Sensory processing in autism and childhood epilepsy

Published: 06-05-2015
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To study sensory processing and hyperexcitability in children with ASD and epilepsy using neurophysiological measurements (EEG/ERP).

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

Summary

ID

NL-OMON44800

Source
ToetsingOnline

Brief title
SPACE-study

Condition

- Neurological disorders NEC
- Developmental disorders NEC

Synonym
autism spectrum disorders - autism

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Autism, E/I balance, Epilepsy, Sensory processing

Outcome measures

Primary outcome

Primary endpoint: The main outcome parameters are EEG markers: brain evoked P50 suppression, P300, mismatch negativity and absolute resting-state power change.

Secondary outcome

Secondary endpoints: Other EEG phenotypes, neurocognitive and behavioural parameters.

Study description

Background summary

Autism spectrum disorder (ASD) is a behaviorally defined syndrome characterized by variable abnormalities in social interactions and communication, in association with restricted interest patterns and unusual stereotyped behaviors (1). The heterogeneity of ASD has obstructed the development of targeted treatments. No individual with ASD is the same in terms of clinical presentation and many different etiological factors have been implicated (2, 3). Nonetheless, preclinical research has revealed the possibility of converging mechanisms that may contribute to a substantial part of ASD. One important mechanism is the balance between inhibitory and excitatory inputs in the brain, also referred to as the E/I balance (4, 5). Many studies in animal models as well as experimental neurophysiological studies have brought evidence that an elevated E/I imbalance lead to disturbance in information processing and functional brain development (6-12). At the same time, it has also been emphasized that not all forms of ASD might be related to elevated E/I imbalances and even that the reverse, e.g. excessive inhibition, might also occur (11, 13). A contribution of hyperexcitable cortical networks, however, is strongly suggested by the frequent concurrence of epilepsy and/or seizures in children with ASD (14). Furthermore, the strong aversive reactions of children with ASD to sensory stimuli further indicates that cortical networks overreact to relative neutral stimuli (15). Indeed, excessive response to sensory stimuli is also thought to facilitate or cause seizures (16, 17). Hence, a continuum of E/I imbalances across ASD and epilepsy is increasingly suggested and may

constitute an important treatment target to reduce excitability and excessive response to sensory stimuli. In fact, novel treatments are currently being developed that can lower excitatory (*glutamatergic*) inputs or enhance inhibitory (*GABAergic*) activity (12). Successful application of these treatment requires the development of clinical markers that can indicate E/I imbalances and/or sensory processing deficits. In this study, we aim to deliver these markers by studying neurophysiological correlates of E/I imbalances in children with ASD an epilepsy. We hypothesize that the presence of seizure susceptibility or epilepsy in these types of ASD indicates the presence of hyperexcitable networks that may be detected by neurophysiological measurements of resting brain states and sensory processing capabilities.
To test this hypothesis, we will investigate sensory processing in children with epilepsy and ASD and compare these with typically developing controls and children with ASD without seizures. Sensory processing and E/I balance correlates will be assessed using electroencephalography (EEG) and event-related potentials (ERPs). With these studies we aim to establish neurophysiological markers of sensory processing deficits and E/I imbalances in ASD.

Study objective

To study sensory processing and hyperexcitability in children with ASD and epilepsy using neurophysiological measurements (EEG/ERP).

Study design

Observational study

Study burden and risks

The risks associated with participation in this study are minimal/ negligible. The burden for the participant is that he or she has to come to the University medical centre Utrecht three times; for neurocognitive and behavioural assessments, and for the EEG assessment. The EEG assessment is not an invasive procedure, although some children might find it uncomfortable to be touched on the head. In addition to the test days, parents of the participants will be asked to fill in multiple types of questionnaires about their child. There will be no direct benefit for the participants. However, in these patients with ASD and, finding evidence for a E/I imbalance via sensory processing deficits might give implications for more targeted treatment of (their) behavioural problems as novel, safe treatments are being developed. Furthermore, this study brings a detailed characterization of behavioural, sensory and cognitive profile for each of the participants, which can facilitate better treatment and guidance. This study will be performed among children with epilepsy and autism as the aforementioned sensory processing deficits are assumed to cause behavioural symptoms of hyperexcitability in both disorders. Finding neurophysiological

correlates of sensory processing and E/I deficits might give implications for better understanding of epilepsy as well as autism, and raises possibilities for treatment of ASD symptomatology. A typically developing control group is added to generate reliable reference data.

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

Ability to comply with the protocol-specified procedures for the duration of the study
IQ above 70
Written informed consent (and assent if appropriate to local laws and regulations),
In case of methylphenidate use, willingness to skip methylphenidate on the testing days
For epilepsy groups: Males and females aged 7-12, Diagnosis of epilepsy and ASD symptoms

(SRS50+ or diagnosis according to ADOS, or probable/definite difference at SP-NLor behavioral problems indicative of sensory processing problems (problems at school, irritability etc)
For ASD group: Males and females aged 7-12, Diagnosis according to ADOS or given by psychiatrist
For control group: Males and females aged 7-15, No psychiatric disorder present

Exclusion criteria

Major visual or auditory impairment
Presence of severe medical disorder
Other (psychiater) disorders other than epilepsy or ASD

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-08-2015
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO

Date:	06-05-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Approved WMO Date:	14-09-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	07-09-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	07-12-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	17-05-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL51700.041.15