Gravitation
Call 2012

Consortium on Individual Development (CID)

Mid-term self-evaluation
Consortium on Individual Development (CID)

*Why some children thrive and others do not*

Application number: 024.001.003

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Approved by the Supervisory Board, the Scientific Advisory Board, and Steering Committee at April 19 2016
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Introduction

Most children develop well and find their way in society without major problems, but some do not. A combination of the child’s disposition and the environment in which he or she is raised is thought to underlie this developmental difference. In order to gain a better understanding of the factors involved, the Consortium on Individual Development (CID) was set up in May 2013 and brings together twenty top researchers (principal investigators, PIs) from different disciplines, working in eight institutes (Appendix 2). Together, we have the necessary expertise in developmental research, including the role of parents, peers and media, epigenetics, interventions, brain development, and animal and statistical models, to advance our knowledge and understanding of why some children thrive and others do not. To this end, we plan to develop a model of how developmental differences between children arise as a result of the interplay between child characteristics and environmental factors, by filling in crucial gaps in our knowledge of the role of brain development, effects of interventions in the environment, and intergenerational transmission.

Over the past years, we have grouped research into four work packages (WPs), each focusing on specific aspects of development: the role of brain development in WP1, effects of interventions in WP2, the role of generational transmission in families in WP3, and animal and mathematical models of development in WP4. In addition, two new study cohorts have been set up, to provide longitudinal data: a longitudinal cohort based in Utrecht (YOUth, WP1) and an intervention cohort based in Leiden (L-CID, WP2). In addition, WP3 makes use of four existing cohorts: TRAILS (Groningen), Generation-R (Rotterdam), RADAR (Utrecht), and NTR (Amsterdam). In each cohort a specific subset of measures is used to monitor the development of two aspects of behavior, namely, social competence and behavioral control, skills that are needed for functioning in society and for reducing the risk of behavioral and emotional problems. Social competence is the ability to engage in meaningful interactions with others. Behavioral control is the ability to control one’s emotions, behavior, and impulses and to adapt to rules.

In addition to the subset of measures for social competence and behavioral control, several instruments are used in all cohorts, thereby allowing (partial) integration of datasets. This broad (social sciences, humanities, biomedical/medical sciences) yet focused multigenerational approach is unique.

A series of interrelated close-knit PhD and postdoc projects on the identification and interplay of factors critical to the development of behavioral control and social competence are now in progress, under the supervision of at least two PIs from different disciplines, in order to stimulate the integration of expertise. These projects are described in detail in Appendix 11. We have also implemented curricular changes and invested in an appropriate infrastructure, so that in the future Dutch science and scientists will continue to have a leading role in the field of child development. Despite the relatively short time since CID started, it is promising that pilot studies have been published and presented at conferences, and that findings have been presented to the public in general, via meetings, newspapers, and other popular media (see also 5.1). Please see the website (www.individualdevelopment.nl) for additional information on our consortium.

This self-evaluation is in accordance with the Terms of Reference (ToR) of NWO for both structure and total number of pages (max. 15). The Italic texts are descriptions of the evaluation criteria given in the ToR.

1 – Participating researchers

1.1 Filling of vacancies

Did the filling of vacancies proceed according to plan? Which changes took place compared to the original plan? What were the reasons for this? What are the consequences of the changes? Optional: How do you deal with gender diversity (opportunities for women)?

All PIs involved in the original proposal are still members of CID, and each has received a budget to fund PhD students and postdocs according to the scientific plan outlined in the proposal. It has also been possible to appoint temporary (scientific) personnel on the cohort budgets. Co-funding budgets have been
used to appoint additional PhD students, postdocs, and research staff. To ensure integration of expertise, it is mandatory that at least two PIs be involved in the supervision of PhD students and postdocs that are appointed on the CID budget (see Appendix 2 for a more detailed overview of the budget and procedures for ensuring scientific integration; the forms that are used to formalize this are in Appendix 14).

Vacancies have been filled as planned. As of February 1 2016, CID consists of 20 PIs, 25 PhD students, 26 postdocs, and 8 other CID researchers; thus there are 51 junior scientists, each supervised by at least two PIs. Thirty-seven researchers (17 PhD students, 18 postdocs, and 2 researchers) are financed through the CID budget (Appendices 3-4; for budget see Appendix 1, Table A and B); 22 researchers are supported by co-funding budgets (Appendices 5-6; for budget see Appendix 1, Table C). In addition to the original plan, 17 more PhD students, postdocs, and researchers have been appointed through co-funding budgets (Appendix 6).

**Gender diversity**
Eleven of the 20 PIs are women and 78% of the appointed PhD students and postdocs are women (Appendices 3-4); women account for 81% of the researchers supported by co-funding budgets (Appendices 5-6).

### 1.2 Future

*Which changes (outlines) do you anticipate over the next five years with respect to the personnel appointed within the consortium? Which adjustments/reinforcements are needed to achieve the objectives?*

PIs will be encouraged to appoint junior staff in the coming 5 years, so that their input is visible within the 10-year scope of Gravitation funding. For the coming 5 years, we will adhere to the plans for PI budgets, cohort budgets, and co-funding as described in in the original application (Appendix 2 and above).

### 2 – Quality of the realization of the research program

#### 2.1.1 Realization lines of research

*Describe the start and the progress of the separate lines of research based on the objectives. Have changes taken place with respect to the original plan? What were the reasons for this? What are the consequences of the changes?*

The four work packages, their scientific methods and objectives, their progress, and any substantial changes to the original research plan are described below. In WPs 1, 2 and 3, research is centered on the new and existing cohorts and thus the research lines mainly focus on the design and development of the cohorts. PhD students and postdocs have started projects along the lines envisaged in the original proposal, which are described in Appendix 11.
WP1

WP leader: Prof. dr. R.S. Kahn
YOUth cohort representative: Prof. dr. C. Kemner
Other PIs: Prof. dr. J. van Berkum, Prof. dr. M. Dekovic, Prof. dr. S. Durston, Prof. dr. H.E. Hulshoff Pol, Prof. dr. P.M. Valkenburg, and Prof. dr. W.A.M. Vollebergh

Aim/objectives: The neurobiological developmental trajectory of newborns, children, and adolescents is not fully understood. In particular, we are only just beginning to learn to what extent genetic and environmental factors influence brain development and how these effects in turn influence behavior. 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, gender, genetic influences, and environmental exposures.

Method/Cohorts: The YOUth cohort includes children from before birth until 18 years of age in two independent but related samples from the general population. The first entry point consists of 3000 babies recruited via their pregnant mothers. The mothers will be tested (including 3-dimensional ultrasound) at 20 and 30 weeks of pregnancy, and their infants will be evaluated at about 5 and 10 months, and at about 3 and 6 years of age. The second entry point consists of a similar number of 8–to 10-year-old children recruited via schools. They will be tested at about 12 and 15 years of age. In both groups, at each visit behavioral development and brain development will be assessed by using EEG/ERP (in the infants and young children), structural and functional MRI (in the school-age children), and eye-tracking, behavioral, and computer tasks. The tasks will focus on behavioral control and social competence, and longitudinal changes therein. Parent-child interactions and IQ (both child and parents) will also be evaluated. In addition, questionnaires will be administered to parents and children, and biological samples will be collected at the various assessment times.

Projects: In WP1, seven PhD students and five postdocs are employed via the CID budget: see Appendix 3-4 and Appendix 11 for progress reports.

Start and progress: Preparations for setting up the cohort started in 2013. This required decisions to be taken about the cohort composition, participant age at testing, and choice of measures and instruments to be used. Tests were developed and tested. A dedicated soft- and hardware structure was designed to incorporate MRI and Biobank data stored at the UMC Utrecht, and questionnaire and experimental data stored at the UU. Personnel for running the cohort have been hired and trained, and protocols covering logistics, and safety and ethical issues have been prepared. We have also developed a strategy for the recruitment and retention of cohort participants and have a dedicated location and facilities for testing children (the Child Research Center (CRC), http://www.kinderkenniscentrum.nl).

The two enrolment moments were described in two protocols submitted to the Institutional Review Board of the UMC Utrecht. These described the general idea of YOUth, including follow-up and inclusion of pregnant women. Subsequently, for each round of assessments an amendment describing the specifics of that assessment round will be submitted for approval. In March and April 2015, the two framework protocols were approved (14-616/NLS1465.041.14 and 14-617/NLS1521.041.14), and the amendments for the first round of measurements were recently approved. Three large pilot studies have been performed: in one data were collected from children at 5 months, and in another data were collected at 10 months, with measurements being performed twice within 2 weeks, to establish test-retest reliability. The third study collected data from children aged 8 to 16 years. Functional Near-Infrared Spectroscopy (fNIRS) is still being piloted in infants, and preliminary data have been used to adapt the measurements and protocols. At the end of May 2015, we started the recruitment of pregnant women, and in March 2016 the first children in the second enrolment period (8–10 years) were recruited.

Changes compared to original proposal: An important change is that the initial number of 4500 subjects in each cohort has been revised to 3000 per cohort and the number of visits in young children has been reduced, mainly for logistic and financial reasons. Even with this reduced number of participants, the study will be amply powered to estimate differences in the primary outcome measures (i.e. typical brain development, social competence, and behavioral control), as these are continuous outcomes. We decided to test children over a wider age range (e.g., the assessment time “9 years” will include children aged 8-10
years), and we have included 3D ultrasound studies of pregnant women, to allow the tracking of brain development prenatally. Also, we decided to collect hair and saliva samples, to allow for more detailed determination of environmental influences. In general, we started recruitment to the YOUth cohort later than envisaged, because of the need to build a dedicated research center and extensive discussion of instruments to be used, etc. Furthermore, recruitment of the cohort of 8- to 10-year-old children was delayed because the dedicated 3T Philips MRI scanner was delivered later than planned: it came in use in February 2016.

WP2

| WP leader: | Prof. dr. M.H. van IJzendoorn |
| L-CID cohort representative: | Prof. dr. M.H. van IJzendoorn |
| Other PIs: | Prof. dr. M.J. Bakermans-Kranenburg, Prof. dr. E.A.M. Crone, Prof. dr. R.C.M.E. Engels |

Aim/objectives: Children are not equally vulnerable to adverse rearing environments and nor do they equally profit from supportive environments. Differential susceptibility theory proposes that vulnerable children, who suffer most from bad environments, also are more receptive to positive changes in the child rearing and wider social environment. Central questions are: Which children are most susceptible to environmental influences, and what are the neurobiological mechanisms by which the environment influences children’s social competence and behavioral control? These questions are addressed experimentally in four longitudinal randomized controlled trials (Leiden-Consortium Individual Development, 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 intervention effects, with the added advantage that the control groups of the four studies partly overlap in such a way that they can be combined in one series of quasi-longitudinal analyses from the first pre-test evaluation in the youngest L-CID cohort to the last post-test evaluation in the oldest L-CID cohort. The four longitudinal studies cover (1) infancy, (2) early childhood, (3) pre-adolescence, and (4) early adolescence. The first 5 years of the 10-year CID program will focus on L-CID cohort 2 (starting at 3 years of age) and L-CID cohort 3 (starting at 7 years of age); thereafter the focus will be on L-CID cohorts 1 and 4.

Projects: In WP2 four PhD students and one postdoc are employed via CID budget: see Appendix 3-4 and Appendix 11 for progress reports.

Start and progress: On the basis of discussions with the Scientific Advisory Board and the research team, we decided to recruit families with same-gender monozygotic (MZ) and dizygotic (DZ) twins and their parents. This approach has the advantage of: (i) more efficient recruitment/data collection/implementation of the intervention, (ii) potential for genetic modeling of intervention effects, and (iii) observation of differential intervention effects between siblings within the same family at a behavioral, (epi-)genetic, hormonal, and neural level. The overall design of the four intervention studies and the main behavioral and biological measures to be included have been established. Experts in various domains were consulted (ambulatory assessments, imaging, hormonal measures, VIPP intervention) to finalize the design.

Several pilot studies have been carried out. The first pilot study investigated the association between behavioral problems and tympanic membrane temperature asymmetry (N=92). In the second study, the Video-feedback Intervention to promote Positive Parenting (VIPP) was revised to include 1 booster session. Internet provision was piloted to see whether it could be used for assessments instead of home visits (with the intention to improve efficiency). Unfortunately, pilot parents and research staff considered it not to be feasible because of technical problems with two-way transfer of videotaped interactions and strict confidentiality requirements. We adapted the VIPP intervention for use with twins and successfully piloted the adapted protocol with three families. In the third study, two paradigms to assess central outcomes, namely, prosocial behavior (Prosocial Cyberball, PCB) and aggressive behavior (Social Network Aggression Task, SNAT) were developed and tested (N=136). PCB and SNAT were adapted to be used in the MRI scanner and with younger children. In the fourth pilot study, the Motionlogger (an actigraph to measure physical activity and sleep characteristics) was used to evaluate chaos in the home environment and the neighborhood. The LENA (Language Environment Analysis), a small apparatus, was used to record and
analyze speech/language and other auditory stimuli in the home environment. In the fifth pilot study, a digital ambulatory assessment app was developed to collect data in real-life contexts and to remind parents to collect saliva samples.

Protocols for the early childhood (cohort 2) and pre-adolescence (cohort 3) studies have been submitted to the Institutional Review Board of the Institute of Education and Child Studies and the Institute of Psychology, revised and submitted to the Medical Ethics Committee of Leiden University Medical Centre (LUMC; obligatory for studies with a neurobiological component), and to the Central Committee on Research Involving Human Subjects. Both protocols have been approved, and the cohorts have been registered in the Netherlands Trial Register (NTR5312).

Recruitment and testing of the early childhood cohort has been successfully completed: 245 families with twins (490 children) have been assessed. By January 2016, 90 families (180 children) had visited the EEG laboratory for the second assessment round, and assessments have been scheduled for another 31 families (62 children); the attrition rate would appear to be low. Preparations for randomization and intervention implementation in cohort 2 are in progress. Recruitment to cohort 3 started in the summer of 2015, and the first 133 families (266 children) have visited the MRI laboratory, with great enthusiasm. Visits for 30 other families (60 children) have been scheduled at the time of writing. Imaging and other tests are conducted in a newly built MRI facility at Leiden University Medical Centre, with two dedicated laboratory rooms, and a mock scanner nearby.

**Changes compared to original proposal:** As explained above, we decided to recruit families with same gender MZ and DZ twins as subjects, to enable comparison of the effectiveness of the intervention in siblings raised in the same family/environment. The VIPP intervention has been adapted to meet the specific needs of families with twins; the aim and general approach of the intervention program remain unchanged. Moreover, since parenting twins can be complicated, the parents of twins are eager to participate in the intervention to get support and advice on sensitive parenting and discipline strategies. We decided to stop recruitment after the inclusion of almost 500 children in each of the two cohorts, instead of the projected 600 children. Implementation of the original design with several rounds of assessments at specific ages would have been impossible because of the overlapping rounds of data collection within and between the two cohorts. The advantage of recruiting twin families is the greater variation in socioeconomic status (and consequently greater statistical power) in the sample relative to that of non-twin families because we have consistently found that families from lower socioeconomic backgrounds are more motivated to participate in research when they have twins.

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<th>WP3</th>
<th>WP leader:</th>
<th>Prof. dr. W.H.J. Meeus</th>
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<td>Cohort representatives:</td>
<td><strong>Generation-R</strong> Prof. dr. F.C. Verhulst</td>
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<td><strong>TRAILS</strong> Prof. dr. A.J. Oldehinkel</td>
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<td><strong>RADAR</strong> Prof. dr. W.H.J. Meeus</td>
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<td>Other PIs:</td>
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<td><strong>NTR</strong> Prof. dr. D.I. Boomsma</td>
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<td>Prof. dr. J. Ormel</td>
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**Aim/objectives:** The WP3 studies investigate how the characteristics of grandparents (Generation 1, G1) impact the development of parents (Generation 2, G2) and – through them – the development of their children (Generation 3, G3). These studies have a multigenerational design and investigate the extent to which genetic and non-genetic transmission between generations causes differences in developmental outcomes in children and adolescents. The three-generation design is used to study behavioral transmission. Two- and three-generation designs are used to study the epigenetics of transmission and to untangle genetic and environmental processes of transmission of processes related to behavioral control and social competence.

**Method/Cohorts:** The WP3 studies will use data collected from existing G1 and G2 cohorts and will collect data from the G3 cohort. These cohorts are part of four strong cohort studies of child and adolescent development currently in progress 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 budget: see Appendices 3-4 and Appendix 11 for progress reports.

Start and progress:

Generation-R
The epigenetic measurements are in progress. We expect the additional methylation data to be available for analysis in March or April 2016. We already have genome-wide epigenetic array data for cord blood from 960 children and will add cord blood methylation data for another 500 children, and measurements repeated at 5 and 9 years of age (G3). These data are unique and constitute one of the largest population-based repeated epigenome-wide datasets for children worldwide. The collection of data on childhood trauma (obtained by maternal interview, G2) has been completed. In total about 5800 primary caregivers completed the structured interview about their child’s life events and traumatic experiences. These data are currently being cleaned, checked for inconsistencies, and prepared for analysis.

NTR
The medical ethical committee approved the data collection protocol in children of twins of the Y(oung)NTR. Preparations have been made to collect data from the children of twins of the YNTR. All twins in the cohorts 1986-1990 (G2) with offspring have been identified (about 700 persons from about 575 families) and are asked, together with their partners and the co-twin of the parent, to fill out a survey about the development of their offspring/cousin(s) (G3). This survey includes measures on psychopathology, well-being, behavioral control, temperament, and the home environment. We already have extensive longitudinal data for these parents on, amongst others, psychopathology and well-being. In young twins, we will try to collect data from their teachers and characterize the school environment.

RADAR
In 2013-2014, we collected data for the Wave 7 assessment of G2 and linked them with earlier collected data for G1. The Wave 8 assessment of G2 took place in fall 2014 and spring 2015. In total, data were collected for 1152 target parents and 567 partners. Attrition between the Wave 1 and Wave 8 assessments was about 15%. We are now cleaning the data of the Wave 8 assessment. Key aspects include measures of personality, behavioral control, parent-child relationships, social competence, peer relationships, and psychopathology. The preparation of questionnaires and observational measures (special attention given to social competence and behavioral control) for G3 was completed in 2014. Data collection for G3 participants is in progress, in close collaboration with TRAILS.

TRAILS
In close collaboration with the RADAR study group, we have investigated measures of a third generation (G3), using 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 include early movements, milestones, temperament, behavioral control, social competence, and psychopathology. Data collection started in April 2015, with screening of the cohort regarding pregnancies, and the first home visits started in September. The coming period will see the inclusion of children born in the last years (> 80).

Changes compared to original proposal: The Generation-R, NTR, and RADAR studies are being carried out according to the original plans. This is also true for the TRAILS study, with the exception that offspring follow-up assessments are planned at 3, 24, and 48 months of age instead of the originally planned twice within 12 months, at 18 months, and once every year thereafter. We made this change to optimize the time window for specific assessments (e.g. early motor activity should be assessed between the 11th and 16th week in order to be informative) and to enable comparisons with the other cohorts of the CID, as far as possible given the budget.

WP4

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<th>WP leader:</th>
<th>Prof. dr. M. Joëls</th>
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<td>Animal cohort representative:</td>
<td>Prof. dr. M. Joëls</td>
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<td>Other PIs:</td>
<td>Prof. dr. J.J. Bolhuis</td>
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<td></td>
<td>Prof. dr. H.J.A. Hoijtink</td>
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Aim/objectives: We aim to gain an understanding of how gene x environment (G x E) interactions influence the development of behavioral control and social competence (relevant to work packages 1-3). To this end, we will use models to study G x E interactions under highly controlled conditions; use experimental methods to examine specific brain connections (down to the level of synapses); investigate trans-generational effects within a time-frame of a few years; and test the validity of specific theoretical frameworks, which in turn can be used to guide future experiments. Like the other WPs, WP4 makes use of shared technology (e.g. neuroimaging) and has a focus on behavioral control and social competence.

Methods/cohorts: In the animal (rodent and bird) cohort, we will focus on genes known to be important in environmental/intervention susceptibility (WP2), e.g. DRD4. We will also investigate the influence (i) of parent-infant interactions in rodents and birds or (ii) of growing up in a complex environment, on the development of various cognitive skills including social communication and behavioral control (WPs 1-3). We will also examine trans-generation parallels in parenting styles and the commonalities/differences in epigenetic programming between humans and rodents (aligned with WP3). We will apply (Bayesian) statistics to existing human/animal datasets to test the interaction between early life stress and stress in adulthood.

Projects: In WP4 four PhD students and five postdocs have been employed via CID budget: see Appendix 3-4 and Appendix 11 for progress reports.

Start and progress:

Use of rodent models/rodent cohorts
This part started in October 2013, with the optimization of the animal models and behavioral tasks. Two animal models for early life adversity (limited bedding/nesting material in mice from postnatal day 2-9; maternal deprivation on postnatal day 3) have been developed, as well as the complex housing environment. We have set up various cohorts: genetically modified mouse lines with Mineralocorticoid Receptor (MR) overexpression or knockout, Glucocorticoid Receptor (GR) knockout and combinations thereof. All behavioral set-ups were optimized in 2013/2014.

We are currently investigating whether the consequences of early life stress on the developing rodent brain can be normalized during the sensitive peripubertal period, by means of environmental or pharmacological interventions, and the role of epigenetic programing. Special attention will be paid to male-female differences. Experimental endpoints include: behavioral control in the 5-choice serial reaction time task, and social competence (play behavior, social interaction behavior, and behavioral flexibility).

Use of avian models/avian cohort
There are two research lines: (1) Gene-environment interactions in the development of social behavior in a cohort of birds, and (2) How do developmental factors affect each other in the development of song and social preferences in birds? In research line 1, we are examining the neurogenetics of birdsong learning. In research line 2, further technical advances in the high-density multielectrode recording set-up have enabled 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). We have recently finished collecting data from a first experiment. One of the goals is to find precursors for good or bad vocal learning. We have completed a first experiment on song recognition in zebra finches, in which the birds were exposed to manipulated songs in phonotaxis preference tests.

Use of statistical models
We have developed inferential procedures that are relevant for CID research in cooperation with CID researchers. In the past year, we have started the following projects:

• Use of data and expert knowledge to estimate and evaluate statistical models
• Development of statistical tools for replication studies in the context of cumulative stress and match/mismatch theories
• Development of statistical tools for theory-based evaluation of contingency tables in the context of eye-tracking studies
An essential component of these projects is consultation and cooperation with PIs from other WPs. The newly developed statistical techniques will be implemented in CID projects.

**Changes compared to original proposal:** At this stage, there have been no changes to the plans described in the original proposal.

### 2.1.2 Added value Gravity funding

**Where does the Gravitation funding make the difference?**

Gravitation grant funding has been indispensable for creating a multidisciplinary community, for building up longitudinal cohorts, and for developing an interdisciplinary training program. The participating cohorts form the backbone of the CID program, and thanks to the Gravitation funding we have been able to set up two new cohorts and integrate four existing cohorts. Longitudinal cohorts are essential to the aim of CID, namely, to understand the many factors that determine *individual development*. Setting up two new cohorts in Utrecht and Leiden and integrating major existing cohorts are costly endeavors – the substantial funding through CID has allowed us to create internationally unique instruments. In addition, funding has allowed us to hire personnel to work on joint research questions. In the relatively short time since CID started, many interdisciplinary cooperative projects have been set up that reflect the envisaged integration of social sciences and substrate-driven neurobiological approaches.

Importantly, funding has allowed us to create a community with a focus on child development, a community that provides a stimulating environment for PhD students and postdocs. This community will be consolidated in the future.

### 2.2 Interaction and coherence between the lines of research

**How do you promote the interaction and coherence between the lines of research? Which changes have been made with respect to the original plan for this interaction/coherence? What were the reasons for this? What are the consequences of the changes? In the annex include a list of any joint publications that emphasize this interaction (Appendix 10).**

CID brings together top researchers from different disciplines. We have established several ways to stimulate interaction, coherence, and complementarity that are in line with our original plans:

- As described in the original proposal, the research of all WPs is specifically focused on understanding the development of social competence and behavioral control. WPs 1-3 are complementary to each other and are carried out in parallel with WP4 in existing rodent and avian models or statistical models.
- To promote complementarity and cooperation further, PhD students and postdocs funded by the CID budget are supervised by at least two supervising PIs (Appendix 2 and Appendix 14).
- Importantly, a specific subset of measures of social competence and behavioral control is used in all cohorts (see our website: [http://www.individualdevelopment.nl/research/measurements](http://www.individualdevelopment.nl/research/measurements)). All twenty PIs agreed on the use of these core measures in a meeting held on January 15, 2014 (see 2.3).
- In addition, several instruments are used in more than one cohort. For example, all cohorts use standardized tasks to measure intelligence: the Wechsler Preschool and Primary Scale of Intelligence (WPPSI) or the Wechsler Intelligence Scale for Children (WISC). The YOUth study uses several questionnaires that are also used in other cohorts, such as Generation-R, TRAILS, and RADAR. Several neurocognitive tasks are common to both YOUth and L-CID: delay gratification and delay discounting (behavior), prosocial cyberball (Utrecht behavior, Leiden fMRI), and stop signal task (Utrecht fMRI, Leiden behavior). Structural MRI and MRI resting state activity are measured in the Utrecht and Leiden studies. The Generation-R, NTR, TRAILS, and RADAR studies of WP3 collaborate with respect to data collection (similar or equivalent measures are used for psychopathology and parent-child relationships) and cooperate in terms of storage and imputation of genetic data. Lastly, we have made every effort to ensure that similar biological materials are collected across all participating cohorts.

These endeavors have led to several co-supervised PhD projects and publications, which further strengthen collaborative efforts within and between different WPs (Figure 1 (collaboration within and between WPs), Appendix 7 (examples of interaction and coherence between WPs) and Appendix 10 (joint publications)).
**Two highlights of CID collaborative efforts:**

First, collaboration between the UMC Utrecht (WP4) and Leiden University (WP2) has led to the use of an animal model to answer questions about the role of environmental factors in the development of behavioral control in children. Results suggest that a complex rearing environment leads to a faster adaptation to changes in the environment, but at the cost of lower behavioral inhibition. (Van der Veen et al. (2015): Complex living conditions impair behavioral inhibition but improve attention in rats. *Frontiers in Behavioral Neuroscience*, doi: 10.3389/fnbeh.2015.00357)

Second, a CID-initiated collaboration between the UMC Groningen, Utrecht University, and Erasmus UMC has led to a publication on whether experiences in parent-child relationships are associated with experiences in relationships with peers and intimate partners. (Kretschmer et al. (2015): Configurations of Adolescents’ Peer Experiences: Associations with Parent-Child Relationship Quality and Parental Problem Behavior. *Journal of Research on Adolescence*, doi: 10.1111/jora.12206)

### 2.3 Joint activities

*Illustrate the interaction and coherence between the lines of research with a list of joint activities that emphasize this interaction.*

#### Joint activities since the start in 2013

*See also the timeline in Appendix 2*

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>22 March 2013, Utrecht:</td>
<td>Brainstorming with all 20 CID PIs about the implementation of the research program.</td>
</tr>
<tr>
<td>10 October 2013, Utrecht:</td>
<td>First Scientific Advisory Board meeting with the Steering Committee and Scientific Advisory Board members; presentations and discussion about all WPs.</td>
</tr>
<tr>
<td>11 October 2013, Utrecht:</td>
<td>Kick-off CID symposium with presentations by international experts (Scientific Advisory Board members and PIs) and poster presentations by PhD students and postdocs.</td>
</tr>
<tr>
<td>30 October 2013, Utrecht:</td>
<td>PI meeting to decide on the core measures for social competence and behavioral control.</td>
</tr>
<tr>
<td>26 November 2013, Utrecht:</td>
<td>Cohort expert meeting. Advice meeting for the YOUth cohort. Experts from other cohorts within the consortium were attending.</td>
</tr>
<tr>
<td>15 January 2014, Utrecht:</td>
<td>PI meeting on core measures for social competence and behavioral control. Core measures were selected for use in each cohort in the consortium: <a href="http://www.individualdevelopment.nl/research/measurements">http://www.individualdevelopment.nl/research/measurements</a>.</td>
</tr>
<tr>
<td>25 June 2014, Utrecht:</td>
<td>CID meeting with all PIs, PhD students, postdocs, and other interested parties. Giving the opportunity to meet each other, to present work and learn about each other activities. Along with a community coffee session, the PI meeting, the Steering Committee meeting, and an informal reception. This meeting is held regularly every 6 months (see below *).</td>
</tr>
<tr>
<td>29 October 2014, Utrecht:</td>
<td>Seminar for directors of primary schools, teachers, internal counselors, and care teams on behavioral problems in children. Organized by the Brain Center Utrecht (CID PI Joëls) and the Child Research Center (CID PI Kemner).</td>
</tr>
<tr>
<td>17 December 2014, Utrecht:</td>
<td>CID meeting with all PIs, PhD students, postdocs, and other interested parties.*</td>
</tr>
<tr>
<td>18 March 2015, Utrecht:</td>
<td>CID meeting with all PIs, PhD students, postdocs, and other interested parties.*</td>
</tr>
<tr>
<td>9 April 2015, Utrecht:</td>
<td>Second Scientific Advisory Board meeting with the Steering Committee and Scientific Advisory Board members; presentations and discussion about all WPs.</td>
</tr>
<tr>
<td>10 April 2015, Utrecht:</td>
<td>Second CID symposium with presentations by international experts (Scientific Advisory Board members and PIs) and poster presentations by PhD students and postdocs.</td>
</tr>
<tr>
<td>31 August 2015, Utrecht:</td>
<td>Jet Bussemaker, Minister of Education, Culture and Science, and Jos Engelen, Chairman of the Governing Board of NWO visited the Child Research Center Utrecht (KinderKennisCentrum Utrecht), base of the WP1 YOUth cohort.</td>
</tr>
<tr>
<td>30 September 2015, Utrecht:</td>
<td>CID meeting with all PIs, PhD students, postdocs, and other interested parties.*</td>
</tr>
<tr>
<td>22 March 2016, Utrecht:</td>
<td>CID meeting with all PIs, PhD students, postdocs, and other interested parties.*</td>
</tr>
</tbody>
</table>
2.4 Future

What is the planning for the next five years with respect to the realization of the research program? Which adjustments/reinforcements are still needed to achieve the objectives?

CID is on track and we will in general continue as planned. More specifically, in WP1, we are currently investigating, in the YOUTH cohort, the possibility of using structural and functional MRI both preterm and in newborns, to study early brain development in greater detail. We are also discussing the possibility of greater cooperation with other partners at the Utrecht campus, to enable a more in-depth assessment of environmental effects (Geosciences) and somatic factors (with the Wilhelmina Children’s Hospital). In addition, we are working on an Internet platform that will allow us to make more measurements and which will be a tool for cohort recruitment and retention.

In WP2, the studies involving cohorts 2 and 3 will continue with several assessment rounds. Protocols for the two remaining cohorts 1 and 4 of L-CID will be prepared, and these studies will be started after prior assessment of the measures that are unique to these cohorts compared to L-CID cohorts 2 and 3. Ethical approval will be sought and the trials will be registered in the Netherlands Trial Register.

In WP3, the data collection of the four studies (Generation-R, NTR, TRAILS, and RADAR) is on track. A cooperative submission for additional funding was made to NWO large investment grant 2015, to support the projected large-scale investigations, specifically for the large-scale collection of data from G3 children in the coming years. Also, WP3 has set up collaboration with Geosciences UU to study the effects of neighborhoods on child and adolescent development.

In WP4, three series of experiments using rodent models will be started in collaboration with WP1 and WP2. The development of avian models and their use in studies will continue as planned. The statistical foundation for theory-based data evaluation and the evaluation of replication studies will be finalized in the coming year. These developments will be used/implemented in different CID projects from WP1, WP2 and WP3.

3 – Institutional and organizational embedding

3.1 Organization structure and management

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

Describe the organization structure. Have changes taken place with respect to the original plan? What were the reasons for this? What are the consequences of the changes? Add an organogram.

The Consortium on Individual Development (CID) started in May 2013. A Consortium Agreement was formulated, specifying the governance structure in more detail than was given in the proposal (amongst others including cohort representatives), the aim of collaboration, the relationship between parties, consortium management, and the rights and obligations of the parties concerning the implementation of research projects and use of project budgets (Appendix 15). Conform the Consortium Agreement, structures for meetings, documentation, administration, and finance have been set up. The Finance Office (manager and controller) set up a financial structure (control sheet, forms) and visited the finance staff of all parties to explain procedures and structures.

The organizational structure of CID can be found in the organogram below and Appendix 2 (e.g., for names of the members of the different bodies). The Program Chair organizes and chairs the meetings of the Steering Committee. She implements the Steering Committee’s policy with respect to scientific direction. The Program Support Office assists and facilitates the work of the Steering Committee and the Program Chair in executing the decisions of the Steering Committee as well as in the day-to-day management of the program. The Steering Committee is composed of the program chair, the four WP leaders and two additional members who were co-applicants. The Steering Committee oversees the general management of the research program and ensures the coherence, cooperation, and complementarity between the different WPs. The Steering Committee monitors scientific progress in each WP and makes decisions about ethical issues, financial, administrative, and contractual matters. It meets every 2 months (every 6 months...
The research program is subdivided into four WPs, each led by a WP leader. The WP leader implements the policy of the Steering Committee for their own WP. The WP leader monitors scientific progress and is responsible for the management of the scientific staff (PhD students/postdocs) associated/assigned to their WP. For each cohort, a CID Cohort representative is responsible for organizing measurements that are needed to achieve the scientific goal of the WP and for organizing the financial management of their cohort. The Scientific Advisory Board is an advisory board to the research program in general and advises the Steering Committee, as specified in the Consortium Agreement.

Changes compared to original proposal
- Up to now, there have been no changes in the participating institutes or in PIs in the consortium. Because of health reasons, Prof. dr. Durston has passed on her role as WP leader and member of the Steering Committee to Prof. dr. Kahn.
- Prof. dr. Robert Plomin (King’s College, University of London) had to withdraw from the Scientific Advisory Board for personal reasons and has been replaced by Prof. dr. Mark Johnson. Prof. dr. Laurence Steinberg joined the Scientific Advisory Board in early 2013.
- We set up a Supervisory Board of deans or division leaders from all consortium partners. This is the consortium’s supervisory and ultimate decision-making body.
- In 2015, an ethical advisor was appointed and she is an additional member of the Scientific Advisory Board. The ethical advisor advises the Steering Committee on various topics, including human and animal research, data protection, Biobank, and database specialties. She is responsible for monitoring the proper application of ethical rules and for advising consortium partners on ethical issues.

Organogram
3.2 Progress and quality assurance

How is the safeguarding of quality and progress arranged? Optional: State how you deal with data management and state how you deal with the ethical aspects of the research (Appendix 12).

The program chair implements the Steering Committee’s policy regarding the scientific direction, coherence, cooperation, and complementarity between the WPs. The Steering Committee steers the scientific progress of the research program and ensures communication between the different WPs. In turn, the WP leaders monitor the scientific progress of their WP, and the Cohort Representatives organize the evaluations and measurements in their cohorts that are needed to achieve the scientific goals of their WP.

We have set up a Supervisory Board of deans or division leaders from all consortium partners (see Appendix 2 for the members of the Supervisory Board). This is the consortium’s supervisory and ultimate decision-making body. The annual reports and accounts submitted by the Steering Committee have to be approved by the Supervisory Board. The governance structure to safeguard the quality and progress of the consortium is specified in the Consortium Agreement. The Supervisory Board has held three meetings: on April 8, 2014, October 12, 2015, and February 17, 2016, during which they unanimously approved the annual reports of 2013–2014 and 2014–2015. Please see Appendix 13 for a summary of the notes.

Ethical aspects and data management: All protocols were submitted to relevant Institutional Review Boards and/or Medical Ethics Committees for approval before participant recruitment was started (see also Appendix 7). All studies are carried out in accordance with the Medical Research Involving Human Subjects Act (WMO). As an example of how the consortium deals with data management and ethical aspects of our research, the protocols for WP1 (YOUth cohort) are given in Appendix 12. The protocol for data management was written in close collaboration with the Department of Information and Technology Services (ITS) of Utrecht University. The protocol is shared with consortium partners.

3.3 Advisory/quality assurance body

Does the consortium have a quality assurance body (e.g. Scientific Advisory Board)? If it does then who are its members? Have meetings/consultations already taken place? In the annex add recent notes of meetings of the quality assurance body, if applicable (Appendix 13).

The Scientific Advisory Board is an advisory organ for the research program in general and advises the Steering Committee, as specified in our Consortium Agreement. An ethical advisor has been added to the Scientific Advisory Board (see Appendix 2 for board members). The Scientific Advisory Board has had two meetings: on October 10, 2013 and on April 9, 2015. A meeting is scheduled for October 27, 2016. Please see Appendix 13 for the most recent notes.

3.4 Embedding and collaboration

How is the embedding and collaboration currently organized in the national and international contexts? Support your argument with a summary of activities from which this embedding and collaboration is apparent (Appendix 7).

The consortium is associated with one of the four strategic themes of Utrecht University, namely, Dynamics of Youth (DoY, www.uu.nl/doy), which focuses on child development, but with an even broader scope and participation (including involvement of all Utrecht Faculties: Social and Behavioral Sciences, Geosciences, Humanities, Law, Economics and Governance, Science, Medicine, and Veterinary Medicine). This clear nucleus of organization at Utrecht University increases the coherence of the program and provides structural embedding (see also 3.6). Local embedding is reflected by the co-funding provided by different institutes, both in material and personnel, as can be seen in Appendix 1, Table C and Appendices 5, 6, and 7. Furthermore, all participating research groups have excellent, state-of-the-art facilities and equipment at their disposal. The institutional embedding of the different sites and examples of national and international embedding are described in Appendix 7. A few highlights are given below:

WP1: Nationally, WP1 collaborates with the Trimbos Institute, Utrecht. Internationally, it cooperates with
the Marie-Curie training school on neurocognitive methods in infants (Brainview), and with the European IMI EU-AIMS consortium involving, among others, the Institute of Psychiatry, London (UK), the Institute of Psychiatry, Mannheim (Germany), Nijmegen, and the Karolinska Institute, Stockholm (Sweden).

WP2: Nationally, L-CID cooperates with the VU University Amsterdam on challenges to child-caregiver relationships. Internationally, it cooperates with Gusto, a large cohort study in Singapore, on epigenetics of parenting, and with Imperial College, London (UK), on video feedback interventions.

WP3: Nationally, NTR collaborates with the Max Planck Institute, Nijmegen, regarding its research on literacy development. Internationally, NTR, Generation-R, and TRAILS collaborate as part of the EAGLE consortium (EARly Genetics and Lifecourse Epidemiology) with other international groups in studies to identify genes underlying childhood psychopathology.

WP4: Nationally, WP4 collaborates with Radboud University Nijmegen. Internationally, WP4 has a close collaboration with the Max Planck Institute for Psychiatry, Munich (Germany), and with the Massachusetts Institute of Technology, Cambridge (USA).

3.5 Talent management

How do you realize talent management (e.g. activities and training courses for the next generation of researchers)? Have changes taken place with respect to the original plan? What were the reasons for this? What are the consequences of the changes? Support your argument with a summary of relevant activities.

We designed a curricular environment in which our Master’s and PhD students can obtain the right mix of deep disciplinary expertise and a wider interdisciplinary outlook. To this end, we determined what is already in place in the participating graduate programs and added specific facilities relevant to our CID junior scientists. A list of specialized courses at Master’s and PhD levels organized by the participating graduate programs for PhD students and postdocs working in CID can be downloaded from the CID website (www.individualdevelopment.nl). The Program Support Office facilitates participation in courses outside its own graduate program for the CID PhD students and postdocs. PhD level courses, Master’s-level courses, and Master classes are regularly organized by CID PIs. In addition:

- All cohorts offer on-the-job training and coaching. They provide students with the possibility to participate for several months (Master’s level) or several years (PhD level). To foster interdisciplinary development, all CID PhD students have a second supervisor with a different disciplinary background from the consortium.
- Graduate program students are regularly invited to attend lectures given by one of the researchers, which address a specific topic from the research program in depth.
- During the course of the research program, Summer Schools rotate over the participating institutes. Students have the opportunity to present their research via mini-presentations.
- Extra to the original proposal, a journal opinion article assignment has been initiated to stimulate the multidisciplinary cooperation between CID PhD students and postdocs. In small groups (2–4 persons) PhD students and postdocs participate in ongoing discourse in scientific communities or media. They write a journal club article, an opinion article in a scientific journal, or an opinion article in the (inter) national media.

We have the following specific goals for the coming years, all in addition to the original proposal:

- We will organize once or twice a year a Tour de Consortium, planned to start June 2016. All CID PhD students and postdocs will be invited to visit a participating institute, to look at its laboratories, facilities, and methods/tools.
- We have reviewed available courses on ethical aspects of research and we are planning to close ethical educational gaps by providing workshops in collaboration with our Ethical Advisor.
- We will organize ‘meet-the-senior’/’speed-date’ sessions for CID PhD students and postdocs with PIs in order to explore their research career possibilities.

3.6 Future

What are the plans for the next five years with respect to institutional and organizational embedding? Which adjustments/reinforcements are still needed to achieve the objectives?
3.7 Anchoring

How will the consortium be anchored after the end of the Gravitation funding and how is that being worked towards? Describe this in as much detail as possible.

We envisage successful anchoring of the consortium after the end of the Gravitation period, as a result of our collaborative efforts, community building, cohorts, and the long-lasting effects of the curricular environment. We have already established extensive cooperation, complementarity, and exchange of ideas between participating PIs, as described in detail in 2.2 and 3.4. Our consortium encompasses a broad integration of top researchers, universities, university medical centers, landmark cohort studies, and scholarly fields, which is unprecedented in Dutch academia and beyond. This confers a critical mass and versatility that will form the basis of a leading position in international child development research over the decades to come.

Furthermore, our integration of longitudinal cohort studies offers a rare but exceptionally powerful opportunity for synergy, which will put us at the forefront worldwide. With additional funding, we will be able to continue the cohorts, and we believe that this large-scale endeavor in child development research in the Netherlands will enjoy broad support in Europe.

Importantly, our interdisciplinary community of CID junior and senior researchers, together with the set-up of our Master’s and PhD level curricular environment, will form an important component of our institutional and organizational embedding. We have set up a curriculum in which the next generation of researchers can thrive and develop their talents to the fullest. This will ensure that we gather critical mass and momentum, not just during the 10 years of this Gravitation project, but also thereafter. Our plans for Talent Management (see 3.5) for the next 5 years will further build on a firm basis for a new generation of highly multidisciplinary researchers.

3.8 SWOT analysis

What are the strengths and weaknesses of the organization and the management of the consortium and what are the opportunities and threats present in the environment?
For further clarification of the SWOT analysis, we refer to Appendix 8, page 43.

<table>
<thead>
<tr>
<th>Internal analysis</th>
<th>External analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Strengths</strong></td>
<td><strong>Opportunities</strong></td>
</tr>
<tr>
<td>S1 CID Community: broad expertise and enthusiasm</td>
<td>O1 Science is changing</td>
</tr>
<tr>
<td>S2 Joint instruments: unique cohorts</td>
<td>O2 Funding possibilities</td>
</tr>
<tr>
<td>S3 Organization: transparent and efficient</td>
<td></td>
</tr>
<tr>
<td>S4 National and international embedding</td>
<td></td>
</tr>
<tr>
<td>S5 Well-developed talent management and strong investments in junior scientists</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Weaknesses</th>
<th>Threats</th>
</tr>
</thead>
<tbody>
<tr>
<td>W1 Timing: starting-up cohorts</td>
<td>T1 Governmental regulations for data handling</td>
</tr>
<tr>
<td>W2 Financing of cohorts</td>
<td></td>
</tr>
</tbody>
</table>

4 – Realization and budget
For the realization and budget we refer to Appendix 1.

All work packages have started up successfully, as evidenced by the funding allocated to principal investigators (Tables A and D). The infrastructure for setting up and maintaining cohorts is well developed (Table B). Table C shows the additional funding provided by the UMCU, UU Faculty of Social and Behavioral Sciences, University Medical Center Groningen, Leiden University, and University of Amsterdam. Additional funding is essential to cover the costs of, for example, recruitment and MRI scans. Tables A-C reflect planned vs. actual costs conform the original application approved by NWO. Tables D-F are specifications: budget for scientific staff subdivided by PI per WP (Table D), and specification of costs of materials and personnel, and full-time equivalents (FTEs) for scientific staff (Table E) and investment costs (Table F).

5 – Knowledge utilization

5.1 Interaction with knowledge users

<table>
<thead>
<tr>
<th>Highlights of CID interaction with knowledge users:</th>
</tr>
</thead>
<tbody>
<tr>
<td>WP1 has actively participated on the Cultural Sundays of October 18, 2015 and April 3, 2016, successful events in Utrecht attracting up to 60,000 visitors. And WP2 co-organized the Braintime Festival in Corpus (<a href="http://www.universiteitleiden.nl/nieuws/2016/02/feest-voor-het-puberbrein">http://www.universiteitleiden.nl/nieuws/2016/02/feest-voor-het-puberbrein</a>), with 300 young participants of the Braintime research.</td>
</tr>
</tbody>
</table>
Appendices
Appendices

Appendix 1 – Realization and budget

CID started in May 2013, 2.5 years ago. Bearing this in mind, the accounts and budgets presented below show that CID has made a successful start and that personnel and infrastructure are in place to support the further development of CID and its research.

First, we show the budget proposal, submitted and approved by NWO. Tables A-C reflect these same tables conform the original application, but now with actual costs up to December 2015. The totals in the year budget columns for 2013 to 2015 as well as the total budget for the period 2013-2023 therefore reflect the budgets from the original tables of the proposal.

Table A: According to the original proposal, every work package was divided into objectives to which specific PIs were assigned. Originally, the scientific staff budget per work package was subdivided into PhD students and postdocs. In order to come to the realization of this budget, we further subdivided the total budget per work package into the different PIs participating (and thereby into the different objectives per WP). The PIs were allowed to use maximally 50% of their allocated budget in the first 5 years (€810,000 = €405,000; other PIs: €540,000 = €270,000; see Table D) for the appointment of PhD students and postdocs, subject to the approval of NWO. There would appear to be a discrepancy between projected and actual costs (see Table A), which can be explained by the fact that PhD students and postdocs are appointed for a number of years, in many cases beyond December 2015. The 5- and 10-year personnel costs given in Table D show that most PIs have allocated their total 5-year budget, as planned (total first 5-year PI-budgets: €6,345,000; total allocated budget: €5,141,906). Monies remaining will be carried over to and merged with the second 5-year period.

Tables B and C: Table B provides an overview of projected and actual investment costs and Table C an overview of co-funding acquired. Every institute gave a short description on the realization (actual) of their budget.

Tables E and F: These Tables provide a further specification of the costs of materials and personnel, and full-time equivalents (FTEs) for the scientific staff (Table E) and for cohort budget (Table F). Please note that the totals in the year budget columns for 2013 to 2015 as well as the total budget for the period 2013-2023 reflect the budgets from the original Table A and Table B respectively, from the proposal.

Table of content:
Original tables conform NWO application
Table A: Scientific staff (PhD student and postdoc costs per work package)
Table B: Investment costs (per cohort for the different work packages)
Table C: Co-funding description (for the institutes specified in the original proposal)
Table D: Specification of Table A (scientific staff) per principal investigator
Table E: Specification of Table A (scientific staff) for material costs, personnel costs and full-time equivalents (FTEs)
Table F: Specification of Table B (investment costs) for material costs, personnel costs and full-time equivalents (FTEs)
Original tables conform NWO application

Table A - Requested scientific staff (in k€ incl. surcharge)

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>WP1: Post doc</td>
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<td>110.00</td>
<td>110.00</td>
<td>110.00</td>
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<tr>
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Table B - Requested investment costs (in k€)

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### Table - Available co-funding

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### Table A – Scientific staff (PhD students and postdoc costs per work package)

**Up to December 2015**

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Please note that the totals in the year budget columns for 2013 to 2015 as well as the total budget for the period 2013-2015 reflect the budgets from the original Table A from the proposal, but now with budget vs. actual for the period including December 2015.

Please note that the total realization (actual) does not reflect the total allocated budget. See Table D for the specification of the total 5-year total allocated budget per PI.
Please note that the totals in the year budget columns for 2013 to 2015 as well as the total budget for the period 2013–2015 reflect the budgets from the original Table B from the proposal, but now with budget vs. actual for the period including December 2015.

(a) YOUth Utrecht (WP1): it took longer than anticipated to set up the cohort, because of careful tuning with the Institutional Review Board and their request for additional information (in the form of, among others, performing several pilot studies). Moreover, the dedicated MRI scanner and relevant software were not delivered on time.

### Table B – Investment costs (per cohort for the different work packages)
Up to December 2015

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<td>162.703</td>
<td>351.000</td>
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<td>455.521</td>
<td>2.574.000 PM</td>
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<td>90.000</td>
<td>91.455</td>
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<td>50.861</td>
<td>240.000</td>
<td>163.719</td>
<td>660.000 PM</td>
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<td>90.000</td>
<td>91.455</td>
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<td>50.861</td>
<td>240.000</td>
<td>163.719</td>
<td>660.000 PM</td>
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<td>4.002.592</td>
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</table>
(b) L-CID Leiden: The investment budget for 2013-2015 has been carried over because collection and analysis of saliva samples and cheek swabs will be done at the same time for all first-wave samples. Measurements are in progress. Delayed ethical approval of the cohort 2 study meant that it started in September 2014 instead of June 2014. This also delayed the appointment of personnel.

(c) TRAILS: The cost of data collection in TRAILS is lower than budgeted, mainly because there were fewer assessments of infants born before the start of CID. The primary focus was to include all new pregnancies, and recruitment of pregnant women was complicated and logistically difficult (problems now solved). An additional problem was that the interviewer training to perform the home visits at 24 months was appointed later than anticipated. The expenditures will be compensated in the upcoming years.

(d) NTR: The costs of the cohort studies are lower than projected, mainly because the PhD student and postdoc started later than planned. The remaining sum will be carried over to 2016 onward.

(e) RADAR: Other funding sources were first used for data collection in Wave 8 (2014–2015). The CID cohort budget will be spent from 2016 onward.

(f) For Generation-R there was a prepayment, resulting in higher actual costs than budgeted for 2014. This was compensated for in the years 2013 and 2015.

(g) Animal costs: Animal costs were lower than projected, because of the long time needed to start-up the different mouse lines (e.g., quarantine and some problems with the bringing on and breeding of mice). At this moment, everything is running on schedule.
Table C – Co-funding description (for the institutes specified in the original proposal)
Up to December 2015

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<td>777.778</td>
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<td>UU Toparea Youth (Topgebied Jeugd) (b)</td>
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<td>1.000.000</td>
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<td>200.000</td>
<td>132.238</td>
<td>200.000</td>
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<td>UL Free MRI Scans (d)</td>
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<td>UL Additional PhDs (e)</td>
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<td>100.000</td>
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<td>100.000</td>
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<td>UL Four additional PhDs (f)</td>
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Please note that the totals in the year budget columns for 2013 to 2015 as well as the total budget for the period 2013-2015 reflect the budgets from the original Table C from the proposal, but now with budget vs. actual for the period including December 2015.

(a) University Medical Center Utrecht (UMCU): The dedicated 3T Philips MRI scanner arrived later than planned, so that the funds dedicated for the scans has not been spent so far. Some of these funds have been used by Division of Neuroscience to pay the baby recruitment team.

(b) Utrecht University (UU): The budget for Toparea Youth (i.e., the strategic theme *Dynamics of Youth*) and the contribution for additional postdocs are received in the first 4 years of the project, whereas actual costs will be spread out over the total 10-year period of the project. Therefore, the numbers in ‘actual’ columns for 2013 to 2015 are given according the proposed budget.

(c) University Medical Center Groningen (UMCG): Up to 2016, one PhD student has been matched by co-funding from the UMCG.

(d) University of Leiden (UL): In September 2015, MRI scans were started. Up to January 2016, 186 MRI scans have been carried out with a total cost of €40,687.50. In the next 3 years, another 1300 scans will be carried out in the current cohorts. This will cost approximately €350,000, which will exceed the proposed matching budget.

(e) University of Leiden (UL): Up to 2016, one PhD student and one postdoc have been matched by co-funding university budgets. Another PhD project will start in spring 2016.

(f) University of Amsterdam (UvA): The co-funding of one PhD student in the first period did not materialize for two reasons. First, it was the intention that the PhD student would work on the WP1 cohort data, but data became available much later than anticipated. Second, the Amsterdam School of Communication Research has received significantly less Government funding in the last 2 years, so that it is no longer possible to fund additional PhD projects.
The column ‘Total Allocated’ reflects the total budget allocated from the 5-year budget per principal investigator (PI). Almost all PIs have allocated most of their 5-year budget, indicating that all work packages have taken off successfully. In some cases, not enough money is left within the PI-budget to appoint an extra PhD student or postdoc. These budgeted funds will be carried over to and merged with the second 5-year period and used to appoint new junior staff.

Table D – Specification of table A (scientific staff) per principal investigator
Up to December 2015

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<tr>
<th>Including December 2015 (€)</th>
<th>Total Budget</th>
<th>5 yr budget</th>
<th>10 yr budget</th>
<th>Total Allocated</th>
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Table E – Specification of Table A (scientific staff) for material costs, personnel costs, and FTE
Up to December 2015

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</table>

Please note that the totals in the columns of ‘Budget’ correspond with the totals in Table A from the original NWO application.

This table reflects the same budgets as Table A (scientific staff), but now specified for material costs, personnel costs, and full-time equivalent (FTE).
Table F – Specification of Table B (investment costs) for material costs, personnel costs, and FTE
Up to December 2015

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<td>1,046,724</td>
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Please note that the totals in the columns of ‘Budget’ correspond with the totals in Table B from the original NWO application.

This table reflects the same budgets as Table B (investment costs), but now specified for material costs, personnel costs, and full-time equivalent (FTE).
**Appendix 2 – Organization and timeline**

### A. Organization (see 3.1, page 14)

#### Main applicant
Prof. dr. C. Kemner

#### Co-applicants
- Prof. dr. D.I. Boomsma
- Prof. dr. S. Durston
- Prof. dr. M. Joëls
- Prof. dr. P.M. Valkenburg
- Prof. dr. M.H. van Ijzendoorn

#### PIs
- 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.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

#### Steering Committee
- Prof. dr. C. Kemner (Program Chair)
- Prof. dr. D.I. Boomsma
- Prof. dr. M. Joëls
- Prof. dr. R.S. Kahn
- Prof. dr. W.H.J. Meeus
- Prof. dr. P.M. Valkenburg
- Prof. dr. M.H. van Ijzendoorn

#### 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  Robert M. and Natalie Reid Dorn Endowed Chair Professor, University of California, Davis, USA
A.L. Bredenoord, PhD  Assistant Professor, University Medical Center Utrecht, Julius Center, Department of PHM, Utrecht, the Netherlands
Prof. dr. B.J. Casey  Director Sackler Institute Developmental Psychobiology, Professor Developmental Psychobiology, Weill Medical College, Cornell University, New York, USA
Prof. dr. M.H. Johnson  Director Center for Brain and Cognitive Development, School of Psychology, Birkbeck University of London, UK
Prof. dr. N. Martin  Professor Genetic Epidemiology, Molecular Epidemiology and Neurogenetics, University of Queensland, Australia
Prof. dr. M.J. Meaney  Scientific Director Ludmer Center for Neuroinformatics and Mental Health, Douglas Mental Health University Institute, Québec, Montreal, Canada
Prof. dr. L. Steinberg  Distinguished University Professor of Psychology, Department of Psychology, Temple University, Philadelphia, USA

Supervisory Board
Prof. dr. W. Raub (Chair)  Dean Social and Behavioral Sciences, Utrecht University
Prof. dr. E.J. Fischer  Interim Dean Social and Behavioral Sciences, University of Amsterdam
Prof. dr. E.J.C. de Geus  Director EMGO Institute for Health and Care Research (VU University Medical Center Amsterdam and VU University Amsterdam)
Prof. dr. V.W.V. Jaddoe  Director Generation-R, Erasmus University Medical Center Rotterdam
Prof. dr. F. Kuipers  Dean University Medical Center Groningen
Prof. dr. F. Miedema  Dean University Medical Center Utrecht
Prof. dr. J.T. Swaab  Dean Social and Behavioral Sciences, Leiden University
Prof. dr. D. Wigboldus  Dean Social and Behavioral Sciences, Radboud University Nijmegen

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

B. Procedures appointments PhD students and postdocs (see 1.1, page 5)
Every application needs to be approved by the WP Leader and the Steering Committee. We set up an application structure encompassing an application form (Appendix 14) and budget specification form. To ensure integration between the four research lines (WPs), the procedure for the appointment of junior staff is both focused on assuring scientific quality of projects (by judgment of the Steering Committee) and on interaction/coherence between different objectives as defined within the WPs (by collaboration between 2 PIs per project).

Cohort representatives receive a fixed amount for the cohorts quarterly. PhD students and postdoc staff appointed on the cohort budget also have to be justified in an application to the Steering Committee (Appendix 14). For the total amount of FTEs within the cohorts, see Appendix 1, Table F.

Finally, PIs contributed to the consortium with additional PhD students, postdocs, and research staff through co-funding budgets, whether or not specified in the original NWO proposal. PhD students and postdocs are also justified to the Steering Committee in an application (Appendix 14).
Consortium Partners

Timeline

- Kick-off symposium: March 2013
  - Brainstorm PI’s
- SAB meeting: May 2013
- Core measurement meeting with all PI’s: May 1
  - Project Start
- Cohort expert meeting: June 2013
- Opening CRC: July 2013
  - CID meeting with all PI’s, PhD-students, postdocs and others interested
  - Visit minister CRC
- Symposium 2015: August 2015
  - Visit minister CRC

Timeline:

- 2013
  - May: Kick-off symposium
  - October: SAB meeting
  - November: Cohort expert meeting
  - January: Core measurement meeting with all PI’s
  - May 1: Project Start
- 2014
  - March: SAB meeting
- 2015
  - April: Opening CRC
  - August: Symposium 2015
  - October: Visit minister CRC
- 2016
  - October: Symposium 2015
  - November: Visit minister CRC
- 2023
Appendix 3 – CID appointed PhD students and postdocs from principal investigator budget

PhD students or postdocs financed by CID through PI-budget, as seen in Realization and budget, Appendix 1, Table A.

<table>
<thead>
<tr>
<th>CID appointed PhD students and postdocs from PI-budget</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WP1</strong></td>
</tr>
<tr>
<td><strong>Dienke J. Bos</strong></td>
</tr>
<tr>
<td>Connected and in control</td>
</tr>
<tr>
<td>Durston, Crone; UMC Utrecht</td>
</tr>
<tr>
<td><strong>Ine Beijens</strong></td>
</tr>
<tr>
<td>The effect of media on ADHD-symptoms</td>
</tr>
<tr>
<td>Valkenburg, Dekovic; University of Amsterdam</td>
</tr>
<tr>
<td><strong>Fraukje Coopmans</strong></td>
</tr>
<tr>
<td>Developmental trajectory of the human connectome in health and disease</td>
</tr>
<tr>
<td>Kahn, Crone; UMC Utrecht</td>
</tr>
<tr>
<td><strong>Karin Fikkers</strong></td>
</tr>
<tr>
<td>The effects of media violence exposure on aggression: A differential susceptibility perspective</td>
</tr>
<tr>
<td>Valkenburg, Dekovic, University of Amsterdam</td>
</tr>
<tr>
<td><strong>Sanne B. Geeraerts</strong></td>
</tr>
<tr>
<td>Development of infant self-regulation within the early caregiver relationship: A cascade model</td>
</tr>
<tr>
<td>Dekovic, Kemner; UU Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td><strong>Roy S. Hessels</strong></td>
</tr>
<tr>
<td>The effects of social stimulation/interaction on perceptual and social development</td>
</tr>
<tr>
<td>Kemner, Hoijtink; UU Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td><strong>Jalmar Teeuw</strong></td>
</tr>
<tr>
<td>Genetic and environmental influences on development of structural and functional brain connectivity</td>
</tr>
<tr>
<td>Hulshoff Pol, Boomsma; UMC Utrecht</td>
</tr>
<tr>
<td><strong>Hannah de Mulder</strong></td>
</tr>
<tr>
<td>The power of stories: exploring the effects of (self) narrative on the development of social competence and behavioral control</td>
</tr>
<tr>
<td>Van Berkum, Valkenburg; UU Faculty of Humanities</td>
</tr>
<tr>
<td><strong>Margot Peeters</strong></td>
</tr>
<tr>
<td>Behavioral control and reward sensitivity as predictors of adolescents’ risk behaviors</td>
</tr>
<tr>
<td>Vollebergh, Oldehinkel; UU Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td><strong>Bauke van der Velde</strong></td>
</tr>
<tr>
<td>Connectivity of the social brain</td>
</tr>
<tr>
<td>Kemner, Kahn; UU Faculty of Social and Behavioral Sciences</td>
</tr>
</tbody>
</table>

*The PhD is financed for 25% from PI-budget Kemner (Appendix 1 Table A), for 25% from co-funding budget from the UMCU (Kahn, Appendix 1 Table C, Appendix 5) and for 50% from cohort budget (Appendix 1 Table B, Appendix 4)*
### WP2

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
<th>Institution</th>
<th>Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Michele Achterberg</td>
<td>Social aggression regulation in childhood and emerging adolescence</td>
<td>Crone, Bakermans-Kranenburg; UL Faculty of Social and Behavioral Sciences</td>
<td>Sep/14 – Sep/19</td>
</tr>
<tr>
<td>Rani Damsteeg</td>
<td>Intervention effects of video/feedback on parenting and social competence in preschoolers: The role of genetic polymorphisms, temperament and tympanic membrane temperature</td>
<td>Bakermans-Kranenburg, Crone; UL Faculty of Social and Behavioral Sciences</td>
<td>May/13 – Mar/18</td>
</tr>
<tr>
<td>Mara van der Meulen</td>
<td>Social aggression regulation in childhood and emerging adolescence</td>
<td>Engels, Crone, Van IJzendoorn; UL Faculty of Social and Behavioral Sciences</td>
<td>Jan/15 – Jan/20</td>
</tr>
<tr>
<td>Claudia I. Vrijhof</td>
<td>Intervention effects of video-feedback on social competence and behavior control in preschoolers: the mediating role of parenting and physiological regulation</td>
<td>Van IJzendoorn, Bakermans-Kranenburg, Crone; UL Faculty of Social and Behavioral Sciences</td>
<td>Nov/13 – Nov/17</td>
</tr>
</tbody>
</table>

### WP3

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
<th>Institution</th>
<th>Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andrik Becht</td>
<td>Why some adolescents thrive and others don’t: The role of uncertainty dynamics</td>
<td>Meeus, Vollebergh; UU Faculty of Social and Behavioral Sciences</td>
<td>Sep/14 – Sep/18</td>
</tr>
<tr>
<td>Tina Kretschmer</td>
<td>Examining the complex interplay between relationship experiences and individual factors to understand adolescent development</td>
<td>Oldehinkel, Meeus, Dekovic; UMC Groningen</td>
<td>Oct/13 – Nov/15</td>
</tr>
<tr>
<td>Odilia M. Laceulle</td>
<td>Investigating developmental models of psychological distress: transactional processes and explanatory models of individual differences</td>
<td>Ormel, Meeus, Van IJzendoorn; UMC Groningen</td>
<td>Oct/13 – Aug/18</td>
</tr>
<tr>
<td>Stefanie A. Nelemans</td>
<td>Development of anxiety symptoms in adolescence and early adulthood: over/time links with biological, psychological, and social factors</td>
<td>Meeus, Oldehinkel; UU Faculty of Social and Behavioral Sciences</td>
<td>Sep/14 – Sep/17</td>
</tr>
<tr>
<td>Alexander Neumann</td>
<td>The epigenetics of intergenerational transmission</td>
<td>Verhulst, Oldehinkel, van IJzendoorn; Rotterdam Erasmus MC</td>
<td>Aug/14 – Aug/18</td>
</tr>
<tr>
<td>Sabine Veldkamp</td>
<td>Intergenerational transmission of reading and cognitive skills</td>
<td>Boomsma, Van Berkum; VU University Amsterdam</td>
<td>May/15 – May/19</td>
</tr>
<tr>
<td>Eveline de Zeeuw</td>
<td>Longitudinal development and intergeneration transmission of psychopathology versus wellbeing</td>
<td>Boomsma, Oldehinkel; VU University Amsterdam</td>
<td>Dec/14 – Dec/17</td>
</tr>
<tr>
<td>WP4</td>
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</tr>
<tr>
<td><strong>Gabriël J.L. Beckers</strong>  &lt;br&gt; <em>A neurogenetic analysis of birdsong learning as a model for infant development</em>  &lt;br&gt; Bolhuis, Joëls; UU Faculty of Social and Behavioral Sciences</td>
<td>Assistant professor  &lt;br&gt; Oct/14 – Oct/17</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sita M. ter Haar</strong>  &lt;br&gt; <em>A neurogenetic analysis of birdsong learning as a model for infant development</em>  &lt;br&gt; Bolhuis, Joëls; UU Faculty of Social and Behavioral Sciences</td>
<td>Postdoc  &lt;br&gt; Mar/15 – Jan/16</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sofia Kanatsou</strong>  &lt;br&gt; <em>Environmental influences on brain development: rodent models</em>  &lt;br&gt; Hoijtink, Joëls; UU Faculty of Social and Behavioral Sciences</td>
<td>Postdoc  &lt;br&gt; Aug/15 – Apr/16</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Jiska Kentrop</strong>  &lt;br&gt; <em>Maternal care as predictor of later life success: possibilities for intervention</em>  &lt;br&gt; Joëls, Bakermans-Kranenburg; UMC Utrecht, UL</td>
<td>PhD student  &lt;br&gt; Jul/14 – Jul/18</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Manila Loi</strong>  &lt;br&gt; <em>Intervention at puberty after early life adversity</em>  &lt;br&gt; Joëls, van IJzendoorn; UMC Utrecht</td>
<td>PhD student  &lt;br&gt; Sep/13 – Sep/15</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Carien Mol</strong>  &lt;br&gt; <em>Twitter evolution: Comparative linguistics of birdsong and child language acquisition</em>  &lt;br&gt; Bolhuis, Kemner; UU Faculty of Social and Behavioral Sciences  &lt;br&gt; <em>The PhD is financed for 67% from PI-budget Bolhuis (Appendix 1 Table A), and for 33% from co-funding budget from the UU (Dynamics of Youth, Appendix 6)</em></td>
<td>PhD student  &lt;br&gt; Oct/15 – Jun/18</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mariëlle A.J. Zondervan-Zwijnenburg</strong>  &lt;br&gt; <em>Formalization and evaluation of prior knowledge based on prior/posterior predictive inference</em>  &lt;br&gt; Hoijtink, van Berkum; UU Faculty of Social and Behavioral Sciences</td>
<td>PhD student  &lt;br&gt; Jul/14 – Jun/18</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Appendix 4 – CID PhD students, postdocs or researchers from cohort budget**

PhD students, postdocs or researchers financed from CID cohort budget, as seen in **Realization and budget, Appendix 1, Table B.**

<table>
<thead>
<tr>
<th>CID PhD students, postdocs or senior researchers from cohort budget</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WP1</strong></td>
</tr>
<tr>
<td><strong>Stefanos Mastrotheodoros</strong></td>
</tr>
<tr>
<td>Branje, Dekovic; UU Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td>PhD student</td>
</tr>
<tr>
<td>Dec/15 – Dec/19</td>
</tr>
<tr>
<td><strong>Dr. N. Charlotte Onland-Moret</strong></td>
</tr>
<tr>
<td>UMC Utrecht</td>
</tr>
<tr>
<td>Associate professor</td>
</tr>
<tr>
<td><strong>Soundry Staats</strong></td>
</tr>
<tr>
<td>Dekovic, Huijding; UU Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td>PhD student</td>
</tr>
<tr>
<td>Mar/16 – Mar/20</td>
</tr>
<tr>
<td><strong>Bauke van der Velde</strong></td>
</tr>
<tr>
<td><em>Connectivity of the social brain</em></td>
</tr>
<tr>
<td>Kemner, Kahn; UU Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td><em>The PhD is financed for 25% from PI-budget Kemner (Appendix 1 Table A, Appendix 3), for 25% from co-funding budget from the UMCU (Kahn, Appendix 1 Table C, Appendix 5) and for 50% from cohort budget (Appendix 1 Table B)</em></td>
</tr>
<tr>
<td>PhD student</td>
</tr>
<tr>
<td>Dec/15 – Nov/19</td>
</tr>
<tr>
<td><strong>WP2</strong></td>
</tr>
<tr>
<td><strong>Bianca G. van den Bulk</strong></td>
</tr>
<tr>
<td>UL Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td>Postdoc</td>
</tr>
<tr>
<td>Aug/14 – Jan/23</td>
</tr>
<tr>
<td><strong>WP4</strong></td>
</tr>
<tr>
<td><strong>Angela Sarabdjitsingh</strong></td>
</tr>
<tr>
<td>UMC Utrecht</td>
</tr>
<tr>
<td>Postdoc</td>
</tr>
<tr>
<td>Nov/13 – Feb/18</td>
</tr>
<tr>
<td><em>The postdoc is financed for 14% from cohort budget (Appendix 1 Table B), and for 86% from co-funding budget (VENI grant, Appendix 6)</em></td>
</tr>
<tr>
<td><strong>Rixt van der Veen</strong></td>
</tr>
<tr>
<td>UMC Utrecht, UL Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td>Postdoc</td>
</tr>
<tr>
<td>Oct/13 – Aug/14</td>
</tr>
<tr>
<td><em>The postdoc is after this period financed from co-funding budget from Leiden University (Appendix 6)</em></td>
</tr>
<tr>
<td><strong>Rinke Klein-Entink</strong></td>
</tr>
<tr>
<td>UU Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td>Senior Research Consultant</td>
</tr>
<tr>
<td>Sept/14 – Aug/18</td>
</tr>
</tbody>
</table>
Appendix 5 – CID researchers from co-funding budgets conform NWO application

PhD students, postdocs or researchers not financed by CID, but directly from the government, from the government through a funding allocation agency or by contracts with third parties and specified within the original NWO application as matching, as can be recognized from Realization and budget, Appendix 1 Table C.

<table>
<thead>
<tr>
<th>CID researchers from co-funding budgets conform NWO application</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WP1</strong></td>
</tr>
<tr>
<td><strong>Marieke E.W. Albers</strong></td>
</tr>
<tr>
<td>UMC Utrecht, Contribution of strategic budget year 1 to 5</td>
</tr>
<tr>
<td><strong>Bauke van der Velde</strong></td>
</tr>
<tr>
<td><em>Connectivity of the social brain</em></td>
</tr>
<tr>
<td>UMC Utrecht, Contribution of strategic budget year 1 to 5</td>
</tr>
<tr>
<td><em>The PhD is financed for 25% from PI-budget Kemner (Appendix 1 Table A, Appendix 3), for 25% from co-funding budget from the UMCU (Kahn, Appendix 1 Table C) and for 50% from cohort budget (Appendix 1 Table B, Appendix 4)</em></td>
</tr>
<tr>
<td><strong>Janna Cousijn</strong></td>
</tr>
<tr>
<td>UU Faculty of Social and Behavioral Sciences, Contribution FSW for additional postdocs</td>
</tr>
<tr>
<td><strong>Caroline Junge</strong></td>
</tr>
<tr>
<td>UU Faculty of Social and Behavioral Sciences, Contribution FSW for additional postdocs</td>
</tr>
<tr>
<td><strong>WP2</strong></td>
</tr>
<tr>
<td><strong>Laura Kolijn</strong></td>
</tr>
<tr>
<td>UL Faculty of Social and Behavioral Sciences, Additional PhDs</td>
</tr>
<tr>
<td><strong>WP3</strong></td>
</tr>
<tr>
<td><strong>Annelene Bloemen</strong></td>
</tr>
<tr>
<td><em>Determinants and consequences of (low) cognitive control</em></td>
</tr>
<tr>
<td>UMC Groningen, Additional PhDs infrastructure TRAILS and intended PhDs</td>
</tr>
</tbody>
</table>

PhD student      Feb/15 – Feb/19
PhD student      Dec/15 – Nov/19
Postdoc          Jan/14 – Nov/15
Postdoc/Assistant professor    Jun/14 – present
PhD student      Starting spring 2016
PhD student      Dec/14 – Dec/17
Appendix 6 – Other CID researchers from co-funding budgets

PhD students, postdocs or researchers not financed by CID, but directly from the government, from the government through a funding allocation agency or by contracts with third parties and not specified within the original NWO application as matching, but contributing to the consortium.

<table>
<thead>
<tr>
<th>Other CID researchers from co-funding budgets</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WP1</strong></td>
</tr>
<tr>
<td><strong>Carlijn van den Boomen</strong></td>
</tr>
<tr>
<td>UU Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td><strong>Jolien van der Graaf</strong></td>
</tr>
<tr>
<td>UU Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td><strong>Marinka M.G. Koenis</strong></td>
</tr>
<tr>
<td>UMC Utrecht</td>
</tr>
<tr>
<td><strong>Renske Koordeman</strong></td>
</tr>
<tr>
<td>UU Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td><strong>Nicolette Munsters</strong></td>
</tr>
<tr>
<td>UU Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td><strong>Matthijs Vink</strong></td>
</tr>
<tr>
<td>UU Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td><strong>WP2</strong></td>
</tr>
<tr>
<td><strong>J. E. (Elisabeth) Bilo</strong></td>
</tr>
<tr>
<td>UL Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td><strong>Dr. Szilvia Biro</strong></td>
</tr>
<tr>
<td>UL Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td><strong>Dr. Anna C.K. van Duijvenvoorde</strong></td>
</tr>
<tr>
<td>UL Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td><strong>Dr. Saskia Euser</strong></td>
</tr>
<tr>
<td>UL Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td><strong>Dr. Renske Huffmeijer</strong></td>
</tr>
<tr>
<td>UL Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td><strong>Dr. Nikolaus Steinbeis</strong></td>
</tr>
<tr>
<td>UL Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td><strong>Rixt van der Veen</strong></td>
</tr>
<tr>
<td>UMC Utrecht, UL Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td><em>The postdoc was first financed from cohort budget from WP4 (Appendix 4)</em></td>
</tr>
<tr>
<td><strong>Ilse C. van Wijk</strong></td>
</tr>
<tr>
<td>UL Faculty of Social and Behavioral Sciences, Additional PhDs</td>
</tr>
<tr>
<td><strong>WP3</strong></td>
</tr>
<tr>
<td><strong>Dr. E. van den Berg</strong></td>
</tr>
<tr>
<td>VU University Amsterdam</td>
</tr>
<tr>
<td>WP4</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Yasin Altinisik</strong></td>
</tr>
<tr>
<td>UU Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td><strong>PhD student</strong></td>
</tr>
<tr>
<td>Mar/14 – Mar/18</td>
</tr>
<tr>
<td><strong>Ruth Damsteegt</strong></td>
</tr>
<tr>
<td>UMC Utrecht</td>
</tr>
<tr>
<td><strong>Research analyst</strong></td>
</tr>
<tr>
<td>Oct/15 – Oct/16</td>
</tr>
<tr>
<td><strong>Nienke Derks</strong></td>
</tr>
<tr>
<td>UMC Utrecht</td>
</tr>
<tr>
<td><strong>PhD student</strong></td>
</tr>
<tr>
<td>Jun/14 – Jun/18</td>
</tr>
<tr>
<td><strong>Carien Mol</strong></td>
</tr>
<tr>
<td>Twitter evolution: <em>Comparative linguistics of birdsong and child language acquisition</em> Bolhuis, Kemner; UU Faculty of Social and Behavioral Sciences</td>
</tr>
<tr>
<td>The PhD is financed for 67% from PI-budget Bolhuis (Appendix 1 Table A, Appendix 3), and for 33% from co-funding budget from the UU (Dynamics of Youth)</td>
</tr>
<tr>
<td><strong>PhD student</strong></td>
</tr>
<tr>
<td>Oct/15 – Jun/18</td>
</tr>
<tr>
<td><strong>Angela Sarabdjitsingh</strong></td>
</tr>
<tr>
<td>UMC Utrecht</td>
</tr>
<tr>
<td><strong>Postdoc</strong></td>
</tr>
<tr>
<td>Nov/13 – Feb/18</td>
</tr>
</tbody>
</table>
Appendix 7 – Examples interaction & coherence and embedding

A. Examples of interaction and coherence between the lines of research (see 2.2, page 12)

**WP1** is collaborating closely with WP2 in its research on the development of connectivity. Cooperation and complementarity with WP3 exists with NTR in its research on (epi)genetics and brain development in a twin model, with RADAR in its research on parenting during adolescence and young adulthood, and with TRAILS in its research on the development of parenting and its role in adolescent adaption. Furthermore, WP1 is collaborating with WP4 in the predictive Bayesian analysis of relevant cohort results and in a project to study social interaction in a hybrid setting, where a live setting of two people interacting is mimicked, under controlled laboratory conditions. As this is a novel method of studying social interaction, there are few tools available to analyze such data, so WP1 and WP4 are developing a tailored statistical tool.

**WP2** has a close collaboration with WP3 and WP4. Generation-R and L-CID are collaborating in epigenetic and genetic-environment interaction studies, for example, in the analysis of the psychometrics of cortisol levels in hair samples collected in the Generation-R study, and in the analysis of structural MRI findings in Generation-R children in relation to parental sensitivity.

**WP3**: NTR is collaborating with L-CID in the application of Genome-wide Complex Trait Analysis (GCTA) for attention and aggression issues, using a combined dataset from Generation-R and NTR in order to obtain a lower bound estimate of Single Nucleotide Polymorphism (SNP) heritability. Similarly, GCTA is currently being used in the analysis of pro-sociality characteristics. WP3 is collaborating closely with WP1 in its research on adolescent identity and drug use, as well as on victimization. TRAILS (WP3) is collaborating with WP4 in its research into the cumulative stress and mismatch hypotheses.

**WP4** is participating in several projects with WP1; for example, the role of epigenetics in early adversity, the relation between exposure to fiction and social competence, the use of theory-based evaluation in the context of eye-tracking data, and the development of language. WP4 is also collaborating with L-CID in its studies of the influence of parenting on cognitive development and the role of genes in susceptibility.

B. Examples embedding and collaboration (see 3.4, page 16)

*For every work package, the institutional embedding is described. Furthermore, for every PI a maximum of 2 national and 2 international examples of cooperation are given.*

**WP1**:  
**Institutional embedding:** Within WP1 there is overlap with the ‘Brain’ strategic research program of the UMC Utrecht. Recently, there have been explorative discussions about the possibilities of cooperation between WP1, *Dynamics of Youth*, the strategic research program *Child Health* of the UMC Utrecht, the Julius Center, the Wilhelmina Children’s Hospital, and the Princess Maxima Center. WP1 also has plans for collaborative studies with the University of Applied Sciences.  
**National embedding:** WP1 is collaborating with the Departments of Media and Culture, Education & Pedagogy, Utrecht University, and the Utrecht Institute of Linguistics in its research on, for example, communication skills as a predictor of behavioral problems in children and adolescents. It is also collaborating with the Erasmus University Medical Center, Rotterdam, in the ongoing large-scale longitudinal study *Flemish Study on Parenting, Personality, and Development* (FSPPD), in the ‘BBMRI-NL2.0 Roadmap for Large-Scale Research Facilities’, and in the NL-Biobank Research Facility Neuroimaging. It is also collaborating with the Radboud University Medical Center, Nijmegen, with a focus on infant research and the *Enhancing Neuroimaging Genetics through Meta Analysis* (ENIGMA) initiatives for ADHD and autism.  
**International embedding:** At an international level, WP1 is collaborating with the ENIGMA Consortium for imaging-genetics studies (Keck University, Los Angeles, USA). Kirby Deater-Deckard (Virginia Tech, USA) and Bruce Ellis (University of Arizona, USA) – experts on the development of self-regulation and differential susceptibility, respectively – both visited the Department of Clinical Child and Family Studies (UU, Faculty of...
Social and Behavioral Sciences) for a few months, financed by NWO visitor travel grants. Furthermore, WP1 is collaborating with Ohio State University, Nanyang Technological University Singapore, and with the European FP7 TACTICS consortium with, among others, the Institute of Psychiatry, London (UK), the Institute of Psychiatry, Mannheim (Germany), the Institute of Psychiatry, Nijmegen, and the Karonlinska, Institute Stockholm (Sweden).

WP2:
**Institutional embedding:** L-CID is part of the Leiden University profile area ‘Health, Prevention and the Human Life Cycle’, and the neurobiological projects of L-CID are also part of the Leiden Institute for Brain and Cognition (LIBC).

**National embedding:** At a national level, L-CID has cooperative links with Generation-R (Erasmus University Medical Center Rotterdam), Brain Center Rudolf Magnus (Utrecht University), NTR (VU University Amsterdam), and Trimbos Institute (Utrecht).

**International embedding:** L-CID is collaborating with the Avon Longitudinal Study of Parents and Children (ALSPAC) in the UK in research into the genetics of parenting and child development, and with Mercy Pregnancy and Emotional Well-being Study (MPEWS) in Melbourne (Australia) in research on stress-related aspects of parenting. Its imaging studies are embedded in a large network, e.g. organized in the Jacobs Foundation Network Initiative on prosocial development. There are collaborative links with the University of Illinois, the University of Oregon, and Harvard University for research into methods for longitudinal imaging analysis in adolescents. Finally, there is ongoing collaboration with the Youth Development Lab at UC Berkeley (USA).

WP3:
**Institutional embedding:** Generation-R is embedded in five different research groups of the Erasmus Medical Center Rotterdam: ‘Mother & Child’, ‘Behavior & Cognition’, ‘Asthma & Atopy’, ‘Diseases in childhood’, and ‘Health & Healthcare’. NTR was founded on February 1 1987 at the Free University Amsterdam and is tightly embedded in this institute. TRAILS is a joint project of the University of Groningen and the Erasmus Medical Center Rotterdam. Other participating universities include Radboud University Nijmegen Medical Center, and Utrecht University. TRAILS is embedded in the departments/faculties of Psychiatry, Sociology, Health Science, Child & Adolescent Psychiatry, and Social Sciences. RADAR is embedded at long-term research lines of Utrecht University and the Free University Amsterdam.

**National embedding:** NTR is collaborating with the VU University Amsterdam in its research on gene-environment interactions. TRAILS maintains close collaborative links with its consortium members, who represent institutes across the Netherlands.

**International embedding:** At an international level, NTR is collaborating with the University of Oxford (UK) in its research on literacy development and is part of a newly established genome-wide association consortium on literacy, named GenLang. RADAR is collaborating with Pittsburgh University (USA) in its research on adolescent delinquency, and with Leuven University (Belgium) in its research on gene-environment interactions. TRAILS has collaborative links with, among others, the University of Arizona (USA) for its research on mechanisms involved in adaptive calibration, and with the University of Denver (USA) for its research on positive affect.

WP4:
**Institutional embedding:** WP4 is embedded in the research program ‘Translational Research’ of the Brain Center Rudolf Magnus of the UMC Utrecht. Furthermore, the research of WP4 is part of Neuroscience & Cognition Utrecht (NCU); its replication studies for TRAILS are carried out within existing research programs of the University of Groningen.

**National embedding:** At a national level, WP4 has collaborative links with Utrecht University, the University of Amsterdam, and Tilburg University.

**International embedding:** WP4 is collaborating closely with the Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig (Germany), the British Heart Foundation and the Department of Neuroendocrinology of Edinburgh University (UK), and the Department of Data Analysis of Ghent University (Belgium).
Appendix 8 – SWOT analysis (see 3.8, page 18)

Strengths
S1 CID community: broad expertise and enthusiasm
CID brings together twenty top researchers (PIs) from several disciplines based at eight institutes. The stipulation that each PhD student or postdoc must be supervised by at least two PIs from different disciplines has generated a multidisciplinary research community. The four work packages of CID are interrelated and two new cohorts have been developed and existing cohorts integrated for joint use (see also below). Lastly, a program of well-attended meetings for CID participants has been set up (see 2.3 and Appendix 2). In the relatively short time since the start of CID, this approach has led to interdisciplinary cooperation that reflects the envisaged integration of social sciences and substrate-driven neurobiological approaches. Importantly, this research community provides a stimulating environment for CID-funded PhD students and postdocs (see also S5).

S2 Joint instruments: unique cohorts
Working on longitudinal cohorts is essential to the aim of CID, to understand the many factors that determine individual development. CID research is therefore dependent on data obtained from the new cohorts and existing cohorts. Recruitment to the two new cohorts has started — a longitudinal cohort based in Utrecht (YOUth) and an intervention cohort based in Leiden (L-CID). In addition, four existing cohorts are available for data collection: TRAILS (Groningen), Generation-R (Rotterdam), RADAR (Utrecht), and NTR (Amsterdam). The scope and size of the resulting datasets are unique, both nationally and internationally. The same subsets of specific instruments assessing social competence and behavioral control are used in all cohorts, and other instruments are used in more than one cohort, which facilitates the combination and integration of data.

S3 Organization: transparent and efficient
The organization of the CID is transparent and effective. It is based on a Consortium Agreement between participants and well-developed structures for meetings, documentation, administration, and finance. The Financial Office (manager and controller) has set up an appropriate financial structure (control sheet, forms) and has visited the financial staff of all parties to explain procedures and structures. The organizational structure of the consortium can be found in 3.1 and Appendix 2.

S4 National and international embedding
The organization of the consortium is well embedded at the coordinator’s site, in connection with the Dynamics of Youth program, which is one of the four strategic themes of Utrecht University in the next 5 years (at least). CID also shares the infrastructure of the Child Research Center. Our collaborative efforts, community building, study cohorts, and curricular environment reflect the embedding of the consortium at different levels. The broad integration of top researchers, universities, university medical centers, landmark cohort studies, and scholarly fields in CID is unprecedented in Dutch academia and beyond. It is an exceptionally powerful combination and confers a critical mass and versatility that will give it a leading position in international child development research in the future.

S5 Well-developed talent management and strong investments in junior scientists
The best way to guarantee a long-term multidisciplinary approach to youth research and care is to set up a curriculum that allows the next generation of researchers to thrive and develop their talents to the fullest. We designed a curricular environment in which our Master’s and PhD students can obtain the right mix of deep disciplinary expertise and wider interdisciplinary outlook, based on existing graduate programs plus additional specific facilities relevant to our CID junior scientists (see 3.5 Talent management).

Opportunities
O1 Science is changing
Academia faces serious challenges – there is an increasing demand for scientists to find solutions for major societal problems, as well as the need for a greater integration of knowledge acquired from different
traditions, in order to stimulate scientific progress. To address these issues, CID is working on the development of our future capital, children (see also O2 below), by stimulating the integration of knowledge and the cross-discipline use of technology and approaches to research. Also, PIs collaborate in large cohort studies that address the current problems in replicability. Being at the forefront of multidisciplinary research will boost the career opportunities of participating (young) researchers.

**O2 Funding possibilities**

In spite of the almost unprecedented level of prosperity in today’s Western society, many children fail to thrive and are at risk of developing behavioral, emotional, and cognitive problems. The themes of CID are of great societal relevance, and since funding to science is becoming increasingly dependent on whether it addresses societal issues, CID is in a good position to obtain funding. For example, CID themes are consistent with many questions on the Dutch National Science Agenda (*Nationale WetenschapsAgenda, NWA*). Internationally, the European Commission launched its Horizon2020 program of funding for 2016-2017 in September 2015, again with several relevant calls. The interdisciplinary teams of CID can and will actively participate in calls for research proposals.

**Weaknesses**

**W1 Timing: starting-up cohorts**

Starting-up the cohorts took more time than foreseen (see also Appendix 1, Table B), mainly because of the long procedures for getting Institutional Review Board approval, both in Leiden and Utrecht. In addition, in Utrecht we were asked to perform several time-consuming pilot studies. Moreover, the delivery and setting up of a dedicated MRI scanner was delayed. While these problems have been resolved, and no further delays are expected, they have affected our planning, as not all children can be tested in the foreseen timeframe. We expect that the delay in data collection in TRAILS, caused by logistic issues, will be eliminated in the coming years.

**W2 Financing of cohorts**

Setting up two new cohorts in Utrecht and Leiden and integrating major existing cohorts are costly endeavors – the substantial funding through CID has allowed us to create these unique instruments. However, it is important that we obtain additional funding to be able to continue the cohorts after Gravitation funding has ended. Also, any delays in setting up the cohorts (see W1) need to be compensated for. Several initiatives to obtain extra funding have been undertaken. For example, WP1 is exploring participation in initiatives (H2020, NWO infrastructure) to align the YOUth cohort with other datasets. Also, additional funding at Utrecht through its strategic theme *Dynamics of Youth* will allow us to expand the number of instruments used in the cohort studies. A positive factor is international recognition of the importance of large-scale projects and big data, and we expect that funding plans for our cohorts will profit from these developments (see also O2).

**Threats**

**T1 Governmental regulations for data handling**

There is increasing governmental attention on the way data are obtained, stored, and shared, and regulations related to this are becoming increasingly restrictive (see also W1). This is in part because of the value placed on subject anonymity and privacy, but is also in part inspired by the negative reports in the media concerning the replicability of biomedical and social sciences studies (at least partly due to small sample sizes, for which our large cohort studies are a remedy). As a result, strategies for data storage and accessibility, but also big data approaches, are becoming increasingly important, not only in the natural and biomedical sciences but also in social and behavioral sciences. The protocols for all the cohort studies were approved by relevant Institutional Review Boards and/or Medical Ethics Committees before participant recruitment started. They all conform to the requirements of the scope of the Medical Research Involving Human Subjects Act (WMO). The protocols for the Utrecht cohort and the related data management are included in Appendix 12. These protocols were written in close collaboration with the Department of Information and Technology Services (ITS) of Utrecht University and are available to other cohort studies. We will carefully monitor any developments in the regulations regarding data handling, to ensure that we continue to fulfill requirements.
Appendix 9 – Examples knowledge utilization and societal relevant activities

A. Examples knowledge utilization (see 5.1, page 19)
For every PI a maximum of 3 examples of knowledge utilization are given.

WP1 has a longstanding cooperation with The Netherlands Youth Institute (Nederlands Jeugdinstituut), the national institute for disseminating knowledge on children and youth matters. In addition to publishing the results in journals, magazines, and websites aimed at clinicians and parents of children, at the end of the project we will also organize a workshop during the annual congress for professionals in youth care, Youth in Research. Furthermore, knowledge is utilized within committees, e.g. the National Initiative Brain & Cognition (Nationale Initiatief Hersenen & Cognitie, NIHC), program committee Education, to integrate developmental brain science with education and research. One example of science communication for WP1 is the research of our CID postdoc Karin Fikkers, which was recently highlighted on NPO Radio 1 and by the NOS (http://nos.nl/artikel/2088530-games-leiden-niet-per-definitie-tot-meer-agressie.html).

WP2 contributes to the Child and Family Blog of the University of Cambridge. Furthermore, there are video blogs (www.brainanddevelopmentlab.nl/index.php/video), and there was the co-organization of the Braintime Festival in Corpus (http://www.universiteitleiden.nl/nieuws/2016/02/feest-voor-het-puberbrein).

WP3 communicates study findings through Twitter (NTR and TRAILS; NTR maintains separate Twitter accounts for science and for participants), study websites, and newsletters for respondents (NTR, RADAR, TRAILS; NTR newsletters may be downloaded from the website). NTR and TRAILS have also Facebook pages.

WP4 provides educational modules for professionals in the teaching world. Furthermore, they published several interviews in national magazines, newspapers, online, on television, and in radio programs. They maintain the website informative-hypotheses.sites.uu.nl, containing free software that can be used by researchers interested in theory based data evaluation and/or the evaluation of replication studies. The website contains an overview of applied papers of researchers that used and published with the approaches from the website.

B. Examples societal relevant activities (see 5.1, page 19)
For every PI a maximum of 5 examples of societal relevant activities are given.

<table>
<thead>
<tr>
<th>Examples of societal relevant activities by CID PIs</th>
</tr>
</thead>
</table>

Dekovic, M.: member of the Accreditation Committee for Behavioral Interventions that helps the Ministry of Security and Justice to develop and implement a high quality program to prevent/reduce recidivism.


Hojitink, H.: Preconference workshop on Informative Hypotheses. IRT meeting at the University of Twente, 2013.


Joëls, M. and de Krom, M.: Translational approaches in developmental disorders and schizophrenia. Course for PhD students (including 5 plenary lectures accessible to a broad audience), Utrecht, May – June 2015.


Every year the Leiden Institute for Brain and Cognition (LIBC) organizes a ‘publieksdag’ (a day-long symposium open to the general public) to which several L-CID members have been contributing. The most recent Publieksdag attracted 800 enthusiastic participants from the general public (http://www.nieuws.leidenuniv.nl/nieuws-2015/800-mensen-kijken-in-de-wereld-van-het-sociale-brein.html).
### C. Study websites

<table>
<thead>
<tr>
<th>Study</th>
<th>Website</th>
</tr>
</thead>
<tbody>
<tr>
<td>YOUth cohort</td>
<td><a href="http://www.youthonderzoek.nl">www.youthonderzoek.nl</a></td>
</tr>
<tr>
<td>Child Research Center</td>
<td><a href="http://www.kinderkenniscentrum.nl">www.kinderkenniscentrum.nl</a></td>
</tr>
<tr>
<td>Dynamics of Youth</td>
<td><a href="http://www.uu.nl/doy">www.uu.nl/doy</a></td>
</tr>
<tr>
<td>L-CID cohort</td>
<td><a href="http://www.samen-uniek.com">www.samen-uniek.com</a></td>
</tr>
<tr>
<td>Generation-R</td>
<td><a href="http://www.generationr.nl">www.generationr.nl</a></td>
</tr>
<tr>
<td>NTR</td>
<td><a href="http://www.tweelingenregister.org">www.tweelingenregister.org</a></td>
</tr>
<tr>
<td>RADAR</td>
<td><a href="http://www.uu.nl/onderzoek/radar">www.uu.nl/onderzoek/radar</a></td>
</tr>
<tr>
<td>TRAILS</td>
<td><a href="http://www.trails.nl">www.trails.nl</a></td>
</tr>
</tbody>
</table>
Appendix 10 – CID publications and PhD student and postdoc activities

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

A. Joint key publications (see 2.2, page 12)

Authors indicated in **bold** are CID researchers, with a specification of their work package (WP).

<table>
<thead>
<tr>
<th>Joint key publications consortium (11)</th>
</tr>
</thead>
</table>
### B. Total CID publications (see 2.2, page 12)

Authors indicated in **bold** are CID researchers. Authors indicated in **bold orange** are CID PhD students or postdocs.

#### Other publications within consortium (67)

<table>
<thead>
<tr>
<th>#</th>
<th>Authors</th>
<th>Title</th>
<th>Year</th>
<th>DOI/URL</th>
</tr>
</thead>
</table>


C. PhD student and postdoc activities (see 2.2, page 12)
See below a list of the most important PhD student and postdoc activities (max. 3 examples per person)

<table>
<thead>
<tr>
<th>CID PhD student and postdoc activities</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beckers, G.</strong> (2015). Invited visit to Max Planck Institute for Brain Research (Frankfurt, DE), Laurent department, for establishing cooperation in sleep research.</td>
</tr>
<tr>
<td>Reference</td>
</tr>
<tr>
<td>--------------------------------------------------------------------------</td>
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<tr>
<td><strong>De Mulder, H., Bergstra, M., Coopmans, P. (2014, July).</strong> ‘I know this is a mit!’: Children’s ability to use speaker certainty in learning novel words. Poster presentation XIII International Congress for the Study of Child Language (IASCL), Amsterdam, The Netherlands.</td>
</tr>
<tr>
<td><strong>Hessels, R. (2015).</strong> Qualitative tests of remote eye-tracker recovery and performance during head rotation. Poster presentation at the European Conference of Eye Movements (ECEM), Vienna, Austria.</td>
</tr>
<tr>
<td><strong>Junge, C. (2015).</strong> Presenter at the course Longitudinal data analysis: current best methods (5-day advanced stats course), Faculty of Social and Behavioral Sciences, Utrecht University, The Netherlands.</td>
</tr>
<tr>
<td>Author</td>
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<tr>
<td>Kentrop, J.</td>
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<tr>
<td>Name</td>
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Appendix 11 – CID PhD student and postdoc projects (progress reports)

Within CID several close-knitted projects focus on identifying critical factors and their interplay during development. CID PhD and postdoc projects study how environment (family characteristics, parents and siblings, peers, and broader societal influences including media) and child characteristics (genetic makeup, temperament, and pre- and perinatal factors) affect the development of social competence (SC) and behavioral control (BC), skills that are essential for functioning in society and for reducing risk of behavioral and emotional problems. Figure 2 shows how CID aims to gain new insights in how developmental differences arise between children as a result of the interplay of child characteristics and environmental factors, by filling crucial knowledge gaps on the role of brain development, effects of interventions in the environment, and intergenerational transmission.

Figure 2. The WPs and how they are interrelated on their focus on the interplay of child characteristics and environmental factors, determining developmental differences, specifically on SC and BC.

All WPs focus on the development of SC and BC (upper right-hand box Figure 2) and use the same core measures, as decided in the PI meeting of 15 January 2014 (see 2.3) and found on our website http://www.individualdevelopment.nl/research/measurements. 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 (upper left-hand box Figure 2).

CID PhD students and postdocs have started projects along the lines envisaged in the original proposal and these are described in short progress reports below.
### 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, Dept. of Psychiatry

**Aim:** The aim of this project is 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.

**Progression 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).

**Dr. Carlijn van den Boomen**, Postdoc, Sept/13 – Sept/16

**Typical and atypical development of visual perception**

Kemner, UU Faculty of Social and Behavioral Sciences

**Aim:** The aim of this project is examining the typical and atypical development of visual and social perception in children, thereby focusing on underlying processes involved in social competence.

**Methods:** This project applies experimental designs. Visual stimuli of basic objects (e.g. stripe-patterns) and faces are shown to children, while we measure behavioral responses or neural processing using electroencephalography (EEG) and functional near infrared spectroscopy (fNIRS). We use existing databases and collect new data. The populations of interest are typically developing children, and children that suffered from cataract, which led to atypical visual development.

**Progression up to now:** In 2015 I published a paper on typical development of basic visual perception. Furthermore, I analyzed and submitted two previously collected datasets on basic visual processing in school-aged children. The first focuses on children that suffered from cataract, the second on typically developed children. In addition, we collected three new datasets in typically developing children: EEG data on emotional face processing in infants aged 5 and 10 months, and behavioral data on face categorization in typically developing children. The data on 10-months are analyzed and submitted for publication. Analyses for the 5-month-olds are ongoing and expected to be submitted in 2016. The data on face categorization could not sufficiently answer the research questions. Additional data will be collected in 2016.

**Karin Fikkers**, Postdoc, Sep/15 – Sep/19

**Understanding children’s and adolescent’s differential use of and susceptibility to violent media entertainment**

Valkenburg; UvA Amsterdam School of Communication Research (ASCoR) and Center for research on Children, Adolescents, and the Media (CcM)

**Aim:** The goal of this project is to understand (1) which children are most likely to consume violent television shows and violent games, as well as (2) which children are more likely to become aggressive of such exposure and why.

**Methods:** We use survey data on youths’ media (violence) exposure, temperament, and self- and parent-reported behavior, in combination with neurological data collected by the CID pilot and main study.

**Progression up to now:** I contributed to the operationalization of media questions in the questionnaire for the main study. We are currently developing ideas for studies that can answer relevant questions using the current and expected data of the CID pilot and main project.

**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:** The aim of this project is to examine the processes through which the early development of infant self-
regulation (behavioral control) within the proximal caregiver relationship influences broad socio-emotional adaptation over time, as proposed by a developmental cascade model. **Methods:** We perform a meta-analysis and use 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 we are working with existing data from the YOUth study of the 10 month old infants. We developed a coding scheme, and moment-to-moment coding of observed parent-infant interactions will take place in the following months. In addition, we are preparing for the data collection of the follow-up study of this pilot, which will take place in the next half year.

**Roy Hessels, PhD student, Jan/14 – Jan/17**

*The effects of social stimulation/interaction on perceptual and social development*

Kemner; Hoijtink; UU Faculty of Social and Behavioral Sciences

**Aim:** The aim of this project is to investigate the effects of social interaction (a critical aspect of social competence) on perceptual and social development. **Methods:** Social development will be studied via two routes. First, by investigating face-scanning behavior of individuals diagnosed with autism, we can model face scanning during abnormal development. If abnormal looking behavior evokes reactive abnormal looking behavior in controls, this can shed light on the role of social interaction in abnormal development. Second, the development of infant face scanning will be investigated in an interactive eye-tracking setup. **Progression up to now:** The setup for investigating social interaction has been developed. As this is a novel setup for studying social interaction there are few tools for statistical analyses available. In our collaboration we develop a tailored statistical tool for analyzing how people make eye contact and look at each other in a live setting. At the moment, the first prototypes are being tested. The results have been described in two publications.

**Dr. Caroline M.M. Junge,** Assistant professor, **Dr. Janna Cousijn,** Postdoc (until 1/12/15) and **Dr. Matthijs Vink,** Assistant professor (since 1/1/16)

*Selecting suitable tasks from infancy to adolescence that tap social competence and behavioral control*

Kemner, UU Faculty of Social and Behavioral Sciences

**Aim:** The aim of this project is to select suitable tasks from infancy to adolescence that tap social competence and behavioral control. **Methods:** For both cohorts, we will use a variety of SC- and BC-tasks repeated at each wave. The tasks are chosen such that they a) can be administered from infancy to adolescence; b) measure a key part of either social competence or behavioral control, and c) are expected to yield meaningful differences at this age. Crucially, we do not only sample behavioral measures, but also eye-tracking and brain-related measures (baby-child cohort: EEG/ERP; child-adolescent cohort: fMRI). Some of the tasks will also be used in other work packages. **Progression up to now:** In 2015, the postdocs from WP1 made a final task selection for the longitudinal cohort studies (baby-child cohort and child-adolescent cohort). In addition, we have piloted as much of the tasks as possible for both cohorts. For the baby-child cohort, we tested a full-day procedure with 5-month-olds (n=44) and with 10-month-olds (n=77). For the child-adolescent cohort, we have piloted the behavioral and eye-tracking tasks in a cross-sectional design (n=135; range 8-16 years). Early 2016 we are fully prepared to test the first waves for both cohorts.

**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, Hoijtink, Valkenburg, Crone; UU Faculty of Humanities

The project consists of two subprojects: 1: From book smart to street smart: does exposure to fiction enhance social competence? And 2: What to say when you talk to yourself: the role of verbal reappraisal in behavioral control. **Aims:** The aim of subproject 1 is to assess the predicted positive impact of exposure to fictional narrative on the child’s development of social competence, in his/her actual behavior (tendency to engage in pro-social behavior) and in relevant cognitive component skills (perspective taking, empathy and moral values). The aim of subproject 2 is 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 (a crucial component of behavioral control) and how general linguistic and narrative abilities mediate this relationship.
Methods: In the cohort study, we use dedicated questionnaires and experimental tasks to assess the various relevant constructs (e.g. exposure to various types of fiction, perspective-taking competence, moral profile), and we will relate those dedicated measures to WP1- and/or CID-wide assessments of social competence and behavioral control, as well as to WP1-wide measurements of brain-anatomical development. In experimental work conducted on non-cohort participants, we use additional lab tasks, as well as additional physiological measures (EEG, facial EMG (electromyography), skin conductance) to assess the effects of emotion regulation.

Progression up to now: In subproject 1 we a) created a fiction exposure questionnaire for use in the cohort (pilot data gathered from a large online study), b) created additional measures to assess fiction exposure for use outside of cohort (data gathered for validation of Author Recognition Test for 8-17 year olds), c) created a Bayesian analysis plan for analysis of data from the YOUTH adolescent cohort (to be implemented once data collection has terminated), and d) are gathering data in an intervention study considering effects of reading particular types of fiction on adults’ social competence (to be modified for use with adolescents at a later stage). In subproject 2 we a) are gathering data in an intervention study considering effects of particular reappraisal strategies on adults’ ability to deal with verbal insults and with social exclusion (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

Aim: 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 intend to focus on the way these two processes interact with each other in impacting developmental trajectories of risk behavior in adolescence.

Methods: We use 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.

Progression up to now: The first results suggest that self-reported behavioral control at age 11 predicts initiation of alcohol use at age 16. Both effortful control and measures of cognitive control at age 11 predict the initiation of cannabis use at age 16. For smoking no such effects were found. In addition, interaction effects between reward sensitivity at age 16 and effortful control at age 11 are found for alcohol and cannabis use, suggesting that lower levels of control in early adolescence combined with higher sensitivity for reward in mid adolescence predict alcohol and cannabis use.

Jalmar Teeuw, PhD student, Jul/15 – Jun/19

Imaging genetics of brain development in healthy adolescent twins
Hulshoff Pol, Boomsma, Brouwer; UMC Utrecht, Dept. of Psychiatry

Aim: The aim of this project is to disentangle the (epi)-genetic and environmental influences on brain development. In particular, brain development and its associations with functioning (intelligence, social competence, behavioral control) of healthy adolescent twins and their siblings are being studied.

Methods: The PhD position is a collaboration between UMC Utrecht and VU Amsterdam / Netherlands Twin Register. Magnetic resonance imaging scans, cognitive test batteries and genetic material have been acquired from monozygotic and dizygotic twins and their older sibling at the ages of 9, 12, and 17 years old. In this project we integrate information from the different MRI modalities (including structural, diffusion, and resting-state functional imaging) to elucidate causal (epi)genetic and environmental influences on the development of the brain. A second approach consists of predicting cognitive and psychiatric conditions in early adulthood using brain measures acquired during adolescence.

Progression up to now: Work on predicting changes in cognitive abilities in relation to cortical thickness during late adolescence has been presented at two internal symposia. This work is currently being extended to include analysis of genetic and environmental influences. In addition, analysis of the resting-state functional imaging data is ongoing.

WP2

Michelle Achterberg, PhD student, Sep/14 – Sep/19

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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 (as a part of social competence and behavioral control).

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 period.

Elisabeth Bilo, PhD student, Apr/15 – Apr/20

Physiological correlates of social and behavioral development in childhood and emerging adolescence  
Bakermans-Kranenburg, van Ijzendoorn, Joëls; 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 the physiological development and the interplay with social and behavioral development in childhood and emerging adolescence (social competence and behavioral control).

Methods: Caucasian families with young twins are invited to participate in our study. Two pretests will be conducted, after which families will be randomly assigned to an intervention or control group. Various measures are used to measure behavioral and hormonal development. To assess hormonal development, both saliva and hair samples are used.

Progression up to now: I have started the project in April 2015 and am fully immersed in data collection and analysis. We started with the data collection of our longitudinal study; since August 2015 89 families (178 children) with a 7- or 8-year-old twin have visited the lab for the first pretest and another 24 families are scheduled for the upcoming weeks. The aim is to recruit at least 250 families by September 2016. In addition to the data collection, I am currently processing and analyzing salivary cortisol data from the first pretest home visit of 239 families with a 3- or 4-year-old twin who also participates in the study. From these families, a total of 2335 saliva samples have been analyzed for cortisol concentration.

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 (a hallmark of social competence) 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.

Progression up to now: Since September 2014 we have recruited 239 families with 3-4-year-old twins (total N = 478). Each family was visited at home for the first pretest. Furthermore, we successfully piloted Video-feedback Intervention to promote Positive Parenting and Sensitive Discipline (VIPP-SD) for twin-families last summer. We have started year 2 of the study in September 2015, during which we invite families to the university for a lab visit. We are currently processing and analyzing data of the home visits from year 1, in which I will focus specifically on parental sensitivity and its relation with prosocial behavior.
**Mara van der Meulen, PhD student, Jan/15 – Jan/20**

**Prosocial development in childhood and emerging adolescence**
Crone, Engels, 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, a hallmark of social competence.

**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 are 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 2015 we started with the data collection of the longitudinal study: we have collected data from 162 participants, and another 66 are scheduled for the upcoming period.

**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.

**Progression up to now:** From September 2014 to September 2015, we recruited and visited 239 families with 3-4 year old twins (total N = 492). 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 May 2015 to September 2015, we successfully piloted the Video-feedback Intervention to promote Positive Parenting and Sensitive Discipline (VIPP-SD) for families with twins. In September 2015 we started with the data collection of year 2. Currently, we are coding and analyzing the data from the home visits of year one.

**Ilse van Wijk, PhD student, Feb/14 – Feb/18**

**Neural correlates of social rejection and aggression in young children**
Van IJzendoorn, Bakermans-Kranenburg, Crone; UL Faculty of Social and Behavioral Sciences

**Aim:** The goal of this project is to study how the developing brain is shaped by genetic and environmental factors (for instance parent-child interactions) using a randomized controlled trial in a longitudinal twin study (six years). Specifically, my project focuses on the development of brain activity differences in frontal asymmetry and the neural correlates of social rejection and aggression.

**Methods:** To study frontal asymmetry a rest measurement during EEG is conducted (6x30 seconds eyes open and closed). Furthermore, social rejection and aggression is measured with a new social judgment task. Participants are shown pictures of peers that judge a personal belonging of the participant (positive, negative or neutral). Participants are requested to react to the peers’ feedback by pressing a button, resulting in destroying the balloons of the peer. Balloon bursts (duration of button press) are used as a behavioral index of aggression.

**Progression up to now:** The social judgment task was tested in a pilot study (N = 50, 23 girls, mean age (SD) = 5.30 (.88)). Participants chose a cuddly animal, which was sent to their home two weeks before testing. Rejection of the
cuddly animal from peers led to more aggression. We are currently analyzing the results from the brain activity and related behavioral tasks (e.g. ToM and questionnaires filled out by parents). In September 2015 the second year of the data collection of the longitudinal twin study started; in this year participants come to the lab for the EEG measurement and the marshmallow task. Additionally, the behavioral tasks from the first year are conducted again. Already 65 families successfully finished the lab visits and until September 2016, we will invite another 167 families.

WP3

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

Determinants and consequences of (low) cognitive control
Oldehinkel, Hartman, UMC Groningen, Dept of Psychiatry, Interdisciplinary Center Psychopathology and Emotion regulation (ICPE)

Aim: Adolescence is characterized by extensive neurodevelopmental changes. It has been hypothesized that disorders with a high incidence during adolescence, such as depression and anxiety, are neurodevelopmental disorders that result from premorbid vulnerabilities of the brain. Low cognitive control is an often-used marker of such brain vulnerabilities. Within the context of CID, cognitive control is highly relevant because it is a prerequisite for behavioral control, one of the two core outcomes. Whereas prior research suggests that low cognitive control is not a strong predictor of depression and anxiety in general, it may still do so in particular subgroups, e.g. youth with a vulnerable temperament. Cognitive control is important in regulating our behaviors and emotions, which may be particularly relevant in the context of specific risk factors. The central aim of this project is to examine the role of cognitive control in relation to the question why some individuals develop psychiatric problems while others do not, and why some remit while others have chronic and even worsening psychopathology. Insight will be gained by investigating how cognitive (behavioral) control may provide a buffer in the context of a vulnerable temperament, stress exposure, comorbid childhood psychopathology, and a high familial presence of psychopathology.

Methods: Existing (multiwave) cohort data will be used from TRAILS (TRacking Adolescents’ Individual Lives Survey), LifeLines, ARIADNE, and NeuroIMAGE. Cognitive control was measured using either paper-and-pencil or computerized tasks. All other variables were measured by interviews or questionnaires.

Progression up to now: Start of the project was 20th of October 2014. Current situation is: one paper submitted; and for the second paper the analyses are finished and we are halfway through writing up the manuscript.

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 up to now: A 1st paper (published) 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. A 2nd paper submitted to Developmental Psychology investigates heterogeneity in development of certainty and uncertainty in identity formation across adolescence and concurrent development of psychosocial adjustment (social competence). For a 3rd paper in progress (finalizing statistical analyses, to be submitted by April 1st) we will investigate socialization of self-certainty (as a part of social competence) across adolescence. We will focus on reciprocal associations between parent and peer quality of relationships and the development of self-certainty, using a 5-year longitudinal, multi-informant approach. We will use a multi-level cross-lagged panel model to investigate within-person change in relationship quality and self-certainty across adolescence. For a 4th paper in progress (currently statistical analyses are conducted), 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. A 5th paper is in progress (not part of my dissertation, but concerns collaboration within the CID-community; to be submitted by February 1st). In this opinion paper, I am the second author, in which I collaborate with colleagues from CID in writing an opinion paper concerning statistical methods to study brain development in childhood and adolescence (Title: Moving beyond the study of mean level brain development: Studying heterogeneity in developmental trajectories).
Examining the complex interplay between relationship experiences and individual factors to understand adolescent development

Oldehinkel, Meeus, Dekovic; UMC Groningen, Dept. of Psychiatry, Interdisciplinary Center Psychopathology and Emotion regulation (ICPE) and Dept. of Sociology

Aim: This project seeks to identify predictors of positive outcomes (educational and occupational success, prosocial behavior, self-competence, empathy; all hallmarks of social competence) and problem development (internalizing and externalizing behavior). In detail, project component #1 asked whether experiences in parent-child relationships are associated with experiences in relationships with peers and intimate partners and project 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 up to now: An article on the link between parent-child relationships/parent characteristics and peer experiences has been published in the Journal of Research on Adolescence (co-authors Sentse, Meeus, Verhulst, Oldehinkel); an article on the link between parent positivity in early adolescence and romantic involvement, commitment, and satisfaction (co-authors Vollebergh, Oldehinkel) is published in the International Journal of Behavioral Development. A third article on bullying development and its negative outcomes (co-authors Veenstra, Dekovic) is under review. This research has also been presented at conferences (European Association for Research on Adolescence, 2014; Society for Research on Child Development, Philadelphia). By the end of 2015, Tina Kretschmer accepted a UD position at the University of Groningen and was followed-up by Jennifer Klop-Richards, who is now preparing a paper on the optimal operationalization of the concept of thriving.

Dr. Odilia M. Laceulle, Postdoc (until 1/9/2015) and dr. Anoek M. Sluiter-Oerlemans, Postdoc (since 1/5/2015)

Developmental models of psychopathology an life outcomes

Oerlemans, Oldehinkel, Vollebergh, Van Uzendoorn, Van Aken, UMC Groningen, Dept. of Psychiatry, Interdisciplinary Center Psychopathology and Emotion regulation (ICPE) and UU Dept. of Developmental Psychology

Aim: In addition to work related to the enrichment of TRAILS study with measurements of a third generation, we started to investigate developmental models of psychopathology. The main aim was to use longitudinal data to disentangle the structure of psychopathology, the complex interplay between individuals and their environments (transactional models) in the prediction of psychopathology and life outcomes.

Methods: Data from all five waves of the Tracking Adolescents’ Individual Lives Survey (TRAILS) are used, though the focus to date has been on measures of mental health, temperament/personality, social relationships, and early adult life outcomes.

Progression up to now: A number of papers have been published and submitted. One article targeted the mediating role of perceived relationship affection in the temperament-stressful events association (European Journal of Personality; co-authors van Aken and Oerlemans). A second article investigated the structure of psychopathology in adolescence (Clinical Psychological Science; co-authors: Vollebergh and Oerlemans). A third paper investigated the relationships between adolescent personality and basal, awakening and stress-induced cortisol responses (Journal of Personality, in press; co-authors Van Aken and Oerlemans). A fourth paper, titled “Sequences of Mal-adaption: Pre-adolescent Self-regulation, Adolescent Negative Social Interactions and Young Adult Psychopathology”, is in progress (co-authors Vollebergh and Oerlemans). Spring 2015, Odilia Laceulle accepted a UD position at the university of Tilburg and left CID September 1, 2015. Her successor, Anoek M. Sluiter-Oerlemans, started September 15, 2015. Currently, Anoek is involved in finalizing two unfinished papers (one investigating life outcomes of psychopathology, and one investigating the scar model of the relationship between psychopathology and personality) and brainstorming with CID PIs on how to elaborate the aim given her skills and interests.

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

Aim: The aim of this project is to 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 (social competence), 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 function 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’ social competence (capacity to involve with peers) 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, Department of Child and Adolescent Psychiatry

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 of this project is the estimation of the factor’s single nucleotide polymorphism (SNP) heritability, the extent to which individuals who share more 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. Parents, teachers and children reported child behavior problems. 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=2115).

Progression up to now: All reported problems, including the child’s self-report, loaded on the general psychopathology factor. The factor was negatively associated with lower IQ (r=-0.13, 95%CI[-0.15; -0.11], p<0.001). We observed a significant SNP heritability of 37% (SE=0.16, p=0.01) for the general factor. A corresponding paper is currently under review.

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, Faculty of Psychology and Education

Aim: The overall aim of my project is to study why some pupils thrive and others do not, with a focus on etiological factors underlying social-emotional (social competence) 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. To be more specific, 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), 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. Data collection: I started with the ongoing survey data collection of primary school teachers.

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

Longitudinal development and intergeneration transmission of psychopathology versus wellbeing
Boomsma, Oldehinkel; VU University Amsterdam

Aim: The aim of the project is to disentangle genetic and environmental influences on psychopathology and wellbeing, 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.

Progression up to now: In the previous years the Netherlands Twin Register (NTR) has been asking parents of young twins whether they themselves were also part of a twin pair. When this was the case they and their co-twins have been invited 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 (~650 families). Several outcome measures are available for both the parents and the children. Measures that are available for both the parents and children are psychopathology, well-being, education, physical activity and physical characteristics. At this moment the analyses of the psychopathology data are being carried out. The data collection in children of twins of the YNTR started in January. All twins in the cohorts 1986-1990 that have offspring of their own have been identified (~700 persons from ~575 families). These twins and their partners are invited to fill out a survey about the development of their own children (also on social competence and behavioral control). Extensive longitudinal data are already available for this sample of parents and the to-be-collected survey for the children will include measures on psychopathology, wellbeing, 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.

Progression up to now: 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. 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. Results have been presented at the SfN Neuroscience 2015 conference in Chicago, and will form the basis of a first manuscript to be submitted in the first half of 2017.
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: We perform neurobehavioral research in combination with innovative genetic techniques: 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. I investigate 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. Also, 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.

Genetic resilience in a combined model of stress early in life and later in adulthood on behavior and neurogenesis in mice

Joëls; UMC Utrecht Dept. of Translational Neuroscience, Brain Center Rudolf Magnus (BCRM) and UvA Swammerdam Institute for Life Sciences, Center for Neuroscience

Aim: The general aim of this project is to model the neurodevelopmental aspects of behavior (social competence and behavioral control) and structural plasticity after stress early in life and later in adulthood in male mice. Mineralocorticoid receptor (MR) function is considered important in mediating stress resilience. We therefore aim to study whether combined exposure of early life stress and stress in adulthood affects memory and neurogenesis and whether these effects can be prevented by increased transgenic overexpression of MR’s.

Methods: We have used a novel approach for developmental behavioral and structural analysis in which mice are assessed in adulthood on a series of behavioral tasks measuring neuroendocrinological markers, locomotor activity, anxiety, learning and memory and adult hippocampal neurogenesis.

Progression up to now: 1) We have established and validated (neuroendocrine and behaviorally) the limited nesting and bedding model (ELS) to induce early life stress in mice through fragmented mother care. 2) We have established and validated (neuroendocrine and behaviorally) the chronic unpredictable stress model (CUS) to induce stress in adulthood in mice through a combination of physical and psychological stressors. 3) We have successfully imported the genetically modified mouse lines necessary to generate the forebrain specific overexpression mice. Recently we have shown that increased MR functionality partially prevents chronic-stress induced reductions in hippocampal memory and structural plasticity in male mice (Kanatsou et al., 2015). Moreover overexpression of MRs protects against the consequences of early life stress on spatial memory, cell maturation and synaptic function in the dentate gyrus in male mice (Kanatsou et al., in preparation). Based on these findings, it is important to further explore the genetic resilience of MRs on behavioral and structural domains in a combined model of stress early in life and later in adulthood.

The effects of early life stress on social competence; possibilities for intervention

Joëls, Bakermans-Kranenburg; UMC Utrecht, Brain Center Rudolf Magnus (BCRM)

Aim: Previous studies have shown that prolonged exposure to high levels of corticosteroids early in life affects stress-sensitivity, cognitive functioning and brain structure. Both early life and adolescence are sensitive periods, where environmental influences can have a critical influence on further brain development. Studies in animal models will help us to better understand the adverse effects of early life stress (specifically on social competence and behavioral control) 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 behavioral control, social competence and pro-social behavior in rats in adolescence and adulthood and 2) to investigate the possibility of reversing these behavioral effects using either environmental or pharmacological interventions in adolescence.

**Methods:** Rats are exposed to 24h maternal deprivation on postnatal day 3. At postnatal day 26 rats undergo a pharmacological or a non-pharmacological intervention. The pharmacological intervention consists of a 3-day treatment with Mifepristone, a glucocorticoid receptor antagonist. The non-pharmacological intervention consists of housing the rats in a complex environment (Marlau™ cages).

**Progression up to now:** Animals with a history of early life stress show less behavioral control as measured with performance on the 5-choice serial reaction time task. Preliminary results suggest that maternally deprived animals have a different play pattern compared to normally reared animals. However, this was only seen when maternally deprived rats also received a 3-day oral gavage treatment on postnatal day 26-28. In addition to a different play pattern, the total amount of play in maternally deprived females was significantly higher compared to control females.

**Manila Loi**, PhD student, Sep/13 – Sep/15

**Intervention at puberty after early life adversity**

Joëls, van Ijzendoorn; UMC Utrecht, Dept. of Translational Neuroscience, Brain Center Rudolf Magnus (BCRM)

**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.

**Progression up to now:** We observed that particularly in male rats (much more 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.
**Genetic resilience to early life stress effects on the behavioral trajectory in mice**

**Joëls; UMC Utrecht, Dept. of Translational Neuroscience, Brain Center Rudolf Magnus (BCRM)**

**Aims:** The general aim of this project is to model the neurodevelopmental aspects of behavioral and cognitive domains after early life stress (ELS) in male and female mice. 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 (behavioral control) 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.

**Progression up to now:** 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.

**Experiences in sensitive periods: Effects on attention and behavioral control**

**Joëls, van Uzendoorn, Bakermans-Kranenburg; Dpt. Translational Neuroscience, UMC Utrecht and Dpt. of Child and Family Studies, Leiden University**

**Aim:** The aim of this project is to examine the effects of maternal deprivation on postnatal day 3 and a complex rearing environment during adolescence on attention and behavioral inhibition (behavioral control) in adult male rats. Next, we investigated whether early life experience (maternal deprivation) interacts with later life experiences (complex housing or a pharmacological treatment with the glucocorticoid receptor antagonist mifepristone during adolescence) to influence attention and behavioral control in adulthood.

**Methods:** 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. Mifepristone was administered by gavage on postnatal day 26, 27 and 28. Animals in the complex rearing environment were housed in large, two floor Marlauch™ cages, together with 10 conspecifics. 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. In the group where animals received a placebo gavage at postnatal day 26-28, maternal deprivation did have a moderate, but significant impairing effect on attention. Mifepristone treatment did not influence this impairment. A paper on the complex housing results has been written and accepted for publication. A paper on the effects of maternal deprivation and mifepristone treatment is in progress.

**Formalization and evaluation of prior knowledge based on prior/posterior predictive inference**

**Hoijtink, van Berkum; UU Faculty of Social and Behavioral Sciences**

**Aim:** The aim of this project is to 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 are 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. We illustrate and apply the models developed to CID data, in which depression (resulting from trials) or contextual memory (resulting from rat-studies) are the target variables.

**Methods:** We performed a simulation study.

**Progression up to now:** We formalized and updated two studies on i) previous literature and ii) expert knowledge 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.
Appendix 12 – Data management plan and ethical aspects (see 3.2, page 16)

Optional: State how you deal with data management (state how you will store research data and render this findable and suitable for re-use; if relevant, add a copy of the repository data contract.

Optional: State how you deal with the ethical aspects of the research (for example the Personal Data Protection Act (WBG), the Medical Research Involving Human Subjects Act (WMO), the Netherlands Code of Conduct for Scientific Practice and the Code of Conduct for the Processing of Personal Data, and any discipline-specific guidelines).

Below we describe how we manage data from the YOUth cohort and deal with the ethical aspects of research. The data management protocol is available to all consortium participants.

Data management

Summary

The project ‘Consortium on Individual Development: Why some children thrive, and others don’t’ will collect data from 6000 children (YOUth Cohort) attending the Child Research Center (CRC) of Utrecht University and the University Medical Center Utrecht (UMC Utrecht). Raw and processed data come from 10 sources, each with different requirements regarding data storage and management. The collected raw data are made available to users under specific conditions incorporated in the Data Transfer Agreement signed by users.

A solid IT data management infrastructure has been developed to store data and consists of systems already in use by the UMC Utrecht (BioBank, XNAT and Research Data Platform (RDP)) and a newly developed facility for managing research data at Utrecht University (YOUth Data; YODA). We have built YODA to achieve the goals set at the start of the project:

- All parties and project researchers should be able to share data in a simple but secure way;
- Data should be stored in systems that preserve the integrity and accessibility of data in the long term;
- Data should be retrievable and accessible to the research community worldwide.

This infrastructure will be extended, as necessary, with facilities to distribute (copies of) data to researchers and to preserve analyzed data. A data management plan provides researchers, laboratory assistants, data managers, and system managers with procedures and guidelines for managing, distributing, and using data. Copies of these documents (at this moment only in Dutch: ‘Datamanagement plan – Gravitation CID, WP1 – YOUth cohort’ and ‘Richtlijnen databeheer en gebruik YOUth cohort’) are available upon request (J.E.Buizer-Voskamp@uu.nl).

Figure 3 provides an overview of all data sources and facilities for storing data.

1. Data Collection

1.1 Data sources

Data will be collected from 10 sources. In some cases, the data will be stored in an intermediate storage facility and afterwards exported to the long-term storage facility (Table 1).
Figure 3. Data sources and storage facilities. KKC: KinderKennisCentrum (Child Research Center); RO2: Research Online 2; YODA: YOUth Data; XNAT: Open-source imaging informatics software platform; RDP: Research Data Platform; FSW: Faculty of Social and Behavioral Sciences; GW: Humanities; UU-ITS: University Utrecht – Information and Technology Services.

Table 1: Data sources and long-term storage

<table>
<thead>
<tr>
<th>Data source</th>
<th>Description</th>
<th>Intermediate storage</th>
<th>Long-term storage</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Questionnaires</td>
<td>Online lists of questions</td>
<td>RO2</td>
<td>RDP</td>
<td>UMC Utrecht</td>
</tr>
<tr>
<td>EEG</td>
<td>Electroencephalography</td>
<td></td>
<td>YODA</td>
<td>Utrecht University</td>
</tr>
<tr>
<td>Parent Child</td>
<td>The parent-child interaction is recorded on video and afterwards coded</td>
<td></td>
<td>YODA</td>
<td>SURFsara</td>
</tr>
<tr>
<td>Interaction</td>
<td></td>
<td>BioBank</td>
<td>UMC Utrecht</td>
<td></td>
</tr>
<tr>
<td>Biodata</td>
<td>Biological samples for analyzing hormones, biomarkers, and DNA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRI scans</td>
<td>MRI scans of the brain</td>
<td>XNAT</td>
<td>UMC Utrecht</td>
<td></td>
</tr>
<tr>
<td>EyeTrack</td>
<td>Recording the position and movement of eyes while performing (computer driven) tasks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Computer Tasks</td>
<td>Data about cognitive and motor aspects while performing computer driven tasks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Echo</td>
<td>Echographs of the brain of the unborn child</td>
<td>PennTask</td>
<td>RDP</td>
<td>UMC Utrecht</td>
</tr>
<tr>
<td>Lab Log</td>
<td>Laboratory data and measurements</td>
<td>LimeSurvey</td>
<td>RDP</td>
<td>Utrecht University</td>
</tr>
<tr>
<td>Cohort Administration</td>
<td>Data about the participants and the appointments</td>
<td>SLIM</td>
<td>RDP</td>
<td>UMC Utrecht</td>
</tr>
</tbody>
</table>

RDP: Research Data Platform; RO2: Research Online 2; YODA: YOUth Data
1.2 Assessment waves
Data from 6000 subjects are collected at fixed intervals called ‘waves’. The subjects are divided into two longitudinal cohorts: a baby-child cohort and a child-adolescent cohort. For the baby-child cohort, data will be collected two times during pregnancy, two times during the first year, once when the child is about 3 years, and once when the child is about 6 years. In the child-adolescent cohort, data will be collected when the child is about 9, 12, and 15 years. In total, about 27,000 measurements will be taken.

1.3 Subjects
The cohort administration is responsible for planning the measurements and communication with the children (subjects) and their parents. The cohort administration is the only place where the identity of subjects is registered.

All data systems use an internally generated, content-less identifier (called pseudo-code) for the subjects. The key linking the pseudo-code with a subject’s identity is held by an independent department. This means that medical and other privacy-sensitive data are not directly linked to the identity of the child or parent. The requirements of the Netherlands Code of Conduct for Scientific Practice (Nederlandse Gedragscode Wetenschapsbeoefening) are incorporated in the informed consent form signed by the child or its parents.

1.4 Types of data
Currently, we collect two types of data:
1. Raw data: the data as measured and/or observed
2. Processed data: the raw data after processing to make them suitable for further scientific analysis (cleaning, reformatting, etc.).

1.5 Users of the data
The type of affiliation/relationship of the researcher to the project determines the order in which access to the data is granted:
1. PhD students, postdocs, and others who have contributed to the collection of the data;
2. Researchers in work package 1 of the Consortium on Individual Development (CID);
3. Researchers affiliated with CID or with the strategic theme Dynamics of Youth;
4. Researchers worldwide.

See paragraph for the retrievability, availability, and accessibility of the data.

2. Data Storage
Four systems at three locations are available for data storage (see Table 1). The systems were chosen based on the source of the data, technical requirements, agreements between the parties in the consortium, and data regulations of the two institutions (Utrecht University and UMC Utrecht). We estimate that about 160,000 experiments will generate up to 500 TB of raw and processed data (excl. backup).

YODA offers a portal for researchers and laboratory assistants to upload their data and checks the completeness and consistency of the uploaded data (e.g., obligatory metadata, data formats, etc.). In 2016, YODA will provide a portal for researchers to upload their analyzed data. These data can then be stored under the same secure conditions as raw and processed data. YODA stores copies (replicas) of the data in an archive at SURFsara (High performance computing & data infrastructure for science and industry). The B2Safe service of EUDAT (www.eudat.eu) is used to transfer the data in a secure way. The replicas at SURFsara are encrypted – SURFsara does not have the encryption key.

The systems are operated by the information technology departments of the institutions, and the services they provide meet the standards for information security, system maintenance, and capacity management required by the institutions. YODA uses the iRODS open source data management software used by research institutions and governmental agencies worldwide.
2.1 After the research project
The data will be available for research for at least 15 years after project completion, although we are as yet uncertain about the choice of data repository. We will meet the obligations to funding organizations, publishers, Utrecht University, and UMC Utrecht.

3. Standards for data formats and metadata
Our guidelines provide instructions about which data formats should be used and which metadata should be provided. The guidelines are based on the protocols of Utrecht University, DANS, Clarin, and UK Archive. When researchers access data, they will be provided with the metadata for establishing the usability of the data. Theoretically, metadata can also be used to retrieve data, but search mechanisms based on metadata have not been implemented yet.

4. Retrievability, availability and accessibility of the data
Storing and preserving research data is not a goal in itself. The data should be used by members of the consortium and by the research community worldwide. This means that data must be retrievable, available, and accessible.

4.1 Making data retrievable
Some of the data and metadata will be copied to the Research Data Platform of the UMC Utrecht. This platform has been specifically developed for the distribution of medical research data and has appropriate security measures. Researchers have to apply for access to the platform, which can only be used for finding relevant links to data, but not the data itself. In the near future, the YODA system will be extended with a catalogue to find and locate YOUth data.

4.2 Making data available
Although the data are retrievable, they are not automatically available to researchers. Research groups have to apply to the Data Management Committee for access to parts or subsets of the data. This committee has set criteria for these requests. For instance, the use of data has to be in agreement with the informed consent of the subject. See the ‘Data management plan – Gravitation CID, WP1 – YOUth cohort’ for an overview of the criteria (only in Dutch, available upon request). Before receiving copies of the data, the requesting party has to sign a Data Transfer Agreement that lays down conditions for the use of data and the publishing of results based on the data.

4.3 Making data accessible
Researchers can download data from the aforementioned Research Data Platform or data copies from a secured server (as part of YODA) for which the researcher has to be authorized. Data managers will be provided with tools to transfer data from the storage locations to the secured server.
Ethical aspects

Several steps have been taken to deal with the ethical aspects of the research. Personal data and research data are encrypted with two different keys and data are stored in a secure environment. Informed consent is in accordance with Dutch privacy law (e.g., the ability to be excluded for just parts of the total investigation and a protocol for the withdrawal of an Informed consent). A form providing information about data storage, data sharing, privacy, and security has to be signed by all employees (see below). Information about data management and sharing is presented above. Lastly, staff must sign a confidentiality agreement if they are not covered by the collective agreement.

<table>
<thead>
<tr>
<th>Code of conduct for data management and data usage (pamphlet)</th>
</tr>
</thead>
</table>

**English summary of the privacy and security aspects**

Employees of the Child Research Center work daily with data that are important for medical research and society in general. Because society has invested strongly in YOUth, by providing funding and study participants, it is our responsibility to handle data with care and to guarantee the transparency, sustainability, and integrity of our research. This guideline summarizes laws and regulations relevant to YOUth, divided into four topics: data storage, data sharing, privacy, and security, of which only the last two are described below.

**Privacy aspects**

- All employees of the Child Research Center work with anonymized data to protect the privacy of research participants.
- All employees of the Child Research Center are individually responsible for maintaining the informed consent of participants each time they come to the center and for protecting their privacy. Personal data (first name(s), initials, title, gender, date of birth, email address, home address, telephone number, social security number, and bank account number) of participants and other indirect data (e.g., zip code) that could be used to identify participants are under no circumstances to be registered (not even in laboratory journals).
- The employees of the Child Research Center are not allowed to use anonymous data files in any way (through links, comparisons, processing) in an attempt to determine the identity of participants.

**Security aspects**

- All employees of the Child Research Center are responsible for all aspects of security in their work environment, e.g. locking the doors at the end of the day, locking computers when leaving the room, anchoring laptops, clean desk, and responding to the presence of unknown individuals in the building.
- If media equipment (e.g., hard disks, but also memory cards from cameras) is to be disposed of or reused, existing information must be destroyed or overwritten.
- All employees of the Child Research Center must use personal login accounts. Accounts must not be shared.
- If any security incident is detected (e.g., unauthorized access to the data or data theft), the Computer Emergency Response Team of Utrecht University (CERT-UU) and the Data Manager should be contacted immediately. The team is available 7 days a week for emergencies.

The relevant Institutional Review Board or Medical Ethics Committee must approve all CID studies before the start of participant recruitment. All study protocols are in accordance with the rules and regulations applying to the Medical Research Involving Human Subjects Act (WMO).
Institutional Review Board protocol of theYOUth study

The YOUth research protocol considered the two enrolment moments (the baby-child cohort starting when the mother is 20 weeks pregnant; and the child-adolescent cohort, when the child is 8, 9 or 10 years old) as individual protocols when it came to gaining Institutional Review Board approval for the study. These protocols described the general idea of YOUth, including follow-up and inclusion of pregnant women. Subsequently, for each round of assessments an amendment describing the specifics of that assessment round will be submitted to for approval.

A summary of the paragraphs regarding the ethical aspects is given below.

Regulation statement
The study will be conducted according to the principles of the Declaration of Helsinki (64th amendment, Fortaleza 2013) and in accordance with the Medical Research Involving Human Subjects Act (WMO).

Informed consent
Parents will be asked to return the completed informed consent form (in duplicate and signed by both parents) by post, using the prepaid return envelope provided or by bringing the forms with them when they visit the Child Research Center. During the first visit, the meaning and relevance of informed consent will be discussed, and parents and their children will be encouraged to ask questions. The research assistant will then sign the duplicate form in the presence of the parents and hand them one copy. The other copy will be stored in the Investigator Site File (see also paragraph 8.3 of the current framework protocol). At each subsequent visit, parents will be again asked to provide their informed consent, and from the second wave onward (in the child-adolescent cohort, at ages 11–14) children will be asked to provide their consent. At all visits, the parents and children will be informed about the possibility to withdraw, without consequences, from the study.

Objection by minors or incapacitated subjects (if applicable)
The code of conduct for minors, as was drawn up by the Netherlands Association for Pediatric Medicine (NVK, 21 May 2001), is applicable. For each individual participant, information will be recorded about whether he or she completed the actual procedure, and any other information of interest. The study procedures will be stopped immediately, without consequences to the participant, if the participant resists or withdraws their consent for whatever reason. Investigators can decide to withdraw a subject because he/she does not meet the inclusion criteria.

Unexpected findings
The YOUth program is not intended as a screening program for health-related problems; however, it is possible that investigators or other team members observe potentially important health-related issues. The YOUth program has drafted a protocol for this situation. According to this protocol, team members should report unexpected findings or observations to the Executive Board of the YOUth cohort, which will then contact a youth health-care physician who is part of the investigation team of the YOUth cohorts. If necessary, the Executive Board or the appointed youth health-care physician will ask a specialist, for instance a clinical psychologist, a child psychiatrist, a pediatrician, or the Biobanking committee from the UMC Utrecht, for advice. As of January 1, 2014, youth health-care physicians are allowed to refer children directly to the relevant specialist. Our youth health-care physician will, if necessary, inform the parents about clinically relevant findings and refer the parents to the relevant specialist. In the case of suspected child abuse or neglect, the youth health-care physician will report this to the relevant authority.

The participant information letter and the informed consent form clearly explain the unexpected findings procedure. Participants cannot participate if they do not agree to being informed about unexpected findings. It is also made clear to potential participants that the study is for research purposes and not for screening for disease.
Appendix 13 – Minutes Supervisory Board & Scientific Advisory Board (see 3.2 & 3.3, page 16)

Supervisory Board meeting
October 12, 2015 | 17:30-19:30h
Academiegebouw | Kernkampkamer | Utrecht

Attendees: Chantal Kemner (program director), Jacobine Buizer (project manager), Werner Raub (UU), Frank Miedema (UMCU), Eco de Geus (VU), Frans Oort (UvA), Hanna Swaab (UL), Daniël Wigboldus (RUN), Vincent Jaddoe (Erasmus MC)
Absent with notice: Folkert Kuipers (UMCG), Eric Fischer (a.i. UvA, replaced by Frans Oort), Mariska Phielix (Financial Office CID)

Chantal Kemner and Jacobine Buizer-Voskamp gave a PowerPoint presentation on the projects, cohorts, finances, and general progression of the consortium. During and after the presentation there was time for discussion and recommendations. Below is a summary of the notes.

1. Discussion during and after the presentation

Regarding WP1: Internationally, multiple cohorts perform MRI on babies and pregnant women. However, this is a major challenge logistically. WP1 is in the IRB procedure for approval of the MRI protocol for babies.

How do you make sure that parents will participate in the study during the whole period of ten years (HS)?
At this moment, we investigate in mailings, presents and postcards for participants. Furthermore, WP1 will develop a website in which parents can find a digital record of their child with results, tests, tips, etc. It will all be about giving knowledge back to the participants. This can be done in groups or individually.
Recommendation: use different sorts of rewards, e.g. presents that will be bigger/more expensive during the testing period.

Cooperation and complementarity with other cohorts in the Netherlands (VJ): Within the consortium, we decided to not harmonize the MRI parts. There are no other cohorts of young children within the Netherlands where the focus is so particularly on (functional) MRI. Furthermore, within Utrecht brain imaging is the main aim, but for the other cohorts, emphasis is on other aspects. However, within CID there is harmonization with Leiden on the performance of MRI: a few measurements, which were used in Leiden, are also taken into account within the YOUth cohort of Utrecht. Finally, we integrated the designs of the cohorts on a specific subset of measures on social competence and behavioral control. We aim to connect with cohorts both within the consortium as internationally.

Regarding WP2: The Supervisory Board discusses the twin design within the L-CID cohort in Leiden. Furthermore, the number of students working within the cohort gives a distorted view. This will be changed in the annual report.

Regarding WP3: The specific subset of measures on social competence and behavioral control will also be used within the cohorts of WP3 for Generation 3.

Regarding WP4: The Supervisory Board is pleased with the new cooperation between Utrecht and Leiden regarding animal models.

Regarding the finances: Table A will be more clear when the total allocated budget will be shown for the upcoming years. This will be changed in the annual report. Table B will be more clear when there is first the column ‘Total budget 5y’, than the column ‘Total budget 10y’, and finally the column ‘Actual’. At this moment, the budgets for the total 10-year period are duplicated in the table. This will be changed in the annual report. Regarding Table C: also PhD students, postdocs and senior researchers can be seen as matching. It is important to show the matching for the total 10-year period.
Recommendations:

**Ethical advisor:** It would be desirable to use the ethical advisor within the education program of PhD students and postdocs. E.g. organize a CID meeting around the ethical aspects of research and give the ethical advisor a prominent role therein. We will draw up an inventory of courses regarding ethical aspects of research and we will close ethical educational gaps by providing workshops in collaboration with our ethical advisor.

**Supervision PhD students:** PIs will always be responsible for the supervision of PhD students. Thereby, the Graduate Schools will guarantee the supervision. The Consortium does not monitor the progress of PhD students on top of that. However, we will keep track on how PhD students are monitored and supervised, including details such as: a supervision document/plan, the number of hours of supervision, and the number of courses (in EC’s) a PhD student has to obtain during their project.

**Interaction with the knowledge users:** Also for CID it is very important to interact with knowledge users, including patient organizations and social organizations. We will draw up an inventory of how individual PIs are already implementing this interaction with knowledge users.

The Tour de Consortium and the journal opinion article assignments are good initiatives to promote the integration bottom-up (starting with junior researchers). Recommendation: it can be considered to make extra money available to give PhD students and postdocs the opportunity to work at other laboratories for a short period of time.

2. Approval of the annual report

All members of the Supervisory Board approve the annual report 2014-2015.

3. Questions to the Supervisory Board

PhD students and postdocs appreciate the initiatives from CID, but note that they experience a ‘heavy load’ if it comes to attending different meetings. They have meetings from their research group, the department, and the consortium. The Supervisory Board notes that without the funding from the consortium, these PhD and postdoc positions would not exist. Furthermore, it was an important aspect in the original proposal that junior researchers would meet within CID. It is probably a part of framing – junior researchers (and PIs) have to acknowledge the CID meetings as part of the education. It is recommended that EC’s will be given for CID retreats. Furthermore, it is very important that senior staff is also present at retreats, as this gives important added value to consortium meetings. The Supervisory Board is unanimously that the priority should be at CID meetings. A strong community will eventually pay off.

4. Any other business

**What about the data management (VJ)?** Within WP1 (YOUth cohort) a protocol for data management was written in close collaboration with the department of Information and Technology Services (ITS) of Utrecht University. This protocol is shared within the consortium and serves a precedent for the other cohorts.

**Spread of knowledge (VI):** It is important to open the CID meetings for non-participants. At one hand, meetings can be organized for the community. On the other hand you need bigger meetings for visibility and PR.
Scientific Advisory Board meeting
April 9, 2015 | 12:30-21:30h
Huize Molenaar | Korte Nieuwstraat 6 | 3512 NM Utrecht

Steering Committee: Chantal Kemner (vz), Dorret Boomsma, Patti Valkenburg, Marian Joëls, René Kahn, Marinus van IJzendoorn, Jacobine Buizer (minutes)
Scientific Advisory Board: Prof. dr. Jay Belsky (University of California, Davis, USA), Prof. dr. B.J. Casey (Weill Medical College of Cornell University, New York, USA), Prof. dr. Mark Johnson (Birkbeck University of London, UK), Prof. dr. Nick Martin (University of Queensland, Australia), Dr. Lieve Page-Christiaens (University Medical Center Utrecht, The Netherlands)

All WP leaders gave PowerPoint presentations regarding their projects, cohort(s) and progression. After each presentation, there was room for discussion. At the end of the meeting, there was one hour of general discussion. After the meeting, the members of the SAB wrote a short evaluation that can be found below.

Work package 1: Brain development

This WP is centered on two large cohort studies designed to better understand the key domains of behavioral control and social competence, in relation to underlying brain development.
In one cohort 3000 babies will be followed through their early development up to 8 years (seen prenatally, at 4-6 months, 9-11 months, 2-5 years and 5-8 years). The second cohort will focus on 3000 adolescents from 8-10 years onwards. Piloting and planning is nearing completion with the studies due to start in the next year.

Advisory Board feedback focused on two issues: (1) the extent to which these studies were coordinated with other international studies of a similar nature (e.g. “The Life Study” in the UK); (2) the pro’s and con’s of sampling different individuals at different age points. We had useful discussion on both issues. Some additional notes for this work package:

• The age of measurement within each developmental period should be randomized. Consider doing this at enrollment, informing the family at the ages the child will be seen over time, so they are prepared for what will be their unique assessment schedule. These could then be built into the protocol delineating from the beginning, when each child will be re-contacted.
• Consider the re-administering of the WAIS at every time period after the initial assessment as the best use of limited protocol time.
• Don’t lose sight of the ever emerging evidence that early-life stress forecasts poor health later in life, meaning that the research should be evaluating this too, perhaps especially with regard to mediating mechanisms (e.g., telomere erosion, inflammation) and organismic moderators (e.g., temperament, genotype).
• Secure teacher ratings of child behavior.
• The theme of the consortium is “Why do some children thrive, and others don’t“. It seems that thriving could be assessed in at least 3 domains: cognitive, behavioral/emotional, and medical. Regarding the first two, it seems that more use could perhaps be made of school results and teacher reports, both on academic performance but also on behavioral aspects such as inattention and hyperactivity. Consider collecting data on the extent to which children perform home chores, such as emptying the dishwasher, walking the dog etc. There is accumulating data assuming such small responsibilities early in life are a predictor of success in later life.
• How extensively is data collected on participation in activities such as sports, scouts, church-youth groups, etc. (as opposed to staying in one’s room playing computer games)? Also, data on length of sleep are being collected, but what about questions on sleep hygiene like no TVs in the bedroom?
• Concerning thriving medically, the consortium will be able to link to medical records, but it could be worthwhile for mothers to fill in simple disease checklists on common ailments such as otitis media, asthma, eczema, hearing problems, eye problems etc. These are likely major factors in childhood
thriving (for example, see D’Onofrio et al. Preterm Birth and Mortality and Morbidity, JAMA Psychiatry. 2013; 70(11): 1231-1240.)

• Collecting hair samples to assess cortisol is being explored. Probably assays from that material can be multiplexed to also obtain testosterone and perhaps some other steroid hormones. It was concerning that Guthrie cards are destroyed after 5 years since we are now doing long-term retrospective studies on e.g. vitamin D and antibodies to viruses and Toxoplasma gondii on long-stored Guthrie cards. The consortium could try and gain exemption from subjects’ cards being destroyed, and more generally, take every opportunity to collect biological samples [blood, saliva, buccal, urine] for future studies.

• The two cohorts within this work package will be large enough to study effects of relative frequent occurrences such as prematurity and intrauterine growth restriction, but not to study the effects of more rare situations such as neonatal intensive care admissions, asphyxia, and rare maternal diseases. It was recommended to survey possible inclusion biases.

Work package 2: Interventions

This work package focuses on parent-mediated interventions in human development, and specifically the VIPP-SD [Video-feedback to promote Positive Parenting with Sensitive Discipline] intervention. Different cohorts will receive the intervention at different age points (e.g. 5 or 9 years old), and data will be collected before and after the intervention period.

Advisory Board feedback included issues of differential susceptibility to the intervention, and how this will be assessed in terms of genetic variation. It was also suggested that with such an internationally unique study it would be important to collect more data on the parents (e.g. the genetic variants of the parents may influence their adherence to the VIPP training protocol – shared genetics variants could then appear as effects in the children). Some additional notes for this work package:

• Pay attention to the possible ethical implications of different patterns of results. What are, for example, the implications if in all trials - at the several ages - only kids (and/or parents) with certain genotypes have any benefit from the intervention?

• The focus is on fostering more harmonious parent-child relationships and, thereby, on down rather than up-regulated physiological reactivity (as indexed by cortisol). Therefore, it could be interesting and exciting to assay telomere length before and after intervention (or even just after given randomization to treatment) to determine whether the intervention might affect “biological aging”. Research on adversity is suggesting this.

Work package 3: Intergenerational transmission

This work package builds on several existing cohort studies in place since 2001-2002, allowing for intergenerational effects (grandparents – parent – child) to be studied. Funding allows for a common protocol to be applied across the different cohort studies. Around 1000 intergenerational families have been identified across the cohorts.

Advisory board comments focused on the options for a behavioral genetic analysis of twins, the composition of the common protocol, and the need for further funding in order to fully exploit the potential from this unique study. Some additional notes for this work package:

• In the case of dizygotic twins, there is the possibility that "due" to genotype one twin in the family will evince greater intergenerational transmission than the other. This will afford determination whether the same genetic moderators of transmission are operative in both twin conditions. If this were the case, it would certainly be notable.

• The consortium should optimize the use of valuable resources. The funding being allocated to these cohorts seems disproportionately small to what they have to offer to CID. For example, some
unique groups that have been identified (in particular the twins who are themselves parents of twins) should be phenotyped in more depth to gain maximum value. In general, it seems that there is little effort being made to harmonize phenotyping of the new cohorts which are being initiated with that already available, for example in making sure a common set of (ASEBA) instruments is used.

**Work package 4: Animal and mathematical models**

A broad and exciting research program on the effects of early social or environmental deprivation stressors on rodent brain and behavioral development was presented. These studies parallel many of the human studies in work packages 1-3 and could more easily address mechanisms of behavioral and brain changes. Additional projects on computational modeling and song learning in birds were also discussed.

The Advisory Board comments focused on issues such as the feasibility of extending the range of rodent pup measures recorded to assess change across development (albeit that this is acknowledged to be challenging), and the degree to which modeling and song bird program were integrated with the other work packages. Some additional notes for this work package:

- Pay attention at investigating physiological, somatic and/or behavioral indicators of reproductive strategy (e.g., puberty, sexual behavior, parenting). Also investigate whether these indicators are affected (as Meaney found as a result of early deprivation experiences).
- Consider evaluating "the prenatal programming of post-natal plasticity" given human evidence that (a) prenatal stress fosters infant/toddler negative emotionality and physiological reactivity and (b) that each of these phenotypic "outcomes" themselves operate as plasticity factors, moderating post-natal environmental effects.

**Overall comments:**

This is a highly innovative and world-leading set of projects in which excellent progress has already been made. In addition, the grant significantly adds value to existing projects and cohorts. Most human projects are at the final planning/piloting stage and it is anticipated that preliminary results from new cohorts may be available for the next Advisory Board visit. The Advisory Board was impressed by the young investigators supported by the consortium and emphasized the importance of continued support of this significant interdisciplinary research.

From an ethical point of view attention was asked for bringing the acquired knowledge and insights to society in general and the medical society in particular. Extensive funding and time spent by professionals and research subjects alike requires justification in the context of health care and clinical utility. The program has a huge potential for exploring determinants of adolescent behavior and to make (prospective) parents and teachers more knowledgeable how to achieve “the best” for future generations.
Appendix 14 – Application forms for appointments PhD students and postdocs

A. Application form for principal investigator budget

NWO Gravitation
Consortium Individual Development (CID)
Application Form Research Proposals PIs

NOTE: For every PhD student or postdoctoral researcher, separate application forms have to be filled in.

<table>
<thead>
<tr>
<th>WORK PACKAGE NUMBER:</th>
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<tr>
<td>WORK PACKAGE LEADER:</td>
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<tr>
<td>FIRST PI (Main applicant):</td>
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<tr>
<td>SECOND PI (Co-applicant):</td>
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**APPLICATION FOR:**

<table>
<thead>
<tr>
<th>PhD student</th>
<th>Postdoctoral researcher</th>
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<tr>
<td>For PhD students we use a standard duration of 4 years.</td>
<td>Duration:</td>
</tr>
</tbody>
</table>

When deviation from the standard duration of 4 years for PhD students is desired, please give an explicit explanation below:

**STARTING DATE**:  
*NOTE: The starting date has to be within maximally 6 months after acceptance*

**GENERAL PROJECT (title or running head)**

### 1. Applicant(s)

#### 1a. Main applicant (First PI)

<table>
<thead>
<tr>
<th>Name, titles</th>
<th>M / F</th>
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**Correspondence address**

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<tr>
<th>Faculty &amp; Department</th>
<th>Address</th>
<th>Postal code</th>
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<td>Telephone</td>
<td>E-mail address</td>
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#### 1b. Co-applicant (Second PI)

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<th>Name, titles</th>
<th>M / F</th>
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**Correspondence address**

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<td>Telephone</td>
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1c. Possible other co-applicant(s)

<table>
<thead>
<tr>
<th>Name, titles</th>
<th>Faculty/Department</th>
<th>M / F</th>
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</table>

2. Title and summary of the proposed project

**English (compulsory)**

**Dutch (optional)**

**Summary of the project (max. 200 words)**

3. Contribution to work package research questions

<table>
<thead>
<tr>
<th>Key theme(s)</th>
<th>Relation to the work package (max. 100 words)</th>
</tr>
</thead>
</table>

4. Budget

**NOTE 1:** Please, note carefully that the maximum budget that can be requested should not exceed the total budget per PI for the first 5 years of the project. This budget can be used for personnel and for material costs.

**NOTE 2:** Please attach the supplementary budget specification and make sure the specification is approved and signed by the financial controller. Only proposals with signed specifications will be taken under consideration.

<table>
<thead>
<tr>
<th>Total costs (as from specification)</th>
<th>k€</th>
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<tr>
<td>Personnel</td>
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<td>Material</td>
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</table>

5. Description of the proposed project (max. 1,000 words, excl. references; address a through d explicitly)

a) Topic and scientific relevance.

b) Methodological approach.

c) Innovative capacity.

d) References (max. 1 page; not included in word count)
6. Signature

I hereby declare that I have completed this form truthfully and that the co-applicant(s) fully support this proposal.

Main applicant:                      City:

Date (D-M-Y):

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THIS SECTION WILL BE FILLED OUT BY PROJECT MANAGEMENT

Date received:                      Procedure agreed (signature project manager):

Judgment WP leader:

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Judgment Steering Committee:

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<td>Signature:</td>
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WBS number (when available):

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### 1. BASIC DETAILS

**COHORT NAME:**

**COHORT REPRESENTATIVE:**

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<th>APPLICATION FOR:</th>
<th>PhD student</th>
<th>Postdoctoral researcher</th>
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<td>For PhD students we use a standard duration of 4 years.</td>
<td>Duration:</td>
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When deviation from the standard duration of 4 years for PhD students is desired, please give an explicit explanation below:

**STARTING DATE¹:**

¹ NOTE: The starting date has to be within maximally 6 months after acceptance

**GENERAL PROJECT (title or running head)**

### 1. Applicant(s)

**Main applicant (Cohort Representative)**

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<th>Name, titles</th>
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**Correspondence address**

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<th>Faculty &amp; Department Address</th>
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**Possible co-applicant(s)**

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<td>Faculty/Department</td>
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</table>

### 2. Title and summary of the proposed project

**English (compulsory)**

**Dutch (optional)**
Summary of the project (max. 200 words)

3. Contribution to the cohort

**Key theme(s)**

**Relation to the cohort (max. 100 words)**

4. Budget

**NOTE 1:** Please, note carefully that the maximum budget that can be requested should not exceed the total budget for the first 5 years of the project. This budget can be used for personnel and for bench fee costs.

**NOTE 2:** Please attach the supplementary budget specification and make sure the specification is approved and signed by the financial controller. Only proposals with signed specifications will be taken under consideration.

| Total costs (personnel and bench fee as from specification) | € |

5. Description of the proposed project (max. 1,000 words, excl. references; address a through d explicitly)

a) Topic and scientific relevance.

b) Methodological approach.

c) Innovative capacity.

d) References (max. 1 page; not included in word count)

6. Signature

I hereby declare that I have completed this form truthfully and that the co-applicant(s) fully support this proposal.

Cohort Representative: __________________________ City: __________________________

Date (D-M-Y): __________________________
**THIS SECTION WILL BE FILLED OUT BY PROJECT MANAGEMENT**

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<tr>
<th>Date received:</th>
<th>Procedure agreed (signature project manager):</th>
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<th>Judgment Steering Committee:</th>
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<th>WBS number (when available):</th>
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C. Application form for PhD students and postdocs from co-funding budgets

**NWO Gravitation**

**Consortium on Individual Development (CID)**

**Form CID personnel not financed by the consortium**

**NOTE:** For every person separate forms have to be filled in.

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<th>WORK PACKAGE NUMBER:</th>
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<tr>
<td>WORK PACKAGE LEADER:</td>
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<tr>
<td>FIRST PI (Main applicant):</td>
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<tr>
<th>APPLICATION FOR:</th>
<th>PhD student</th>
<th>Postdoctoral researcher</th>
<th>Other:</th>
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<td>Duration:</td>
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**Details CID employee not financed by the consortium:**

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<th>Name</th>
<th>Faculty &amp; Department</th>
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**This person is financed by:**

- Directly from the government
- From the government through a funding allocation agency
- By contracts with third parties, namely:
  - Other:

**STARTING DATE¹:**

¹ **NOTE:** The starting date has to be within maximally 6 months after acceptance

**GENERAL PROJECT TITLE**

1. Applicant(s)

1a. Main applicant (First PI)

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<th>Name, titles</th>
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**Correspondence address**

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1b. Possible co-applicant(s)

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<th>Name, titles</th>
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| Faculty/Department | |

2. Title and summary of the project

**English (compulsory)**

**Summary of the project (max. 200 words)**
### 3. Contribution to work package research questions and CID

<table>
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<tr>
<th>Key theme(s)</th>
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<tr>
<th>Relation to the work package (max. 100 words)</th>
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<tr>
<th>Contribution to CID (max. 100 words)</th>
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<tr>
<th>CID data used for this project (max. 100 words) - Optional -</th>
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### 4. Signature

I hereby declare that I have completed this form truthfully and that the co-applicant(s) fully support this proposal.

Main applicant: 

City: 

Date (D-M-Y):

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**THIS SECTION WILL BE FILLED OUT BY PROJECT MANAGEMENT**

Date received: 

Procedure agreed (signature project manager):

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Judgment Steering Committee:

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CONSORTIUM AGREEMENT
regarding
GRAVITATION PROGRAMME (ZWAARTEKRACHTPROGRAMMA)
‘INDIVIDUAL DEVELOPMENT’

BETWEEN

1) UNIVERSITEIT UTRECHT, a legal entity established under the laws of the Netherlands and governed by public law under section 1.8 of the Higher Education and Research Act (Wet op het hoger onderwijs en wetenschappelijk onderzoek) and having its registered offices at Heidelberglaan 8, Utrecht, the Netherlands, hereinafter also referred to as “Universiteit Utrecht” or “Coordinator”;

AND

2) UNIVERSITY MEDICAL CENTER UTRECHT, a legal entity established under the laws of the Netherlands and governing by public law under section 1.13 of the Higher Education and Research Act (Wet op het hoger onderwijs en wetenschappelijk onderzoek) having its registered office at Heidelberglaan 100, 3584 CX Utrecht, the Netherlands, hereinafter also referred to as “UMCU”,

AND

3) VU UNIVERSITY AMSTERDAM, a constituent part of the legal entity “VU-VUmc Foundation”, a legal entity established under the laws of the Netherlands having its registered office at De Boelelaan 1107, 1081 HV Amsterdam, the Netherlands, hereinafter also referred to as “VU”,

AND

4) UNIVERSITY OF AMSTERDAM, a legal entity established under the laws of the Netherlands having its registered office at Spui 21, 1012 WX Amsterdam, the Netherlands, hereinafter also referred to as “UvA”,

AND

5) LEIDEN UNIVERSITY, a legal entity established under the laws of the Netherlands having its registered office at Rapenburg 70, 2311 EZ Leiden, the Netherlands, hereinafter also referred to as “LU”,

AND

6) UNIVERSITY MEDICAL CENTER GRONINGEN, a legal entity established under the laws of the Netherlands having its registered office at Hanzeplein 1, 9713 GZ Groningen, the Netherlands, hereinafter also referred to as “UMCG”,

AND

7) RABOUD UNIVERSITY, a legal entity established under the laws of the Netherlands having its registered office at Geert Grootplein-Noord 9, 6525 EZ Nijmegen, the Netherlands, hereinafter also referred to as “RU”,

AND
8) **ERASMUS UNIVERSITY MEDICAL CENTER ROTTERDAM**, an institution organized in accordance with public law of the Netherlands (article 1.13,2 WHW), with principal place of business at 's-Gravendijkwal 230, 3015 CE Rotterdam, The Netherlands, acting exclusively for and on behalf of its Department of Child and Youth Psychiatry, hereinafter also referred to as "Erasmus MC."

Together also the "Parties" and each a "Party", as the case may be,

**REQUITALS:**

A. Parties all have considerable experience and knowledge in the field of developmental research;
B. Parties have submitted a research proposal for the Gravitation Programme (Zwaartekrachtprogramma) of OCW, as attached to this Agreement in Annex 1;
C. OCW has granted on November 9, 2012, to Utrecht University in its capacity as main applicant a subsidy of €14.800.000,- for the period 2012-2016 for the Consortium Individual Development: "Why some children thrive, and others don't", as attached to this Agreement in Annex 2. This grant relates to a period of five (5) years; and may be extended by OCW for another period of five (5) years, depending an evaluation at the end of the fourth year;
D. Parties wish to cooperate and share knowledge with regard to this specific subject matter by making contributions in cash or in kind (by means of research);
E. Parties therefore wish to enter into a consortium agreement formalizing these intentions on the terms and conditions set out herein.

**THE PARTIES HEREBY AGREE AS FOLLOWS:**

**Clause 1. Definitions**

1.1 In this Agreement:

"Access Rights" means licenses and use rights;
"Administrative Manager" means the consortium body as described in Clause 5.1;
"Agreement" means this Consortium Agreement between Parties including all Annexes;
"Annex" means an annex to this Agreement;
"Background IP" means the Intellectual Property Rights that are owned by each Party prior to the commencement of a Research Project and / or developed independently from a Research Project but during the term of the Agreement, and listed as Background IP in a Project Agreement.
"Clause" means a clause of this Agreement;
"Cohort Representative" means the leader of a cohort, as identified in Annex 5 to this Agreement;
"Confidential Information" means any information including, but not limited to business information, Know How, Foreground IP or Background IP the Parties communicate to or share with each other in...
relation to the performance of a Research Project, and which has been clearly marked or identified as "confidential";

"Coordinator"
"Existing Know How"
means Universiteit Utrecht;
means Know How that each Party owns at the date of this Agreement as well as Know How that each Party acquires or develops during the term of this Agreement unrelated to a Research Project;

"Foreground IP"
means the Intellectual Property Rights arising from the performance of a Research Project, and excluding Background IP and Existing Know How;

"Know How"
means all know how, knowledge, information, drawings, designs, specifications, range-charts, photo’s, models, processes, procedures, regulations, instructions, reports, publications, articles, correspondence, as well as all other technical or commercial information, company information, research information, research results, data and documents of whatever nature, whether acquired verbally, in writing or on any (other) data carrier;

"Intellectual Property Rights"
means all rights relating to any copyright (auteursrecht), patent (octrooi) patent application, trade name (handelsnaam), trademark (merk), database (databank), plant variety rights (kwakersrecht), designs and models (teken- en modellen), utility models, chips, topography of semiconductor products (topografie van halfgeleiderprodukten), neighboring right (naburig recht), including applications for registration of any of them under the laws of the Netherlands and any similar or equivalent forms under any law or jurisdiction;

"Joint Foreground IP"
has the meaning ascribed thereto in Clause 8.2.2 below;

"Member"
means a natural person appointed by a Party as its representative in a specific consortium body;

"New Know How"
means Know How that each Party acquires or develops in the course of a Research Project during the term of this Agreement;

"Party" or "Parties"
has the meaning ascribed thereto underneath paragraph 2) above;

"Postponement Notice"
has the meaning ascribed thereto in Clause 7.3 below;

"Principal Investigator" or "PI"
means a natural person responsible for the execution of a specific Research Project;

"Project Agreement"
means an agreement related to this Consortium Agreement with regard to a
specific Research Project;
means the budget with regard to carry out a
specific Research Project, as set out in an
Annex to the related Project Agreement;

"Programme Chair"
means the consortium body as described in
Clause 5.1;

"Programme Budget"
means the budget with regard to carry out the
Research Programme as initially set out in
Annex 3;

"Publication Notice"
has the meaning ascribed thereto in Clause
7.2 below;

"Research Programme"
means the Gravitation Programme
(Zwaartekrachtprogramma), financed by the
Ministry of OCW, and further elaborated into
several Research Projects, including the terms
and conditions under which the award was
made, as attached to this Agreement in Annex
2;

"Research Project"
means a research project as described in a
separate Project Agreement;

"Workpackage"
means the workpackage as defined in the
Research Programme;

"Workpackage Leader"
means the leader of a Workpackage, as
identified in Annex 5 to this Agreement;

"Work Plan"
means a cluster of tasks or specific work to be
performed for a Research Project under a
Project Agreement, as identified as such in the
Research Programme.

1.2 In this Agreement headings are used for ease of reference only and shall
not control or affect the meaning or construction of any Clause or
provision hereof.

Clause 2. Purpose of the Agreement and execution of the Research
Programme

2.1. The purpose of this Consortium Agreement is to specify the aim of
 collaboration regarding the Consortium Individual Development, the
relationship among the Parties, in particular concerning the organisation of
the work between 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.

2.2. Parties all have considerable experience and knowledge in the field of
developmental research or are otherwise active in this field and wish to co-
operate and share knowledge with regard to this specific subject. Parties
envisage that – for the duration of this Agreement – research will be
conducted, knowledge will be shared and financial contributions will be
made in order to implement the Research Programme.

2.3. Parties shall carry out their activities under the Agreement in accordance
with the subsidy conditions of the Research Programme, including
complying with the administrative requirements thereunder.

2.4. The contributions of Parties shall be in-kind and/or cash. For each Research
Project relevant Parties shall draft a Project Budget in which the financial
specifics of its in-kind and/or cash contribution will be laid down. Each
Project Budget will be annexed to the relevant Project Agreement and shall form an integral part of that Agreement.

2.5. Each Party shall carry out a specific part of the Research Programme, divided into several Research Projects. Each Research Project will be laid down in a Work Plan as attached as annex to the relevant Project Agreement.

2.6. Each Party undertakes to every other Party to use reasonable endeavours to perform and fulfil, promptly, actively and on time, all of its obligations under this Agreement. Each Party further undertakes in accordance with all applicable laws and regulations and to the best of its ability and on the terms and conditions set out in each Project Agreement, Research Project, Programme Budget and in this Agreement.

Clause 3. Performance obligations all Parties and Coordinator

3.1 Following Clauses 2.5 and 2.6 above each Party has to take into account the following obligations:

a) Ensure that all relevant information and communications is sent to the Administrative Manager, so that Administrative Manager is able – if necessary - to distribute this information to the other Parties;

b) Take all necessary and reasonable measures to ensure that the research as described in the Research Project is carried out accordingly and in accordance with the applicable laws and regulations and with the terms and conditions of this Agreement.

c) Make appropriate arrangements for the proper performance of the work it is responsible for, as identified in the Research Project. For this purpose, Party shall designate one representative who shall act as a liaison officer for that Party and work in cooperation with the Administrative Manager. The name and contact details of that representative designated shall be included in the list of names and contact details;

d) Inform Administrative Manager of any event which substantially affects the execution of the Research Project and/or the carrying out of the research as described in the Project Agreement;

e) Ensure that any agreements entered into between the Party and any third party, contains terms and conditions not less stringent as the terms and conditions set out in this Agreement;

h) Take all reasonable steps to avoid commitments that to the best of its knowledge are incompatible with the obligations provided for in this Agreement and inform the other Parties – via the Administrative Manager - of any obligations which may arise during the duration of this Agreement which may have implications for any of its obligations under this Agreement;

i) Upon receipt of a written request, provide all relevant data requested by the Administrative Manager for the administration purposes required under the conditions of the Research Programme.

3.2 Each Party which has to execute a Research Project shall supply to the other Parties via the Administrative Manager the following deliverables in
order to keep every Party informed of the progress of the Research Project:

- bi-annual update-reports (every six months); and
- annual reports (every twelve months); and
- a comprehensive report after completion of the Research Project.

3.3 Coordinator

3.3.1 The Coordinator shall be the intermediary between the Parties and OCW and shall perform all tasks assigned to it as described in this Consortium Agreement.

3.3.2 In particular, the Coordinator shall be responsible for:

- Monitoring compliance by the Parties with their obligations;
- collecting, reviewing to verify consistency and submitting reports and other deliverables (including financial statements and related certifications) to OCW;
- Transmitting documents and information connected with the Research Programme to any other Parties concerned; and
- Administering the financial contribution of OCW and fulfilling the financial tasks described in Clause 4.

3.3.3 The Coordinator shall not be entitled to act on behalf of or to make legally binding declarations on behalf of any other Party.

3.3.4 The Coordinator shall not enlarge its role beyond the tasks specified in this Consortium Agreement.

Clause 4. Financial provisions and payments

4.1 General Principles

4.1.1 Distribution of Financial Contribution

The financial contribution of OCW to the Research Programme shall be distributed by the Coordinator according to:
- the Programme Budget as included in the Research Programme; and
- the provisions of payment in Clause 4.2.

A Party shall be funded only for its tasks carried out in accordance with the Research Programme or any amendment thereof approved by the Parties.

4.1.2 Justifying Costs

In accordance with general accounting and management principles and practices, each Party shall be solely responsible and liable for justifying its costs with respect to its activity in each Research Project towards OCW. Neither the Coordinator nor any of the other Parties shall be in any way liable or responsible for such justification of costs towards OCW.

4.2 Payments

4.2.1 Payments to Parties are the exclusive tasks of the Coordinator.

In particular, the Coordinator shall:

- notify the Party concerned promptly of the date and composition of the amount transferred to its bank account, giving the relevant references
- perform diligently its tasks in the proper administration of any funds and in maintaining financial accounts

4.2.2 Payment schedule

The payment schedule, which contains the transfer of pre-financing and interim payments to Parties, will be handled according to the following:

Funding of costs included in the Research Programme will be paid to Parties after receipt from OCW without undue delay, provided that:
- relevant Research Projects and Project Budgets are approved;
- Parties are not defaulting nor otherwise in breach of its obligations under this Agreement.

The Coordinator is entitled to withhold any payments due to a Party identified by the Steering Committee to be in breach of its obligations under this Consortium Agreement. The Coordinator is entitled to recover any payments already paid to a defaulting Party.

Clause 5. Governance structure

5.1 General structure, tasks & decisions

The organisational structure of the Consortium shall comprise of:

- the Supervisory Board;
- the Steering Committee;
- Programme Chair;
- Programme Support Office;
- Ethical Advisory Board;
- Scientific Advisory Board;
- Workpackage Leaders;
- Cohort Representatives;

5.1.1 Supervisory Board

- The Supervisory Board shall consist of one representative of each Party, being the dean or the division leader of the involved faculty or division of each Party. The Programme Chair of the Steering Committee shall chair all meetings of the Supervisory Board, unless decided otherwise in a meeting of the Supervisory Board. The function of the Programme Chair of the Steering Committee is not compatible with the function of Member of the Supervisory Board.

- The Supervisory Board is the Consortium’s supervisory and ultimate decision-making body. Each Party shall have one vote. The Steering Committee requires the approval of the Supervisory Board on the annual reports and the annual accounts.

- The Supervisory Board has the right to give advice to the Steering Committee on all matters mentioned in Clause 5.1.2, fourth paragraph, as well as on its own initiative.

5.1.2 Steering Committee and Programme Chair

- The Members of the Steering Committee shall be the main applicant and the four Workpackage Leaders, as identified in the Research Programme attached as Annex 1 to this Agreement. As from the start of the Research
Programme, two additional Members, who are co-applicants but not Workpackage Leaders, shall also be part of the Steering Committee. However, these two Members shall not be replaced in case of their retirement. The Members of the Steering Committee are identified in Annex 5 to this Agreement.

- The Steering Committee shall be chaired by a Programme Chair, who shall be a representative of Universiteit Utrecht.

- The Programme Chair has the following tasks:
  o Organize and chair the meetings of the Steering Committee;
  o Implement the Steering Committee's policy with respect to scientific direction, coherence and cooperation between the WPs;
  o Quick resolution of all conflicts related to this Agreement.

- The Steering Committee ensures the general management of the Research Programme and has four main tasks:
  • Steer the scientific progress of the Research Programme and ensure communication, coherence and cooperation between the different WPs;
  • Maintain an up-to-date training program in cooperation with the Participants Graduate Programmes;
  • Monitor scientific progress within each WP, decide on ethical issues, approve project output to be dispatched to OCW;
  • Decide on financial, administrative, and contractual matters, within the limits set by the Supervisory Board.

- The Steering Committee shall be free to act on its own initiative to formulate proposals and take decisions in accordance with the procedures set out herein. In addition, all decisions made by the Supervisory Board shall also be implemented and acted upon by the Steering Committee. The Steering Committee informs the Supervisory Board of all major developments.

- The following decisions shall be taken by the Steering Committee:
  o modifications to the Research Projects, Project Budgets and Programme Budget;
  o approval of the Research Projects, Workplans and Project Budgets, as well as alterations of these documents;
  o entry of a new party to the Consortium and approval of the settlement on the conditions of the accession of such a new party;
  o withdrawal of a Party from the Consortium and the approval of the settlement on the conditions of the withdrawal;
  o declaration of a Party to be a defaulting Party;
  o remedies to be performed by a defaulting Party within 30 days after declaration of default;
  o termination of a defaulting Party’s participation in the Consortium and measures relating thereto;
  o all other decisions as laid down in this Agreement, both implicit as well as explicit.

- The Steering Committee shall seek advice from the Supervisory Board on ways to rearrange tasks and budgets of the Parties concerned. Such rearrangement shall take into consideration the legitimate commitments taken prior to the decisions, which cannot be cancelled.
5.1.3 Programme Support Office

- The Programme Support Office shall be appointed by the Coordinator.
- The Programme Support Office shall consist of the Administrative Manager, a financial officer and a communication officer.

- The Programme Support Office shall assist and facilitate the work of the Steering Committee and the Coordinator for executing the decisions of the Steering Committee as well as the day-to-day management of the Programme.

Administrative Manager

- The Administrative Manager shall be appointed by the Coordinator.

- The Administrative Manager shall be responsible for:
  - The day-to-day management of the Research Programme;
  - monitoring compliance by the Parties with their obligations;
  - collecting, reviewing of, verifying consistency and submitting reports and other deliverables to the Steering Committee and OCW;
  - preparing the decisions and agenda of meetings of the Steering Committee;
  - implementing the decisions of the Steering Committee;
  - organising administration of the Research Programme;
  - execute all other specific tasks which are laid down in the various clauses of this Agreement.

Financial officer

- The financial officer shall be appointed by the Coordinator.

- The financial officer shall be responsible for fulfilling the financial tasks under this Agreement.

Communication manager

- The communication manager shall be appointed by the Coordinator.

- The communication manager shall be responsible for managing dissemination of project results in cooperation with the Administrative Manager.

5.1.4 Ethical Advisory Board (EAB)

- The Ethical Advisory Board is an advisory board to the Research Programme in general and will advise the Steering Committee.

- The Ethical Advisory Board is composed of at least four experts with detailed knowledge of ethical policies. Experts who make up the committee shall represent the various interests involved, including human and animal research expertise, data protection, biobank and database specialties. Nominations for membership of the Ethical Advisory Board may be submitted to the Steering Committee by any Party. The Steering Committee shall ensure that the composition of the EAB is appropriate to provide the guidance required. Members of the EAB shall be approved by
the Steering Committee.

- The Ethical Advisory Board will meet according to the needs of the Research Programme but at least once a year during the Research Programme.

- The Ethical Advisory Board will be general responsible for:
  (a) monitoring the proper application of the ethical rules by Parties;
  (b) providing advice to Parties on ethical issues and
  (c) providing advice on the compliance with European ethical laws and regulations and with different guidelines, laws and regulation of countries where studies are being performed.

5.1.5 **Scientific Advisory Board (SAB)**

- The Scientific Advisory Board is an advisory board to the Research Programme in general and will advise the Steering Committee.

- The Scientific Advisory Board shall:
  (a) meet upon request;
  (b) provide advice to the Steering Committee upon request of the Steering Committee; and
  (c) provide recommendations to the Steering Committee upon request of the Steering Committee as decision making support.

- The Scientific Advisory Board shall consist of at least three members. Nominations for membership of the Scientific Advisory Board may be submitted to the Steering Committee by any Party. The Steering Committee shall ensure that the composition of the SAB is appropriate to provide the guidance required to achieve Research Programme goals and shall invite nominees to the SAB accordingly. Members of the SAB shall be approved by the Steering Committee.

- Upon request of the Steering Committee, the Scientific Advisory Board will be able to call to meetings additional experts covering particular fields of expertise on a case by case basis.

5.1.6 **Work Package Leader**

- The Research Programme is subdivided in the following Work Packages (WP), each led by a Work Package Leader (WP Leader):

  Work Package 1 Brain development;
  Work Package 2 Interventions;
  Work Package 3 Intergenerational transmission;
  Work Package 4 Animal and mathematical modelling.

- Each WP Leader has the following main tasks:
  
  - Implementation of the Steering Committee's policy with respect to scientific direction, coherence, and cooperation between the WPs for their own WP. This is done in cooperation with their co-researchers, the Cohort Representative(s) of the relevant cohorts and, in projects that require cooperation with other WPs, with the leaders of those WPs;

  - Monitoring of the scientific progress of their WP. Each WP Leader organizes a quarterly meeting with the co-researchers and relevant Cohort Representative(s) to discuss progress and the compare the actual
achievement with the goals and deliverables set in the WP work plan. All project results are communicated with the Administrative Manager who collects the outputs of all WPs;

- Active participation in the dissemination of the project results through contribution to workshops, information bulletins, courses, and television production.

- Organisation of the management of the scientific staff (PhD/postdoc) that is related/assigned to their WP. The WP leader advises on the term/position (PhD or postdoc) of employment, in consultation with the PIs that will be responsible for supervision.

5.1.7 Cohort Representatives

- Two new cohorts will be implemented in the Research Programme: a longitudinal cohort (based in Utrecht) and an intervention cohort (based in Leiden). In addition, four other existing cohorts are involved: Trails (Groningen), GenerationR (Rotterdam), Radar (Utrecht), NTR (Amsterdam). For each cohort a CID representative will be appointed, who should be one of the Principal Investigators. The Steering Committee decides on the appointment.

- The Cohort Representative is responsible for the organisation of measurements that are needed to achieve the scientific goal of the WP they are related to. Decisions in this respect are made in cooperation with the associated WP Leader.

- The Cohort Representative is responsible for the organisation of the financial management of their cohort (or the part that is relevant for the WP), in cooperation with the associated WP Leader. The Cohort Representative manages the budget and establishes financial reports with local support, following the instructions of the financial officer of the Programme Support Office.

- The Cohort Representative is involved in a data management committee that will be concerned with possibilities of data exchange between cohorts and availability of the data to members of the consortium and third parties.

- Procedure decision on cohorts:

1) The Cohort Representative, in cooperation and agreement with the WP leader involved, writes a proposal (a cohort plan) that includes the planned measurements and the requested budget.
2) The Steering Committee decides on funding, and decides whether the proposal fits in with the dedicated budget.
3) If approved by the Steering Committee, the Programme Chair informs the financial officer to transfer costs to the Party or Parties involved, following the procedure of Clause 4.2.2.
4) For the new cohorts, it will be possible to request funding by writing a proposal (a cohort plan) on the structure and requirements of the cohort.

- Procedure for decision on proposals and implementation (PhD/postdoc) project:
1) Principal Investigator writes a research proposal in a specified format in cooperation with the WP leader, who should agree both on content and on timeline(s), and whether the requested funding fits within the CID budget of the PI.

2) The format should include specifically how the proposal relates to the WP, who will be the second supervisor from a different theoretical background (this should in principle be one of the other PIs).

3) The Steering Committee decides.

4) If approved, the Programme Chair informs the financial officer to transfer funds to the Parties.

5) The funding will initially be for one year; the WP Leader and the Steering Committee evaluate the progress of the project and decide on funding for the rest of the period.

5.1.8 PI meeting

At least annually all Principal Investigators involved in the Research Programme shall meet and discuss informally the progress of the Research Programme and the Research Projects.

5.2 Meetings and agenda

5.2.1 The Steering Committee meets at least 4 (four) times a year or at any time upon written request of any Member of the Steering Committee.

5.2.2 The Supervisory Board meets at least once a year or at any time upon written request of (a Member of) the Steering Committee and/or (a Member of) the Supervisory Board.

5.2.3 The Programme Chair shall prepare and send each Member and to all of the Members of the Supervisory Board, a written (original) agenda no later than 14 (fourteen) calendar days before the meeting of the Supervisory Board or the Steering Committee as the case may be.

5.2.4 Any Member of the Steering Committee or the Supervisory Board may add an item to the original agenda by written notification to all of the other Members of the Steering Committee or the Supervisory Board.

5.2.5 Meetings of the Steering Committee may also be held by teleconference or other telecommunication means.

5.2.6 Decisions will only be binding once the relevant part of the minutes has been accepted.

5.3 Voting rules and quorum

5.3.1 The Steering Committee as well as the Supervisory Board shall not deliberate and decide validly unless two-thirds (2/3) of its Members are present or represented (quorum).

5.3.2 Each Member of the Steering Committee and the Supervisory Board shall have 1 (one) vote. Each Member may appoint a replacement to attend a meeting on his/her behalf.

5.3.3 Defaulting Parties may not vote, nor shall its presence account for the necessary quorum.
5.3.4 Decisions shall be taken by majority of the votes. The Programme Chair does not have the right to clear an even voting scenario by a tie-breaking vote. In case of an even voting a new voting shall take place in order to achieve consensus.

5.3.5 A change in the Programme Budget and/or the total contribution from one of the Parties requires the consent from all those Parties affected.

5.3.6 Each Member may give a power of attorney to another Member. A Member can have a power of attorney of no more than one other Member.

5.4 Veto rights

5.4.1 A Party which can show that its own work, time for performance, costs, liabilities, intellectual property rights or other legitimate interests would be severely affected by a decision of the Steering Committee, may exercise a veto with respect to the corresponding decision or relevant part of the decision.

5.4.2 A Party may not veto decisions relating to its identification as a defaulting Party. The defaulting Party may not veto decisions relating to its participation and termination in the Consortium or the consequences of them.

5.4.3 A Party requesting to leave the Consortium may not veto decisions relating thereto.

5.4.4 A decision can only be vetoed during the meeting it was taken, unless the decision was related to a point not on the original agenda, as sent out in accordance with Clause 5.2.3.

5.5 Minutes of meetings

5.5.1 The Administrative Manager of the Programme Support Office shall produce written minutes of each meeting which shall be the formal record of all decisions taken. He shall send, on behalf of the Programme Chair, the minutes by e-mail to all Members of the Steering Committee, and to all of the Members of the Supervisory Board, within ten (10) calendar days of the meeting.

5.5.2 The minutes shall be considered as accepted if, within fifteen (15) calendar days from sending, no Member has objected in writing to the Programme Chair with respect to the accuracy of the draft of the minutes.

5.5.3 The Programme Chair shall send the accepted minutes to all the Members of the Steering Committee, the Supervisory Board and to the Administrative Manager, who shall safeguard them.

5.5.4 In event of objections by a Party, the Programme Chair shall discuss with the objecting Party and other involved Parties and attempts to find a solution to the general satisfaction of all Parties.

5.5.5 The objected decision shall not come into force until the Steering Committee has come to a new decision. This decision can be made in an extraordinary meeting or outside a meeting by email or other telecommunications means. If this decision is made outside the meeting, all Members of the Steering Committee must decide unanimously. To this decision no further appeal is open.

Execution copy 31 May 2013
Clause 6. Confidentiality

6.1 Each Party agrees to treat the Confidential Information as confidential and agrees not to disclose the same to any third party without the prior written consent of the Party providing the Confidential Information, without prejudice to the right of a Party to disclose all results of the Research Project at any time as set out in Clause 7 (Publication).

6.2 A Party may not disclose any of the Confidential Information to its own officers and employees except to those directly engaged in the performance of this Agreement for whom it is necessary to know such information for the sole purpose of performing the obligations under this Agreement, and only to the extent necessary for this purpose. Prior to the disclosure of the Confidential Information, the relevant officers and employees will be required to agree in writing to keep the relevant Confidential Information confidential in accordance with the terms of this Agreement during and after the termination of their employment or other arrangement with the relevant Party.

6.3 The obligations set out in Clause 6.1 and 6.2 no longer apply where the Confidential Information:

6.3.1 is or becomes publicly known without the involvement of the receiving Party;

6.3.2. at the time of receipt is already known to the receiving Party and is not subject to any (other) obligation of confidentiality, to be notified to the other Party immediately and to be proofed on demand by sufficient written evidence;

6.3.3 will after the time of receipt be obtained by the receiving Party from an independent source, under which circumstances the receiving Party disclosing the Confidential Information may not reveal that it has already received the relevant Confidential Information from the providing Party;

6.3.4 has been independently developed by the receiving Party to be proofed on demand by sufficient written evidence;

6.3.5 is disclosed pursuant to the requirement of any statute or regulation or the order of any Court of competent authority. If such a situation occurs, Parties shall inform each other promptly of such requirement or order in order to assist in minimizing the disclosure.
Clause 7.  Publication

7.1 Parties are entitled to publish in written form, oral presentation or making public in any other form (including electronic publication on the internet) (the "Publication") results of the Research Project, including but not limited to the Foreground IP, both during the term of the Agreement as well as after the termination thereof, taking into account clause 6 (Confidentiality).

7.2 The publishing Party shall inform all other Parties involved by sending a written notice (the "Publication Notice") attaching the draft Publication.

7.3 Within fifteen (15) days of the date of the Publication Notice, the other Party may request postponement of a maximum of sixty (60) days after the date of the Publication Notice, or alterations of the Publication by submitting a written notice (the "Postponement Notice") in order to protect any Foreground IP or to remove any of its Confidential Information under this Agreement of the other Party without infringing the scientific integrity (wetenschappelijke integriteit) of the publishing Party.

7.4 If the publishing Party has not received a Postponement Notice within fifteen (15) days of the date of the Publication Notice, the publishing Party shall be free to publish the Publication.

7.5 If needed, Parties may make additional working arrangements on the publication policy and (co)authorship. Proposals for such arrangements may be added to the agenda of the Steering Committee by each Party.

Clause 8.  Intellectual Property Rights - Ownership

8.1 Ownership of Background IP

Each Party shall remain the owner and shall retain control of the Background IP owned by it.

8.2 Ownership of Foreground IP

8.2.1 Foreground IP

Foreground IP shall be the property of the Party whose employees, researchers, research fellows, individuals equivalent to those persons make the inventive step, or the creative step (in case of non-patent IP), carrying out the work generating that Foreground IP.

8.2.2 Joint Foreground IP

Foreground IP shall be the property of both or more Parties in the event employees, researchers, research fellows, individuals equivalent to those persons jointly make the inventive step, or the creative step (in case of non-patent IP), carrying out the work generating that Foreground IP and where their respective share of the invention or the work as the case may be cannot be ascertained.

8.3 Protection, maintenance and costs of Foreground IP

8.3.1 Each Party is responsible for the application, acquisition and/or maintenance of its own Foreground IP and shall bear the costs relating to it.
8.3.2 In the event of Joint Foreground IP Parties together are responsible for the application, acquisition and/or maintenance of that Joint Foreground IP. Joint owners of any Joint Foreground IP shall enter into an agreement to determine their participation in such Joint Foreground IP; the costs of application, acquisition and/or maintenance of the Joint Foreground IP and the revenue distribution shall follow such participation.

8.3.3 In the event of Joint Foreground IP, Parties shall make additional arrangements with regard to application, acquisition and/or maintenance of that Joint Foreground IP and shall designate a lead Party. The lead Party shall timely discuss with the other Party applications, reports etc. in order to give the other Party the opportunity to comment there on.

8.3.4 In the event of Joint Foreground IP each Party shall, and shall ensure that its employees, researchers, research fellows, individuals equivalent to those persons, give full cooperation and shall execute all documents, deeds and so forth as may reasonably be required in connection with the registration, protection and/or maintenance of that Joint Foreground IP.

Clause 9. Access Rights

9.1 Parties hereby grant each other non-transferrable, non-exclusive, royalty free, fully paid up Access Rights to the Background IP and Existing Know How contributed by it for the duration of the Research Project to the extent needed to enable the performance of the Research Project and to the extent each Party is authorized to grant such Access Rights. Any other rights are discretionary to each Party.

9.2 Parties hereby grant each other non–transferrable, non-exclusive, royalty free, fully paid up Access Rights to the Foreground IP and New Know How owned by it, to the extent necessary to enable the performance of the Research Project and to the extent each Party is authorized to grant such Access Rights.

9.3 Parties hereby grants each other non–transferrable, non-exclusive, royalty free, fully paid up Access Rights for internal research and educational purposes for non-commercial use on Foreground IP or Joint Foreground IP and New Know How.

9.4 In the event of Joint Foreground IP, none of the owning Parties is entitled to grant Access Rights or transfer or assign or make available in any other way any Joint Foreground IP to any third party without prior written consent of the other owners. The Parties owning the Joint Foreground IP shall in good faith determine and negotiate the terms and conditions to grant Access Rights or transfer or assign or make available in any other way any Joint Foreground IP to that third party.

9.5 If a Party needs Access Rights to Background IP and/or Existing Know How for the commercial use of its Foreground IP, the other Party may grant that Party Access Rights on market terms and conditions as applicable in the relevant international market to be further determined in good faith at that time and insofar a party is free to do so. For the avoidance of doubt, a Party is not obliged to grant Access Rights to its Background IP and/or Existing Know How.
Clause 10. Know How

10.1 Each Party shall remain the owner and shall retain control of Existing Know How owned by it.

10.2 All New Know How directly arising from the Research Programme under this Agreement shall be the property of or controlled by the Party whose employees, researchers, research fellows, individuals equivalent to those persons have developed it.

Clause 11. Subcontractors

A Party that enters into a subcontract or otherwise involves third parties in the Research Programme remains solely responsible for carrying out its relevant part of the Research Programme and for such third party’s compliance with the provisions of this Agreement. It has to ensure that the involvement of third parties does not affect the rights and obligations of the other Parties under this Agreement.

Clause 12. Contact Persons

12.1 Parties hereby appoint the hereunder mentioned persons as contact person on behalf of the Parties:

<table>
<thead>
<tr>
<th>University</th>
<th>Contact Person</th>
</tr>
</thead>
<tbody>
<tr>
<td>Utrecht University</td>
<td>Prof Chantal Kemner, main applicant</td>
</tr>
<tr>
<td></td>
<td>prof Johan Bolhuis, PI</td>
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<td></td>
<td>prof Maja Dekovic, PI</td>
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<td></td>
<td>prof Herbert Hoijtink, PI</td>
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<td>prof Wim Meeus, PI</td>
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<td></td>
<td>prof Wilma Vollebergh, PI</td>
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<td></td>
<td>prof Jos van Berkum, PI</td>
</tr>
<tr>
<td>University Medical Centre Utrecht</td>
<td>prof Marian Joëls, co-applicant</td>
</tr>
<tr>
<td></td>
<td>Prof Sarah Durston, co-applicant</td>
</tr>
<tr>
<td></td>
<td>Prof Hilleke Hulshof Pol, PI</td>
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<td></td>
<td>Prof René Kahn, PI</td>
</tr>
<tr>
<td>VU University Amsterdam</td>
<td>Prof Dorret Boomsma, co-applicant</td>
</tr>
<tr>
<td>University of Amsterdam</td>
<td>Prof Patti Valkenburg, co-applicant</td>
</tr>
<tr>
<td>University of Leiden</td>
<td>Prof Rien van IJzendoorn, co-applicant</td>
</tr>
<tr>
<td></td>
<td>Prof Marian Bakermans-Kranenburg PI</td>
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<td>Prof Eveline Crone PI</td>
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<tr>
<td>University Medical Centre Groningen</td>
<td>Prof Albertine Oldehinkel PI</td>
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<td></td>
<td>Prof Hans Ormel PI</td>
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<tr>
<td>Radboud University Nijmegen</td>
<td>Prof Rutger Engels, PI</td>
</tr>
<tr>
<td>Rotterdam Erasmus Medical Center</td>
<td>Prof Frank Verhulst, PI</td>
</tr>
</tbody>
</table>

12.2 Parties are obliged to inform each other at shortest notice on changes in the Contact Persons.

Clause 13. Liability and Indemnification

13.1 All Parties will perform the Research Programme in accordance with all applicable laws and regulations and to the best of its ability consistent with scientific research principles. It does not guarantee the usefulness of the results obtained nor the consequences of the application thereof.

Without limiting the generality of the foregoing, neither Party shall accept any liability for damage or loss which arises due to the fact that the results of the Research Programme do not qualify for patenting or because rights
of third parties are infringed when applying the results. Each Party hereby indemnifies and holds harmless the other Parties and its respective personnel against any and all claims by third parties relating to the results of the Research Programme and the use thereof by the indemnifying Party.

13.2 No Party shall be liable towards the other Party for acts or omissions commit by it in the performance of the Research Programme and its obligations under this Agreement, unless such liability is the direct result of a Party’s gross negligence or willful misconduct (in Dutch “opzet of bewuste roekeloosheid”).

Clause 14. No warranties

14.1 All Background IP, Know How and Confidential Information made available in the context of this Agreement are made available “as is” and each Party understands and agrees that such Background IP, Know How and Confidential Information may be experimental in nature and are made available without any representation or warranty, express or implied, including any implied warranty of merchantability, satisfactory quality or fitness for any particular purpose or any warranty that the use of the same will not infringe or violate any patent or other proprietary rights of any third party.

14.2 No Party shall be deemed to have made any warranties of merchantability or fitness for any particular purpose of Foreground IP or for the patentability of any ideas in the Research Programme.

Clause 15. Duration / Termination of the Research Programme

15.1 The Research Programme commences on May 1, 2013 and terminates on the date OCW terminates the subsidy (the “Termination Date”), unless Parties mutually agree otherwise taking into account the provisions of this Clause.

15.2 Either Party may terminate this Agreement prior to the Termination Date in the event of:

15.2.1 the other Party’s continuing failure to perform its obligations under this Agreement after being requested to do so by a notice in writing; or

15.2.2 the other Party breaching any of the terms of this Agreement and failing to remedy the breach within 30 days after being requested to do so by a notice in writing.

15.3 The termination of this Agreement for any reason shall not affect:

15.3.1 any obligations or rights of the Parties which shall have accrued on or before the date of termination; and

15.3.2 the coming into force or continuance in force of any provision of this Agreement expressly or by implication intended to come into force or continue in force on or after termination.
Clause 16. Use of logo and name Parties

Each Party is not entitled to use the logo and name of the other Party or any of its employees or staff members for commercial purposes without prior written consent of the authorized body of that Party.

Clause 17. Evaluation

17.1 OCW has granted on November 9, 2012, to Utrecht University in its capacity as main applicant a subsidy of €14,800,000,- for the period 2012-2016 for the Consortium Individual Development: "Why some children thrive, and others don't". This grants relates to a period of five (5) years; and may be extended by OCW for another period of five (5) years, depending an evaluation before the beginning of the fifth year.

17.2 If OCW does not warrant the extension of the subsidy after 2016 or a Party's participation is terminated in the Research Programme, this Consortium Agreement shall automatically terminate in respect of the affected Party or Parties, subject to the provisions surviving the expiration or termination under Clause 17.3 of this Consortium Agreement.

17.3 Survival of rights and obligations: The provisions relating to Access Rights and Confidentiality, for the time period mentioned therein, as well as for Liability, Governing law and jurisdiction shall survive the expiration or termination of this Consortium Agreement. Termination shall not affect any rights or obligations of a Party leaving the Consortium incurred prior to the date of termination, unless otherwise agreed between the Steering Committee and the leaving Party. This includes the obligation to provide all input, deliverables and documents for the period of its participation.

Clause 18. Legal entity

The conclusion of this Agreement and the rights and obligations deriving thereof will in no way constitute a legal entity (rechtspersoon) or any other form of corporate entity (juridische entiteit) and Parties do not intend to create any such legal entity or corporate entity.

Clause 19. Assignment

Neither Party may assign any of its rights and obligations under this Agreement to a third party without the prior written consent of the other Party.

Clause 20. Governing law and jurisdiction

20.1 This Agreement shall be governed by and construed in accordance with the laws of the Netherlands.

20.2 All disputes that might arise as a result of this Agreement, or of further agreements, will be submitted to the competent court in Utrecht, the Netherlands.
Executed by the Parties

For and on behalf of:
**UNIVERSITEIT UTRECHT**

By: Prof. dr. G.J. van der Zwaan
    plaatsvervangend voorzitter
In: Utrecht
On: June, 6 2013

For and on behalf of:
**UNIVERSITY MEDICAL CENTER UTRECHT**

By: [NAME]
In: [PLACE]
On: [DATE]

For and on behalf of:
**VU UNIVERSITY AMSTERDAM**

By: [NAME]
In: [PLACE]
On: [DATE]

For and on behalf of:
**UNIVERSITY OF AMSTERDAM**

By: [NAME]
In: [PLACE]
On: [DATE]

For and on behalf of:
**LEIDEN UNIVERSITY**

By: [NAME]
In: [PLACE]
On: [DATE]
Executed by the Parties

For and on behalf of:
UNIVERSITEIT UTRECHT

By: [NAME]
In: [PLACE]
On: [DATE]

For and on behalf of:
UNIVERSITY MEDICAL CENTER UTRECHT

By: [NAME]
In: [PLACE]
On: [DATE]

For and on behalf of:
VU UNIVERSITY AMSTERDAM

By: [NAME]
In: [PLACE]
On: [DATE]

For and on behalf of:
UNIVERSITY OF AMSTERDAM

By: [NAME]
In: [PLACE]
On: [DATE]

For and on behalf of:
LEIDEN UNIVERSITY

By: [NAME]
In: [PLACE]
On: [DATE]
Executed by the Parties

For and on behalf of:
UNIVERSITEIT UTRECHT

By:  [NAME]
In:  [PLACE]
On:  [DATE]

For and on behalf of:
UNIVERSITY MEDICAL CENTER UTRECHT

By:  [NAME]
In:  [PLACE]
On:  [DATE]

For and on behalf of:
VU UNIVERSITY AMSTERDAM

By:  Drs. M.M. van Aken RC
In:  Amsterdam
On:  01-07-2013

For and on behalf of:
UNIVERSITY OF AMSTERDAM

By:  [NAME]
In:  [PLACE]
On:  [DATE]

For and on behalf of:
LEIDEN UNIVERSITY

By:  [NAME]
In:  [PLACE]
On:  [DATE]
Executed by the Parties

For and on behalf of:

**UNIVERSITEIT UTRECHT**

By: [NAME]
In: [PLACE]
On: [DATE]

For and on behalf of:

**UNIVERSITY MEDICAL CENTER UTRECHT**

By: [NAME]
In: [PLACE]
On: [DATE]

For and on behalf of:

**VU UNIVERSITY AMSTERDAM**

By: [NAME]
In: [PLACE]
On: [DATE]

For and on behalf of:

**UNIVERSITY OF AMSTERDAM**

By: [NAME] Ett de Haan
In: [PLACE] Amsterdam
On: [DATE] 5/6/2013

For and on behalf of:

**LEIDEN UNIVERSITY**

By: [NAME]
In: [PLACE]
On: [DATE]
Executed by the Parties

For and on behalf of:

**UNIVERSITEIT UTRECHT**

By: [NAME]
In: [PLACE]
On: [DATE]

For and on behalf of:

**UNIVERSITY MEDICAL CENTER UTRECHT**

By: [NAME]
In: [PLACE]
On: [DATE]

For and on behalf of:

**VU UNIVERSITY AMSTERDAM**

By: [NAME]
In: [PLACE]
On: [DATE]

For and on behalf of:

**UNIVERSITY OF AMSTERDAM**

By: [NAME]
In: [PLACE]
On: [DATE]

For and on behalf of:

**LEIDEN UNIVERSITY**

By: [NAME]
In: [PLACE]
On: [DATE] 28-6-2013

Execution copy 31 May 2013
For and on behalf of:
UNIVERSITY MEDICAL CENTER
GRONINGEN

By: [NAME]
In: [PLACE]
On: [DATE]

For and on behalf of:
RADBOUD UNIVERSITY
NIJMEGEN

By: [NAME]
In: [PLACE]
On: [DATE]

For and on behalf of:
ROTTERDAM ERASMUS MEDICAL CENTER

By: [NAME]
In: [PLACE]
On: [DATE]
For and on behalf of:
UNIVERSITY MEDICAL CENTER
GRONINGEN

By: [NAME]
In: [PLACE]
On: [DATE]

For and on behalf of:
RADBOUD UNIVERSITY
NIJMEGEN

By: Mw. prof. dr. H.P.J.M. Dekkers,
dean FSW
In: Nijmegen
On: 05-06-2013

For and on behalf of:
ROTTERDAM ERASMUS MEDICAL
CENTER

By: [NAME]
In: [PLACE]
On: [DATE]
For and on behalf of:
UNIVERSITY MEDICAL CENTER
GRONINGEN

By: [NAME]
In: [PLACE]
On: [DATE]

For and on behalf of:
Radboud University
Nijmegen

By: [NAME]
In: [PLACE]
On: [DATE]

For and on behalf of:
Rotterdam Erasmus Medical Center

By: [NAME]
In: [PLACE]
On: [DATE] 07 JUNI 2013

Execution copy 31 May 2013
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ANNEXES

Annex 1 Application Gravitation Programme

Annex 2 Grant letter OCW, including the NWO subsidy terms and conditions

Annex 3 Budget Research Programme

Annex 4 Model Project Agreement
   - Annex 1. Project Budget
   - Annex 2. Work Plan
   - Annex 3. Background IP to Research Project

Annex 5 List of Members of the Steering Committee, Workpackage Leaders and Cohort Representatives.
The Consortium on Individual Development gratefully acknowledges the support of the Gravitation Program of the Dutch Ministry of Education, Culture and Science (OCW) and the Netherlands Organization for Scientific Research (NWO grant number 024.001.003).

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