on the link between parent positivity in early adolescence and romantic involvement, commitment, and satisfaction (c-authors Vollebergh, Oldehinkel) is in press with the International Journal of Behavioral Development. A third article on bullying development and its negative outcomes (co-authors Veenstra, Decovic) is under review. I have also presented this research at conferences (European Association for Research on Adolescence, 2014; Society for Research on Child Development, Philadelphia). In addition, I have contributed to planning and obtaining of ethical approval for the TRAILS next study, a CID project in which TRAILS participants who are now parents and their babies are followed over 48 months.

Dr. Stefanie A. Nelemans, Postdoc, Sep/14 - Sep/17

Development of anxiety symptoms in adolescence and early adulthood: over-time links with biological, psychological, and social factors
Meeus, Oldehinkel; UU Faculty of Social and Behavioral Sciences, Department of Youth and Family

Aim: Provide more insight in the development of Generalized Anxiety and Social Anxiety symptoms from adolescence to emerging adulthood, and over-time links with individual characteristics and social relationships (including the parent-child relationship).
Methods: This project uses existing longitudinal data from RADAR, CONAMORE, and potentially TRAILS. Questionnaire data and (physiological and cognitive) data from a laboratory setting will be used. Analyses include a combination of person-centered and variable-centered longitudinal modeling techniques.
Progression up to now: In 2014-2015, my research has generally focused on biological and (psycho)social correlates, predictors, and outcomes Generalized Anxiety and Social Anxiety symptom development from early to late adolescence. With respect to biological factors, we have focused on basal functioning of the human stress response system (i.e., HPA axis) in relation to adolescent anxiety symptom development (Nelemans, Hale, Branje, Van Lier, et al., 2014), as well as on the role of stress reactivity (of the HPA axis and ANS) in the persistence of adolescent Social Anxiety over time (Nelemans et al., under review). Regarding the social environment, we focused on potential bidirectional associations over time between critical parenting and the development of adolescent Generalized Anxiety symptoms (Nelemans, Hale, Branje, Hawk, & Meeus, 2014), and on how adolescents' peer environment may potentially explain associations between adolescent Social Anxiety symptoms and adolescent cannabis use from early to late adolescence (Nelemans, Hale, Raaijmakers et al., 2015). Currently, I am focusing on adolescent Generalized Anxiety and Social Anxiety symptom development and cognitive functioning (i.e., reward sensitivity and behavioral inhibition) in a laboratory setting.

Alexander Neumann, PhD-student, Aug/14 - Aug/18

The epigenetics of intergenerational transmission
Verhulst, Oldehinkel, van IJzendoorn; Rotterdam Erasmus MC

Aim: Studies in children, adolescents, and adults have identified a general psychopathology factor associated with a high risk for different psychiatric disorders. We defined a general psychopathology factor in school-aged children and tested its validity. The primary goal was the estimation of the factor's SNP heritability, the extent to which individuals who share more single nucleotide polymorphism (SNP) alleles also are more similar phenotypically
Methods: Children from the multi-ethnic population-based Generation-R cohort were repeatedly assessed between ages 6-8 years. Child behavior problems were reported by parents, teachers and children. Confirmatory factor analysis estimated a general psychopathology factor using various psychiatric problem scales; the factor was specified to be independent from internalizing, externalizing, and instrument-specific factors. Genome-wide Complex Trait Analysis (GCTA) was used to estimate SNP heritability of the general psychopathology factor (507,065 autosomal SNPs) in a subset of children with European ancestry (n=2,115).
Progression up to now: We finished analyses and found that all reported problems, including the child's self-reported, loaded on the general psychopathology factor. The factor was associated with lower IQ, more behavioral executive function problems, poorer effortful control, and higher negative affectivity, but not with surgency. Importantly, we observed a significant SNP heritability of 37% (SE=0.16, p=0.01) for the general factor.

Sabine Veldkamp, PhD-student, May/15 – May/19

Why some pupils thrive and others do not. The role of genes and the environment
Boomsma, Van Berkum; VU University Amsterdam

Aim: The overall aim of this project is to study why some pupils thrive and others do not, with a focus on etiological factors underlying social-emotional and cognitive development. This project aims to unravel causes of individual differences in academic skills (literacy and numeracy), bullying behavior

and victimization (at ages 7, 9 and 12). The project will be divided in two parts: behavioral genetics and molecular genetics. The main research questions are: 1) What are the causes of individual differences in academic skills and bullying/victimization? Is the individual variation and co-variation mainly caused by genetic differences or environmental effects? Does the etiology depend on school characteristics? 2) Which genomic regions are associated with academic skills, bullying behavior and victimization?
Methods: To answer these research questions, the study will be conducted in twin pairs and their non-twin siblings in the Netherlands Twin Register (NTR) cohort. If available, parent data will also be added. The focus is on cross-sectional and/or longitudinal multiple rater data and school-test scores. This project builds on and will extend the database of the NTR on cognition and DNA / epigenetic variants. In addition, data about different school characteristics will be collected. Data that will be collected: 1) survey data of the primary school teachers, as well as scores on tests of the Pupil Monitoring System (Cito, 2014), 2) DNA/ epigenetic variants, and 3) publically available data of school characteristics. Part 1) and 2) are ongoing processes, whereas part 3) will be a new addition to the data collection.
Progression up to now: I studied whether twins are at high or low risk compared to non-twin children regarding bullying and victimization and whether bullying and victimization in twins depend on whether the co-twin is 1) genetically identical, 2) in same class or not, 3) of same or opposite sex, and whether 3) changes as children age. Moreover, some interactions and non-twin specific characteristics are investigated, namely gender and age. The next step is to estimate the heritability of both bullying and victimization.

Dr. Eveline de Zeeuw, Postdoc, Dec/14 – Dec/17

Longitudinal development and intergeneration transmission of psychopathology versus well-being
Boomsma, Oldehinkel; VU University Amsterdam

Aim: The aim of the project is to disentangle genetic and environmental influences on psychopathology and well-being, understand the genetic versus cultural mechanisms and contrast the findings for psychopathology to those for wellbeing.
Methods: The mechanisms will be investigated using, amongst others, the (grand)parent-offspring and children-of-twins (COT) model. Four types of intergenerational data will be collected: parents of young twins who are twins themselves, young twins who become parents themselves, adult twins with adult offspring and grandparents of twins.
Progress up to now: The Netherlands Twin Register (NTR) asked parents of young twins whether they themselves were also part of a twin pair. When this was the case they and their co-twins were asked to fill out surveys about themselves. These twin pairs, of which one of the twins is the mother or father of a twin pair, and their twin children have been identified in the different data sets (Y(oung)NTR and A(dult)NTR). Several outcome measures are available for both the parents and the children. Preparations have been made to start the data collection in children of twins of the YNTR. All twins in the cohorts 1986-1990 that have offspring of their own have been identified. These twins will be approached in the coming months to invite them to fill out a survey about the development of their own children. Extensive longitudinal data are available for this sample of parents, and the to-be-collected survey for the children will include measures on psychopathology, well-being, behavioral control, temperament and the home environment.

WP4

Dr. Gabriël J.L. Beckers, Assistant professor, Oct/14 - Oct/17

Tracking sleep slow waves during avian vocal development
Bolhuis, Joëls; UU Faculty of Social and Behavioral Sciences

Aim: Sleep is strongly involved in learning, including vocal learning in songbirds and grammar learning in human infants. However, the underlying neurophysiological mechanisms that enable this, and that require the brain to be `off-line' during sleep, remain poorly understood. The aim of the current project is to provide insight into the role of slow-waves, which are large-scale cortical oscillations that occur during deep sleep, in perception and learning of vocalizations in zebra finches, *Taeniopygia guttata*. This songbird is a prominent animal model system for neuroscientific research into speech and language acquisition in human infants.

Methods*:* As a first step, we record action and local field potential activity with high-density multi-electrodes in cortical areas of isoflurane anesthetized birds. This type of anesthesia is an accepted model for deep sleep, and makes it possible to record from 64 intracerebral electrodes in parallel. This essentially yields a neuroimaging technique enabling us to accurately determine fast and complex temporospatial propagation patterns of slow-wave activity. Earlier research has shown that zebra finch cortex has a response bias to learned vocalizations during sleep and anesthesia.
Progress*:* We successfully recorded slow-wave activity in 9 birds and obtained good spontaneous, auditory evoked and event-related action and local field potential activity in sub-millisecond precision over long recording episodes. These recordings amount to approximately 400 Gb of neural data, and will form the basis of a first manuscript. Partial analyses so far look promising and show sensitivity, particularly in secondary auditory cortices, to vocal sequence structure. These systems may be involved in perception and learning of phonological syntax.

Dr. Sita M. ter Haar, Postdoc, Mar/15 – Jan/16

A neurogenetic analysis of birdsong learning as a model for infant development
Bolhuis, Joëls; UU Faculty of Social and Behavioral Sciences

Aim: This research aims to study the neurogenetic mechanisms behind song learning in zebra finches, which is extensively used as a model for speech and language acquisition in human infants. The first question to be answered is whether individual differences in learning performance are associated with differences in gene expression
Methods: Neurobehavioral research in combination with innovative genetic techniques. More specifically: song analyses, behavioral responses and RNA-sequencing or microarray
Progression up to now: An ethical proposal has been written for the animal experimentation committee to be able to start the research on animals. The plans have been discussed with a genetic birdsong expert collaborator (Prof. Claudio Mello). Before we can start genetic analyses we need to develop methods to quantify individual differences in development. In order to be able to distinguish gene expression patterns in good and poor learners, it is necessary to find precursors in vocal development that indicate good or poor learning. Therefore I have started to analyze vocal development of already existing song recordings during development. The two first parameters I investigate are 1) whether specific song elements or syllables (the units of which song consists) are acquired early in development and if this acquisition is more accurate and/or faster in good learners than poor learners. 2) I study if fast development (i.e. early song stabilization) leads to better or worse song performance as an adult. Once we know the developmental precursors, we can start measuring genetic variation associated with individual differences.

Jiska Kentrop, PhD-student, Jul/14 – Jul/18

The effects of early life stress on social competence; possibilities for intervention
Joëls, Bakermans-Kranenburg; UMC Utrecht, UL

Aim: Stressful events early in life can have a major impact on adult functioning and previous studies have shown that prolonged exposure to high levels of corticosteroids early in life affect stress-sensitivity, cognitive functioning and brain structure[1]. Both early life and adolescence are sensitive periods, where environmental influences can have a critical influence on further brain development. This study will help us to better understand the adverse effects of early life stress on social competence and explore the possibilities of manipulation of the stress system in an attempt to counteract the effects of early life challenges. The aims of the project are 1) to determine the effects of early life stress on social competence in rats in adolescence (social play) and adulthood (social approach) and 2) to investigate the possibility of reversing these behavioral effects using either an environmental or pharmacological intervention in adolescence.
Methods: Wistar rats are exposed to 24h maternal deprivation on postnatal day 3 to induce early life stress. At postnatal day 26, during adolescence, rats undergo a pharmacological or a non-pharmacological intervention. The pharmacological intervention consists of a 3 day treatment with Mifepristone, a glucocorticoid receptor antagonist. This is hypothesized to change the balance between brain MR and GR. The non-pharmacological intervention consists of housing the rats in a complex environment (Marlau™ cages) until the end of testing.

Progress up to now: Thus far, behavioral testing is finished and the data set is complete. Data analyses for adolescent social play behavior and adult social approach are ongoing.

Manila Loi, PhD-student, Sep/13 - Sep/15

Intervention at puberty after early life adversity
Joëls, van IJzendoorn; UMC Utrecht

Aim: Early life adversity is a risk factor for the development of psychopathology in humans. The aim of this project was to understand *how* early life stress in a well-controlled rodent model affects various cognitive domains and whether this can be reversed by pharmacological intervention applied during a critical peri-pubertal developmental stage.
Methods: Wistar rat pups were removed from the mother for 24 h on postnatal day (PND) 3. Weaning was at PND21. Between PND26 and 28 the pups were treated twice daily with a glucocorticoid receptor antagonist (mifepristone), since this receptor is known to exacerbate damage to the brain. In adulthood (after PND90), rats were tested for spatial memory and decision making.
Progress: We observed that particularly in male rats (much more so than in females), cognitive function was disturbed by maternal; deprivation. This was normalized by brief peri-pubertal treatment with mifepristone. A very similar pattern was observed for glutamatergic transmission in key areas involved in these behaviors. Given the rapid but lasting reversal due to mifepristone treatment, we tested the possibility that this compound works through epigenetic programming. Indeed, the efficacy of mifepristone to restore cognitive function disturbed by maternal deprivation was hampered by co-treatment with a methyl-donor and facilitated by a histone deacetylase inhibitor infused into the area of interest.

Carien Mol, PhD-student, Oct/15 – Jun/18

Twitter evolution: Comparative linguistics of birdsong and child language acquisition
Bolhuis, Kemner; UU Faculty of Social and Behavioral Sciences

Aim: Both human language and birdsong involve complex, patterned vocalizations, implying that human infants and songbirds must solve common tasks, such as segmenting sounds into 'chunks' and pattern recognition, what has been termed 'phonological syntax' in birdsong. The aim of this study is to investigate the role of specific acoustic features in birdsong production, perception and learning, and directly compare this to human language and speech acquisition.
Methods: We will use zebra finches as model species for human speech and language. Firstly, we will study song recognition by exposing adult zebra finches to manipulated songs in phonotaxis preference tests. Secondly, we want to obtain high-quality recordings of zebra finch songs, and analyze rhythmic patterns and other prosodic cues. Moreover, we will investigate the presence of "fatherese", comparable with "motherese" in human speech, which means that adults modify their vocal behavior in response to juveniles. Thirdly, we will monitor the development of a song in young zebra finches using tape-tutoring and investigate the effect of specific song manipulation on song imitation.
Progression up to now: We developed an experimental set-up to conduct preference tests. Also, the first preference tests are conducted and, at the moment, I am writing a research paper about the results of these tests. Furthermore, we developed a more detailed plan for the coming years and discussed with linguists (Profs. René Kager and Martin Everaert) which acoustic features are most interesting for the comparison with human language and speech.

Dr. Angela Sarabdjitsingh, Postdoc, Nov/13 – Feb/18

Genetic resilience to early life stress effects on the behavioral trajectory in mice
Joëls; UMC Utrecht

Aims: to model the neurodevelopmental aspects of behavioral and cognitive domains after early life stress in male and female mice. Additionally, mineralocorticoid receptor (MR) function is considered important in mediating stress resilience. We therefore aim to study the contribution of high/low brain-specific MR expression to ELS and the behavioral trajectory.
Methods: we have used a novel approach for developmental behavioral analysis in which mice are assessed at different developmental stages on a series of behavioral tasks measuring general health,

neurological reflexes, locomotor activity, anxiety, short- and long-term memory and cognitive flexibility (Molenhuis et al., 2014). We use this longitudinal testing battery to assess the effects of early stress in males and females. Additionally we look at the contribution of changed MR expression in the brain.
Preliminary results: 1) We have established and validated (neuroendocrine and behaviorally) the limited nesting and bedding model to induce chronic early life stress in mice through fragmented mother care. 2) We have successfully imported the genetically modified mouse lines necessary to generate the forebrain-specific MR knockout and overexpression mice (6 lines in total). We have now started to breed the experimental animals and maintain the colonies.
3) We have experimentally validated the longitudinal test battery. Preliminary data show that early life stress affects social and cognitive domains in male mice. Besides continuing the current experiments, we now have the opportunity to address the behavioral developmental trajectory in females and in our genetic mouse models in which the expression of MR is either increased or decreased.

Dr. Rixt van der Veen, Assistant professor, Oct/13 - Aug/14

Experiences in sensitive periods: Effects on attention and behavioral control
Joëls, van IJzendoorn, Bakermans-Kranenburg; UL Faculty of Social and Behavioral Sciences; Dpt. Translational Neuroscience, UMC Utrecht and Dpt. of Child and Family Studies, Leiden University

Aim: To examine the effects of a complex rearing environment during adolescence on attention and behavioral inhibition in adult male rats. And investigate to what extend these effects can be influenced by an adverse early life challenge, maternal deprivation.
Methods: Animals in the complex rearing environment were housed in large, two floor MarlauTM cages, together with 10 conspecifics. The early life challenge consisted of 24h maternal deprivation on postnatal day 3, where the mother was taken away and the pups kept warm on a heating plate. In adulthood, animals were tested in the 5-choice serial reaction time task, to measure attention and behavioral inhibition.
Progression up to now: We found that animals in the complex environment showed improved attention, but impaired behavioral inhibition in the 5-choice serial reaction time task. The early life challenge of 24h maternal deprivation on postnatal day 3 led to a decline in bodyweight during adolescence, but did not by itself influence responses in the 5-choice task in adulthood, nor did it moderate the effects of complex housing. Our data suggest that a complex rearing environment leads to a faster adaptation to changes in the environment, but at the cost of lower behavioral inhibition. A paper on these results has been written and submitted for publication.

Mariëlle A.J. Zondervan-Zwijnenburg, PhD-student, Jul/14 - Jun/18

Formalization and evaluation of prior knowledge based on prior/posterior predictive inference
Hoijtink, van Berkum; UU Faculty of Social and Behavioral Sciences

Aim: Develop and evaluate methods with which formalized knowledge derived from animal studies, completed waves of cohorts, or expert elicitation can be compared to new data, and answer the question: to what degree is the new data supported by the formalized knowledge? When the formalized knowledge, and new data provide coherent information, an interesting option is to combine both sources of information in an analysis by means of Bayesian statistics, and arrive at an updated conclusion about the current state of knowledge.
Methods: Simulation study.
Progression up to now: In two studies, previous literature, and expert knowledge respectively have been formalized and updated with new data. Currently we are working on the formalization of knowledge from animal studies for comparison with data on adolescents, and the formalization of knowledge from previous cohorts of children to evaluate replication among studies in new ways. A simulation study has been conducted assessing the performance of six methods to evaluate the (dis)agreement between formalized knowledge and new data. This simulation study will be further extended in order to provide a complete report on the performance and use of methods to compare formalized knowledge with data.

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