COgnitive Dynamics in Early Childhood

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2 OBJECTIVES2.1 Primary Objective: To address the existing knowledge gaps and advance our understanding of cognitive variability, the CODEC study aims to integrate experience sampling methods, longitudinal designs, deep phenotyping cohorts, and...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON56515

Source
ToetsingOnline

Brief title
CODEC

Condition

- Other condition

Synonym
not applicable

Health condition

geen sprake van aandoening

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: ERC

Intervention

Keyword: Cognitive variability, Development, Individual differences, longitudinal modelling

Outcome measures

Primary outcome

8.1.1 Main study parameter/endpoint

For the behavioural arm:

Cognitive task battery on tablet, implemented on the m-Path platform (https://m-path.io/landing/). This battery will measure a series of classic cognitive tasks: working memory, vocabulary, simple reaction time, exploration ability, and fluid reasoning. Each task will yield a set of estimated phenotypic parameters including speed, accuracy, trends, autoregression and variability.

Working memory

In this task, participants will see a grid of dots. A number of dots will turn white in sequence. The participants are asked to recall the right sequence by selecting each dot in the same order

Fluid reasoning

Participants will see a 3 by 3 grid, and are asked to select, out of 4 options, which option best fits the blanked out grid.

Reaction time

Participants will see a grid, where a cartoon mole will appear unpredictably. Their task is to tap the mole as quickly as they can.

Vocabulary

Participants will see a word, and are asked which of four alternatives best fits the description of the word, or is an antonym (*tegenovergestelde*), to measure their vocabulary.

Exploration

Participants see a large grid (example from Meder et al., 2021). Under each tile, a *treasure* is hidden of differing values. Participants may select a number of tiles to discover treasure, which is either randomly dispersed (*rough*) or correlated (*smooth*) across the grid, favouring different strategies.

For all 5 tasks we will record speed (response time), accuracy (as binary or continuous/press location) and ambient background noise (as decibels, not identifiable sounds).

The measurements will entail a *burst* measurement, yielding a week of data on N=600 across all tasks. Fitting a DSEM to this wave of data will yield a rich set of variability estimates. These will be used to generate a completely novel descriptive measure to capture individual differences: The

Variability Performance Profile (VPP).

Additional measures will include:

• two slider items before each block, on mood (smiley face to sad face) and sleep (alert face to sleepy face)

• Decibels of the surroundings during testing will be recorded by the tablets (This will only be measured in decibels and not record true audio).

For the imaging arm:

Before of the imaging session in the scanner, the child participants will finish a set of tailored questionnaires and tasks. These are:

• A digital mood scale (slider)

• A digital sleep scale (slider)

• Highly Sensitive Child scale - HSC short form (12 items, ~5 minutes; Pluess et al., 2018)

• Mind Excessively Wandering Scale - MEWS (~5 minutes; Frick et al., 2020)

• Alternative uses tasks (name alternative uses for 4 physical objects, each 2 minutes, based on Van Dijk et al. 2020)

There will be two cognitive task batteries during the MRI session. Two blocks of fluid reasoning (~8 minutes each) will be performed by the child during MRI scanning. These tasks will be explained and practiced in the mock scanner prior to the actual MRI scan. Outside of the MRI scan, children will

perform each of the 5 original cognitive tasks as used in the behavioural part for 3 minutes (15 minutes).

The imaging session will include the following sequences:

• MP-Rage and Sparse MP2-Rage

Gold standard structural scans. MP2-Rage allows for greater specificity of myelination, one of the core research questions.

• Diffusion weighted imaging

This diffusion weighted sequence balances a realistic acquisition time with high quality imaging data.

• Task block 1: fMRI [Fluid Reasoning, low time constraints]

This task will be familiar to the children, as they will have performed it previously outside the scanner in the behavioural arm. One block will be performed under low time constraints (maximum 25 seconds per trial). The other block will be performed under higher time constraints (approximately 8 seconds, varying per person). The order of time constraints will be counterbalanced. The time constraints are known to induce different task strategies which is a key question of interest.

• Task block 2: fMRI [Fluid Reasoning, high time constraints]

• During the two task blocks (2*8.5 minutes) we will record gaze direction and pupil dilation (through the Eyelink 1000 Plus eye tracking system). This will require a brief period of calibration (2 minutes) at the start of each fMRI task block.

• Naturalistic viewing fMRI

o During this task, participants will watch a short video clip (~8 minutes), featuring a social scene from an age-appropriate, mainstream movie (Despicable Me). We hypothesize that variability in resting state fMRI on this block will be related to cognitive variability.

Additionally, parents who agree will respond to a set of questionnaires about their child. The set of questionnaires consists of :

• SES (highest level of education, job type and status, postcode without house number, ~5 minutes)

• Strengths and difficulties questionnaire (25 items, ~10 minutes)

• MEWS (Mind Excessively Wandering Scale; 12 items, ~5 minutes; Frick et al., 2020)

• BRIEF-2 (executive functions). 50 items, ~15 minutes (Huizinga, et al., 2023)

Secondary outcome

8.1.2 Secondary study parameters/endpoints

For the behavioural arm:

• Academic results from the child, obtained through the school (e.g., Cito-scores)

For the imaging arm:

• Cognitive task battery identical to the one used in the behavioural arm, performed by the parent(s) accompanying the child, if parent(s) agrees/signs dedicated informed consent form.

8.1.3 Other study parameters

Some demographic measures will be collected to be able to characterise the population and understand our sample, such as sex, SES measures and languages spoken at home.

For the behavioural and imaging arm:

• Demographic measures of the child (e.g., age, sex, is Dutch the main language at home, education grade/level)

Study description

Background summary

1 INTRODUCTION AND RATIONALE
1.1 Background
This study aims to investigate the nature and implications of cognitive variability, which refers to the fluctuations in performance that individuals exhibit across cognitive tasks over time. While cognitive abilities such as reasoning, memory, and vocabulary have been extensively studied, the focus has predominantly been on mean performance, neglecting the rich and informative dimension of variability. Traditionally, cognitive abilities have been regarded as stable traits with lifelong implications (Deary, 2014). However, this perspective has overshadowed cognitive variability across diverse contexts and situations.

Literature has highlighted the substantial implications of cognitive variability on real-life and educational outcomes (Gottfredson & Deary, 2004). For instance, individuals exhibiting higher variability in cognitive performance are more prone to being misallocated into inappropriate educational settings, leading to long-term consequences (Woodrow, 1932). Moreover, cognitive variability has been identified as a potential early warning marker for adverse outcomes and neurodevelopmental disorders like attention deficit hyperactivity disorder (ADHD) (Fagot et al., 2018; Kofler et al., 2013).

Despite speculations about the importance of cognitive variability persisting for almost a century (Nesselroade, 1991), empirical research on this topic has been limited due to logistical challenges and the lack of appropriate quantitative techniques. However, recent studies have provided evidence that individuals exhibit variability in cognitive performance across different trials, hours, days, and even seasons (Kelly & Beltz, 2020; Licher et al., 2019; Rabbitt et al., 2001; Sievertsen et al., 2016). Notably, this variability is particularly pronounced during periods of rapid cognitive development, such as childhood and old age (Galeano Weber et al., 2018; MacDonald et al., 2006; Siegler, 1994).

Understanding cognitive variability is crucial for several reasons. Firstly, individuals with greater variability are more likely to be inaccurately stratified in schools or careers, resulting in lifelong consequences and emphasizing the need for fair and accurate assessment methods (Cattell, 1966). Secondly, variability in performance implies that individuals may spend a significant proportion of time performing below thresholds of adequate performance, which can have serious implications, particularly in high-stakes professions such as piloting or surgery (MacDonald et al., 2006). Additionally, cognitive variability has been linked to neurodevelopmental disorders like ADHD, and interventions targeting variability have shown promise in alleviating symptoms (Kofler et al., 2013). Lastly, reducing cognitive variability holds potential for enhancing day-to-day functioning and reducing challenges for vulnerable individuals (Li & Lindenberger, 1999; MacDonald et al., 2006).

In this unique longitudinal design using gamified versions of classic cognitive domains we will measure variability across a range of tasks at multiple levels of temporal resolution: months, days, occasions and trials. 600 children (from which 200 will also be in the neuroimaging arm) will be measured for a period of three years. Once per year they will take part in a burst: A week where they will be measured three times a day; and up to two other measurement occasions if classrooms or parents of individual participants agree. We will use cutting edge methodology to understand the behavioural, neural and environmental mechanisms of variability, as well as the longitudinal consequences of variability on cognitive development and the emergence of mental health symptomatology such as ADHD. By combining the strengths of deep phenotyping with cutting edge quantitative modeling, we will be able to test and develop theories of cognitive development, demonstrate the role of brain structure and function in supporting cognitive dynamics and determine the effect of cognitive variability on developmental outcomes.

Testing young children is important in the CODEC study because cognitive variability is particularly pronounced during periods of rapid cognitive development such as early childhood (Galeano Weber et al., 2018; MacDonald et al., 2006; Siegler, 1994). By focusing on young children, the study aims to capture and analyse the dynamic changes and fluctuations in

cognitive performance during this critical developmental stage. Additionally, understanding cognitive variability in early childhood is essential to identify potential risk factors and early warning markers for neurodevelopmental disorders such as ADHD (Fagot et al., 2018; Kofler et al., 2013). By assessing cognitive variability in young children, the study can contribute to early detection and intervention strategies. Previous MRI scanning experiences at the Donders Institute have shown that starting at the age of 8 years, children can clearly understand what is happening, articulate any questions or concerns, and yield high quality data. Hence, only children from the age of 8 years on will be included in the imaging arm. In the behavioural arm, which only has minimal risk, 7-year-old-children can be included to avoid exclusion of younger children in the same class as the 8-year-olds. They will be allowed to participate in the imaging arm from the moment they turn 8. Furthermore, as previously mentioned, since children change school settings (primary to secondary) at the age of 11-12 years, we aim to focus recruitment on children aged 8-10 years at the first measurement to best balance the minimal burden and scientific insight into a key developmental period, allow for maximum retention across the three years while they are still attending primary school.

1.2 Measurement and Modelling

To understand the causes and consequences of variability, we must first measure it, and measure it well (Flake & Fried, 2020). In previous studies, a wide range of variability metrics have been used. However, they suffer from a range of practical and theoretical limitations. For instance, simple summary metrics such as iSD (individual standard deviations) or ICV (coefficient of variation) can be biased due to neglect of autoregressive structure (de Haan-Rietdijk et al., 2016), individual differences in mean performance or trend-like changes over time. Moreover, simplistic measures such as iSD or iSD2 ignore measurement error inherent in variability (Wang & Grimm, 2012). The challenges of modelling these sources of variation in a principled manner have hitherto precluded widespread, accurate measurement of variability. To overcome these challenges, we will use the new, flexible, integrative mathematical framework of Dynamic Structural Equation Modeling (DSEM) (Asparouhov et al., 2018; Hamaker et al., 2018; McNeish & Hamaker, 2020 - see 'methodology'). DSEM allows us to simultaneously estimate all components of the time course. Moreover, using a tailored multilevel SEM framework and Bayesian estimation, each of these sources of variability can be estimated as a random effect (i.e. as varying between individuals). Crucially, variability can then be modelled as dependent and/or independent variable in a fully integrated manner.
The first measurement occasion will entail a *burst* measurement, yielding a week of data on N=600 across all tasks. Fitting a DSEM to this wave of data will yield a rich set of variability estimates. These will be used to generate a completely novel descriptive measure to capture individual differences: The Variability Performance Profile (VPP). This VPP is specific to each individual and will capture a rich description of how variable a child is across cognitive domains (reasoning, speed, memory, language, exploration) and

temporal scales (trials, occasions, days). Further measuremen

Study objective

2 OBJECTIVES
2.1 Primary Objective:
To address the existing knowledge gaps and advance our understanding of cognitive variability, the CODEC study aims to integrate experience sampling methods, longitudinal designs, deep phenotyping cohorts, and state-of-the-art statistical methodologies to investigate three core questions:
1. How does cognitive variability differ between individuals?
2. What are the neural, psychological, and environmental mechanisms that underlie cognitive variability?
3. What are the long-term consequences and outcomes associated with differences in cognitive variability?

2.2 Secondary Objective(s):
1. Measurement and Modelling:
• To develop a comprehensive and accurate measurement of variability using DSEM
• To explore variability across different domains and temporal resolutions
2. The mechanisms of Variability:
• To explore the role of strategy exploration and exploitation as drivers of variability.
3. Long-term consequences of variability:
• To investigate variability as an early marker for atypical development, particularly in neurodevelopmental disorder such as autism and ADHD

Study design

Study Design: longitudinal observational cohort study with children aged 7 to 10 at first measurement. We will use a flexible design, meaning that we will aim to start measuring 8-year-old-children to follow them for the duration of 3 years (while they are still in primary school), although to allow for a big enough sample size, we will also measure children eager to participate from ages ranging between 7 and 10 at the first testing session (behavioural part) and between 8 and 10 at the first testing session for the imaging part.* * Duration: 3 years; Participants for the behavioural testing only, will be examined for a *burst period* (1 week of testing for 2-3 times a day) once a year for the duration of 3 years (3 burst periods in total) and up to two additional brief (25 minutes per occasion) measurements a year depending on classroom or parent agreements. Participants also taking part in the imaging study will also be scanned once at the start of the study (year 1) and once at the end of the study (year 3).

Setting:
-The majority of data collection will be in classrooms of collaborating schools.

-A subset of individuals may use our individual enrolment route, and thus perform their tasks at home.
-200 children will take part in 2 imaging sessions, which will take place at the Donders Institute for Brain, Cognition, and Behaviour at Radboud University.

Justification of the Design:
The study aims to investigate the cognitive development of children over time and the impact of cognitive variability on various tasks. A longitudinal cohort study design is appropriate for this research as it allows for the examination of changes in variability of cognitive abilities over time. Frequent sampling is required to separate different temporal resolutions (e.g. trial to trial, occasion to occasion, day to day), ensure appropriate power, and separate developmental effects from retest effects.

Study burden and risks

The risk for participants taking part in this study is negligible. The full sample will participate in a tablet based cognitive study similar to tasks already implemented as part of widely used educational platforms. A subgroup of the participants will also take part in the neuroimaging phenotyping arm. MRI is a non-invasive technique. MRI has been widely used in*children of similar (and younger) ages without apparent harmful consequences when inclusion criteria are followed. As the aim of the study is to understand individual differences in cognitive variability in early childhood, this study requires the participation of children. The study will run for the duration of 3 years and children will participate in behavioural testing several times a year (one week of high intensity testing - *burst-week*, and up to 2 other measurement occasions per year if classrooms or parents of individual participants agree). The subset of 200 children taking part in the MRI study will have an MRI session in the first year, and a follow up scan after an interval of approximately 3 years. Since children change school settings (primary to secondary) at the age of 11-12 years, we focus recruitment on 7-to-10-year-old-children to allow for a maximum retention across the three years while they are still attending primary school. Based on previous positive experiences with scanning children at the Donders Institute starting from 8-year-old-children, only children aged 8 or older will be allowed to take part in imaging sessions.
The burden for the behavioural part will consist of repeated participation (several times a year: 1 burst-week and up to two other measurement occasions per year if classrooms and individual participants agree) on short mood and sleep scales accompanied by cognitive measures, tested in a playful way on our tablet-based platform (m-Path). For the duration of 1 week (i.e., burst-week) each year (for 3 years), children will play 3 games for a duration of 15 minutes (5 minutes per game), 2 or 3 times a day (depending on the possibilities within the classrooms or at home). Further testing occasions will consist of children playing all 5 games once for a total duration of 25

minutes (5 minutes per game).
The burden for the imaging arm will consist of 2 on-site visits at the Donders Institute for parent(s) and child. For the children, the burden associated with participation comprises two imaging sessions (once at the beginning of the study and once approximately 3 years after). While 8-11-year-old children do not rate their participation in MRI research as scary or annoying according to the DISCO-RC questionnaire (DISCOmfort in Research with Children; Staphorst et al., 2017; https://vragenlijst.kindenonderzoek.nl/resultaten/mri-scan/), some children mention feeling tired or bored. During scan sequences which allow it, a silent animation video will play to decrease boredom, and we will regularly interact with participants in between scan sequences. The MRI session will take a total of ~2 hours and will involve a screening and welcome (15 minutes), answering a set of short questionnaires on mood and tiredness (15 minutes), a mock scan to familiarise children (30 minutes), the actual MRI session (~55 minutes), and a thank-you note/debrief with a small gift (5 minutes). In order to further reduce potential discomfort in the scanner, children will receive hearing protection suitable for their age and their head will be supported with foam pillows. During the two task-based fMRI blocks (2*8.5 minutes) we will record gaze direction and pupil dilation using the Eyelink 1000 Plus system. During the scan session, children will have continuous contact with the experimenters and can ask to leave the MRI scanner at any time without consequences.* *
The accompanying adult will be asked to complete a range of questionnaires at each visit, which will take approximately 35 minutes and/or to take part in the same 5 cognitive games as the child previously took part in during the behavioural part (25 minutes). Participation of the parents on the questionnaires and cognitive tasks will require consent on a different form to the child*s consent. Parental participation is not required for the child to take part in the imaging arm.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

600 children will be recruited from schools and on individual bases to take part in the behavioural testing. A subgroup of 200 children (tested on-site and with participant insurance) will be further recruited to participate in the imaging part of the study at the Donders Institute.

In order to be eligible to participate in the behavioural arm of this study, a subject must meet all of the following criteria:
• Between the ages of 7 and 10 years at the moment of the first assessment.

In order to be eligible to participate in the imaging arm of this study, a subject must meet all of the following criteria:
• Between the ages of 8 and 10 years at the moment of the first assessment.

Exclusion criteria

A potential subject will be excluded from participation in the study if the participant indicates not understanding the instructions of the behavioural tasks due to a language barrier.
In the imaging arm of the study, a potential subject who meets any of the following criteria will further be excluded from participation in the imaging arm of the study:
• History of neurological or psychiatric illness.
• History of using psychotropic medications.
• Contraindications for MRI.
• Metal parts that cannot be removed, are present in or on upper body, e.g. plates, screws, aneurysm clips, metal splinters, piercings or medical plasters. (exception: dental fillings, crowns, a metal wire behind the teeth, tattoos and contraceptive coils).

• Body containing metal fragments, in particular in the eye, e.g., caused by injuries when working with metal.
• History of brain surgery.
• Active implant(s) (e.g. pacemaker, neurostimulator, insulin pump, ossicle prosthesis)
• Using a medical plaster that cannot or may not be taken off (e.g. nicotine plaster)

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-11-2024
Enrollment:	600
Type:	Actual

Ethics review

Approved WMO Date:	21-02-2024
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-04-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-10-2024

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL84688.091.23