Study on Working Memory in Adolescents with Autism in the Netherlands (amendment regarding an extension using fMRI)

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Primary objectives: 1) Study EF in general and WM capacity specifically in intelligent adolescents with HFA on a neuronal and cognitive level, as well for abstract information as for social relevant information, using neuropsychological assessments...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Developmental disorders NEC
Study type	Observational non invasive

Summary

ID

NL-OMON38231

Source
ToetsingOnline

Brief title
SWAAN

Condition

- Developmental disorders NEC

Synonym
High functioning Autism

Research involving
Human

Sponsors and support

Primary sponsor: Epilepsiecentrum Kempenhaeghe

Source(s) of monetary or material Support: Stichting Kempenhaeghe

Intervention

Keyword: Adolescents, High Functioning Autism, Neuropsychology, Working Memory

Outcome measures

Primary outcome

The neuropsychological WM parameters and behavioral WM parameters as obtained by the questionnaires. The endpoints for the neuropsychological tasks and behavioral data as obtained by the questionnaires are standardized (z-) scores. This will all be processed in terms of: (i) correlation between neuropsychological test results, and behavioral questionaires data results, (ii) differences between adolescents with HFA and normal controls.

AMENDMENT

The neuropsychological WM parameters and MRI technique parameters as obtained by the neuropsychological task and the MRI scan. The endpoints for the neuropsychological task are standardized (z-) scores. The MRI data will be pre-processed, activation maps will be made and compared between normal controls and adolescents with HFA (GLM). Functional connectivity values from ROIs will be compared and functional connectivity maps will be generated. This all will be processed in terms of: (i) correlation between neuropsychological test results, MRI results and behavioural questionnaires data results, (ii) differences between adolescents with HFA and normal controls.

Secondary outcome

The study parametres of the Delphi procedure are the answers of the experts on

the (based on the main study)questionnaires. The endpoints of this procedure

are the mean scores of the final round of the experts' forecasts.

Study description

Background summary

Approved neuropsychological study:
Autism spectrum disorder (ASD) is a heterogeneous neurodevelopment syndrome in category of pervasive developmental disorders. The aetiology of ASD is still unknown, and in spite of many studies the main cognitive theories of ASD - Theory of Mind deficit hypotheses, Weak Central Coherence account, and the Executive dysfunction theory - fail to explain the broad spectrum of symptoms found in ASD.
In the Netherlands a growing number of high average intelligent (HAVO/VWO) adolescents with autism is in the need for special secondary education due to their social, executive function (EF) and specific learning problems. Although these adolescents experience many problems in their everyday life, it is very difficult to objectify these problems in clinical or laboratory settings due to the compensation strategies these adolescents apply in these structured settings. This makes the need for finding new ways to objectify their problems and to link these problems with their behavioural difficulties outside the laboratory especially high.
Although there have been many studies that looked at working memory (WM) as a core domain of EF in adolescents with high functioning autism (HFA), the results remain inconclusive. In these studies it is assumed that WM only processes abstract information, and only two studies made a direct link between behaviour outside the laboratory and EF and/or WM. However, in our view a proper functioning WM is not only important for cognitive processes as language, memory etc. (i.e. *cold* cognitive information), but is also essential for successfully navigating in the social world (i.e. *hot* cognitive information).

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Also functional MRI studies strongly support a WM deficiency underlying the broad spectrum of problems high functioning adolescents with ASD have. However, structural imaging studies point to a more global connectivity problem in the autistic brain. Abnormal growth patterns do indicate a ground for the WM problems found in adolescents with ASD, but unfortunately, there are to our knowledge no studies that combine behavioral, functional and structural imaging

data from the same cohort of subjects, so no direct conclusions can be made over the clinical implications of these findings.

In light of these earlier findings, our hypothesis is that WM plays a more central role in remembering, uploading and selecting social cues from the environment, hence in processing both *cold* and *hot* cognitive information. WM capacity problems therefore may play a leading role in the multiple symptoms (both *cold* and *hot* cognitive) displayed by intelligent adolescents with HFA.

Study objective

Primary objectives: 1) Study EF in general and WM capacity specifically in intelligent adolescents with HFA on a neuronal and cognitive level, as well for abstract information as for social relevant information, using neuropsychological assessments and MRI techniques , 2) find in this group of adolescents a link between their WM capacity, functional WM network, micro structural changes and their daily behaviour (questionnaires), and 3) propose a new way of objectifying the problems of this specific group of adolescents and 4) to make an attempt to translate these results to the social (school) settings where these adolescents experience their problems.

Primary Objective(s):
• Do high average intelligent (HAVO/VWO) adolescents with HFA have more EF problems on a behavioural and/or cognitive level than matched normal developing adolescents?
• Do high average intelligent adolescents with HFA have more WM capacity problems than matched normal developing adolescents?
• Do the social and specific learning problems found in high average intelligent adolescents with HFA find their origin in WM capacity problems?
• Is there a relationship between the behavioural problems and the strength that is put on WM in adolescents with HFA and if so, is there a difference between processing social relevant and abstract information?
• Are functional WM network properties different between high functioning adolescents with ASD and normal controls? And if so, can this be related to micro structural changes in the brain and/or with the problems these adolescents have in everyday life?

Secondary Objective(s):
• If these high average intelligent adolescents with HFA show WM capacity problems, are there new and better ways of objectifying their problems?
• Attempts will be made to translate the result of this study to the social (school) settings where these adolescents experience their problems.

Study design

This study will be a case-control study. The study will be performed at Epilepsy Centre Kempenhaeghe, Heeze, special secundairy education school de Berkenschutse Heeze and Radboud University Nijmegen.

Study burden and risks

Adolescent, parent / caregiver, and teacher / mentor will be asked to complete two questionnaires at home or at school. The neuropsychological assessment in the HFA group will last approximately 4 hours. The neuropsychological assessment in the normal control group will last approximately three hours. For this, one appointment will be made. The neuropsychological assessment is non-invasive and hardly stressful. Therefore, the risks of participating in this study is minimal. All tests and tasks are in a quiz or game fashion and will be offered on a computer or as a pen-paper task. The adolescent may work in his / her own work pace, and if desired, additional breaks will be inserted. Minors aged 12 years and older will participate in this study. Following the WHO guidelines, we stress that the 'not unless' principle applies to this study and that based on this principle approval for this study should be granted.

During adolescence, major changes take place in the neural systems that sub serve higher cognitive functions as EF. A normal development of these neural systems and EF is necessary to become an independent adult. Until now, the relation between the neural changes, the cognitive problems and the behavioural problems of adolescents with HFA is unknown, but the implications of this deviant development are huge: As these children grow from early adolescents into young-adults, more expectations of independence and social competence from their environment arise, expectations that they often fail to meet. This makes the need to get more insights in the neurocognitive system behind the HFA problems of these adolescents, to try and find a new way to objectify their problems and to find new ways to counteract these problems especially high. One possible way to counteract these problems in the future could be in the form of a WM training. Because the impact of training is bigger in an immature brain as opposed to a mature brain, this training could best be given during adolescence, when the development of WM is in full progress. This combination of factors makes it essential to study the problems found in individuals with HFA during adolescence. Because there are differences in WM strategies, capacity and neuronal networks in adolescence and adulthood, it is not possible to do this research with adult participants.
It is this combination of factors (neurodevelopmental changes, cognitive developmental factors, and behavioural and environmental factors) that make it essential to study the EF problems and social problems found in individuals with HFA during adolescence. This all with the goal to get more insights in the neurocognitive system behind the HFA problems of these adolescents, and to try and find a new way to objectify their problems and find new ways to counteract

these problems.
Because all effects found in this study will be relative effects (not absolute effects) a comparison with a matched normal development group is required to be able to understand and interpret the results.

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If the adolescent and his parent(s)/caregiver(s) wish to participate in the MRI assessment of the SWAAN study, a date for a MRI scanning session and the ADI-R will be scheduled. During this session (of 1 hour) a parent/caregiver will be present. The MRI-techniques and neuropsychological assessment that are applied in this study are non-invasive and scarcely stressful. Therefore, the risks of participating in the study are minimal. The adolescent can work in his/her work pace, and if desired additional breaks will be taken. This study involves minors of and above the age of 12 years. Following the WHO guidelines, we argue that the *not unless* principle should grant permission for this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

For adolescents with HFA:
- Age of 12 to 16 years.
- Autism disorder or Asperger disorder diagnosis made conform the diagnosis criteria as formulated in the DSM-IV.
- A signed informed consent (IC) from the adolescent and the parent/ caregiver.
- A high average intelligence conform a HAVO/VWO education level.;For normal control adolescents:;- Age of 12 to 16 years
- A signed IC from the adolescent and the parent/ caregiver.
- A high average intelligence conform a HAVO/VWO education level.

Exclusion criteria

For adolescents with HFA:
- A diagnosis for other (co-morbid) psychological disorders or psychiatric diseases as formulated in the DSM-IV, such as: attention-deficit and disruptive behaviour disorders, anxiety disorders and mood disorders.
- Appearance of additional variables that can influence cognitive functioning such as pathology of the Central Nervous System (CNS), significant hearing impairment, and medicinal treatment for epilepsy.
- Use of Methylphenidate. In consultation with the responsible doctor, parent/caregiver and adolescent are asked if they are willing to not take the medicine on the day of the neuropsychological assessment. If all agree, the adolescent may participate in the study.
- Inability to speak/understand the Dutch language.
- Vision less than +4.5D or - 4.5D.
• Claustrophobia.
• Metal implants or other contraindication for MRI.;For normal control adolescents:
- A diagnosis for a psychological disorder or psychiatric disease as formulated in the DSM-IV, such as: pervasive developmental disorders, attention-deficit and disruptive behaviour disorders, separation anxiety disorders, selective mutism, reactive attachment disorder of infancy or early childhood, anxiety disorders and mood disorders.
- Appearance of additional variables that can influence cognitive functioning such as pathology of the CNS, significant hearing impairment, and medicinal treatment for epilepsy.
- Use of Methylphenidate. In consultation with the responsible doctor, parent/caregiver and adolescent are asked if they are willing not to take the medicine on the day of the neuropsychological assessment. If all agree, the adolescent may participate in the study.
- Inability to speak/understand the Dutch language.

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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:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-02-2011
Enrollment:	276
Type:	Actual

Ethics review

Approved WMO Date:	22-12-2010
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	08-03-2012
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)

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	NL32788.068.10
Other	TC2519