Neuropsychological functioning of children and adolescents (6-16) born with Congenital Adrenal Hyperplasia (CAH)

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Objective of this pilot study is to investigate differences in neuropsychological functioning between CAH patients and healthy controls. Differences in neuropsychological functioning may influence the quality of life and daily functioning of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Endocrine disorders congenital
Study type	Observational non invasive

Summary

ID

NL-OMON40664

Source
ToetsingOnline

Brief title
Neuropsychological functioning CAH

Condition

- Endocrine disorders congenital

Synonym
CAH congenital adrenal hyperplasia

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud

Source(s) of monetary or material Support: Onderzoeksgeld afdeling kinderendocrinologie

Intervention

Keyword: CAH, Children, Cognition, Psychological

Outcome measures

Primary outcome

Cognitive functioning

To measure global intellectual functioning we will use the Wechsler Intelligence Scale (WISC-III). This intelligence test is standardized for children in the age range of 6-16 years old. The WISC-III-NL consists of 13 subtests, grouped as Verbal and Performal subtests. One subtest is complementary and two are optional.

The Behavioural Assessment of the Dysexecutive Syndrome for Children (BADS-c) will be used to measure problems in daily functioning emerged from abnormalities in planning- and organizational skills. We are assessing two subtasks of this battery, namely the key test (a test for strategy formation) and the zoo map test to measure planning abilities.

The sort version of The Test of Everyday Attention for Children (TEA-Ch) will be used to measure different aspects of attention. We will investigate outcomes of four subtasks to examine attention. The sky search task will be used to measure selective attention, the count task to measure sustained attention, the creature counting task to measure attentional control and the sky search dual task to measure divided attention.

Social cognition

To measure social cognition we will use the Theory of Mind test-R (ToM test-R). Information is collected regarding the manner in which children between 4 and 12 years process social understanding, insight and sensitivity. With this test we can analyze strengths and weaknesses concerning social cognitive skills. The test is standardized for children in the age range of 4-12 years old.
The Emotion Recognition Task (ERT) measures the recognition of six basic emotions in facial expressions: fear, happiness, sadness, surprise, anger and disgust. There will be shown video clips of different length, starting with a neutral face that changes in a facial expression of different intensity (20-100%).

Psychological functioning

With the Dutch Social-Emotional-Questionnaire (SEV) we will check if there are certain social-emotional problems involved in children*s lives. This questionnaire will be filled in by the child*s caregiver.
The Pediatric Quality of Life Inventory (PEDS-QL) will measure quality of life. There are results in four different domains: physical, social, emotional and school performances. Children above 8 years can fill in this questionnaire themselves, for children aged 6 or 7 caregivers can fill in this inventory.
The Child Behavior Checklist (CBCL) is a checklist parents complete to detect emotional and behavioural problems in children and adolescents. The CBCL/6-18 is to be used with children aged 6 to 18. It consists of 113 questions, scored on a three-point Likert scale (0=absent, 1= occurs sometimes, 2=occurs often).

The time frame for item responses is the past six months.

The 2001 revision of the CBCL/6-18, is made up of eight syndrome scales: anxious/depressed, depressed, somatic complaints, social problems, thought problems, attention problems, rule-breaking behavior, aggressive behavior.

These group into two higher order factors-internalizing and externalizing.

The Dutch Competention-Experience Scale for Children and Adolescents (CBSK and CBSA) gives a standardized insight in the manner in which a child experiences itself and how the child assesses his/her own skills and adequacy of different areas of life. We can subdivide the 35 items in six subscales: school performance, social acceptance, sportive skills, physical appearance, behavioural attitude and feeling of own value.

Secondary outcome

The level of parenting stress will be measured with the Nijmegen Parenting Stress Index - short form questionnaire (NOSIK). The NOSIK is a diagnostic questionnaire to investigate if parents experience a certain degree of stress within the context of raising a child.

The Schok Verwerkingslijst (SVL) will be used to meassure a certain degree of trauma by parents, in the context of the birth of their child. The SVL meassures two key characteristics of a trauma, re-experiencing and avoidance. The SVL contains of 15 items of which seven relate to re-experiencing and eight relate to avoidance of thoughts and feelings about the event.

Study description

Background summary

Cognitive functioning in CAH
A disturbed hormone balance as a result of Congenital Adrenal Hyperplasia (CAH) may influence cognitive development in children living with this syndrome. Different studies investigated the influence of hormones and neonatal salt loss on brain development by comparing patients with CAH with healthy controls. The first study investigating intelligence and cognitive functioning in CAH patients was published by McGuire et al. (1975). No differences were found between IQ of the CAH patients and healthy controls.
More recent studies focused on more differences within the cognitive profile, trying to find support for a more male like cognitive profile in CAH girls. This assumption was supported by Helleday et al. (1994). They found higher differences between performal IQ and verbal IQ in favor of performal in CAH girls compared to controls. Other studies also took different forms of CAH into account: the salt wasting versus simple virilised type. Johannson et al. (2006) found lower IQ scores in the salt wasting type, however other studies could not support this (Malouf et al. 2006).
Other recent studies focused on different cognitive outcomes in CAH patients prenatally treated with dexamethasone versus no prenatal treatment. There seems to be a slight positive short term effect of dexa on cognitive functioning in affected patients, however there seems to be a negative effect in non affected prenatally treated persons (Maryniak et al. 2012; Meyer-Bahlburg et al. 2012). In addition, prenatal dexamethasone treatment could influence the verbal working memory (Hirvikoski, 2007).

Results on cognitive functioning in CAH are mixed. Differences in IQ and cognitive functioning seem to be more related to details of treatment and disease course than to general CAH as such. In future research all these factors should be taken into account.

Quality of life/psychological functioning in CAH
In this pilot study, besides cognition, we also want to investigate quality of life and psychological functioning in children and adolescents with CAH. From limited previous results we know that CAH children experience more difficulties developing relationships, have a disturbed self-concept and body image and patients with CAH choose jobs where they don*t have to work with people more often, compared to healthy controls.
Results of studies on quality of life in CAH are mixed (Johannsen et al. 2006; Reisch et al. 2011). Han et al. (2013) investigated the association between quality of life and different other factors like medicine treatment with corticosteroids, disease control and health factors like metabolism (obese, insulin resistance). They conclude that treatment with strong corticosteroids is associated with worse metabolism and a disturbed quality of life. The

causality of this relationship isn*t clear and needs further investigation.

Social cognition in CAH
Structural imaging reveals reductions in amygdale volume in both CAH boys and girls relative to healthy controls (Merke et al. 2003). fMRI research also reveals a difference in amygdale function during emotional processing between CAH patients and healthy controls. Ernst et al. (2007) discover that patients show heightened responsivity to negative material in areas associated with face processing (fusiform gyrus), the precuneus, temporal areas and the striatum). Another interesting finding is that recognition memory is worse for negative but not neutral scenes and faces in CAH adolescents (Maheu et al. 2008; Mazzone et al. 2011). fMRI data of emotional memory processing reveals aberrant activity in limbic circuitry in CAH including the amygdale, the hippocampus and the anterior cingulate cortex.
The amygdala is an important structure involved in social cognition (Adolphs, 2010). According to different imaging studies the amygdala plays an important role interpretating thoughts, beliefs and desires of others. A construct also known as *Theory of Mind* (Shaw et al. 2003; Stone et al. 2005).
It should be relevant for society to combine above-mentioned research to find out if CAH patients differ from healthy controls in social cognition.

Study objective

Objective of this pilot study is to investigate differences in neuropsychological functioning between CAH patients and healthy controls. Differences in neuropsychological functioning may influence the quality of life and daily functioning of children with CAH. Thats why we want to map out all these different factors that can influence neuropsychological functioning in CAH children and adolescents.

Questions that can be answered:

1) Is there a significant difference in psychological functioning at the age of 6-16 years between CAH patients and healthy controls? Which factors may be associated?
2) Is there a significant difference in cognitive functioning at the age of 6-16 years between CAH patients and healthy controls? Which factors may be associated?
3) In de second question we also want to take social cognition into account.

Clinicians need more knowledge about neuropsychological functioning in CAH patients so that they can intervene more suitable to problems especially experienced in CAH. Simultaneously the advice that's provided to children, teachers and parents will contain more quality.

Study design

Method(s)
The incidence rate of CAH in Holland is 15-20 new patients a year. In the period 1997-2007 there will be a maximum of 100 patients in the range from 6 till 16 years old.
For this pilot only children treated in the Radboud UMC hospital in Nijmegen will be recruited. Therefore our amount of participants will be considerable less.

We will only recruit children and adolescents still under treatment for CAH in the Radboudumc. The attending endocrinologist will contact patients to give them a description of the study. The study will be an extension of the already existing care and clinical appointments. Children and their parents get the chance to gain more information about the child*s functioning. The doctor will use application forms and afterwards the researcher will contact the child and their caregivers to give further information about the study.

Caregivers, or children older than the age of 12, will sign an informed consent. Healthy controls will be matched on age and gender and are siblings of children with CAH. They will also be recruited via the doctor of children with CAH.

This study will consist of one visit where children and adolescents will perform some neuropsychological tests. Children older than the age of 11 will also fill in some questionnaires, this will be done digitally in a internet programme. One of the caregivers will also fill in some questionnaires digitally at home.

When we know the research results the children and their caregivers will receive them written by mail. If there are uncertainties or questions parents can contact the researcher by phone.

Study burden and risks

The whole study will consist of one visit. This visit will occupy a maximum of approximately three hours for the child. We will ask the parents if they can fill in some questionnaires digitally. There will be no further risks connected to this study. Parents will conceive a rapport with study results of their child. This offers them an overview of the neuropsychological functioning of their child.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

Children and adolescents between age 6 and 16 under treatment for CAH in Radboudumc

Exclusion criteria

Comorbidity: disease that might influence neuropsychological functioning

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other

Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-05-2017
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO

Date:	26-11-2014
Application type:	First submission
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	NL48454.091.14