Deafblindness
Theory-of-mind, cognitive functioning and social network in Alström syndrome
To my family
Deafblindness
Theory-of-mind, cognitive functioning and social network in Alström syndrome
Abstract


This thesis addresses young adults with Alström syndrome (AS). AS causes acquired deafblindness, a severe, progressive, combined auditory and visual impairment affecting daily life and self-reliance to a degree that full participation depends on help from others and society. AS is an autosomal, recessively inherited single-gene disorder that affects the ALMS1 gene. AS has a multi-systemic pathology including a high incidence of additional multiple endocrine abnormalities, cardiomyopathy, pulmonary fibrosis, restrictive lung disease and progressive hepatic and renal failure leading to reduced life expectancy. The focus in the present thesis is on the development of Theory-of-mind (ToM) and on how ToM relates to the development of certain cognitive skills and the characteristics of the individual social network. ToM refers to the ability to understand the thoughts and feelings of others.

The results reveal that individuals with AS displayed a significantly higher degree of heterogeneity in the performance of ToM tasks, and some individuals with AS performed on an equal level with nondisabled individuals. ToM performance was predicted by verbal ability and executive functioning (EF), whereas working memory capacity (WM) proved to be an indirect predictor. Later onset of visual loss further characterized AS individuals with better ToM. The sizes of the social networks of individuals with AS were smaller relative to those of nondisabled individuals, and many of the acquaintances were professionals working with individuals with AS. The number of friends correlated with ToM performance.

Methods to improve verbal ability and EF, and interventions to enhance social participation in childhood of individuals with AS might prove to be fruitful. In addition assistive technology to establish and maintain friendships in adulthood is required.

Keywords: Alström syndrome, Deafblindness, Theory-of-mind, Communication, Verbal ability, Executive functions, Working memory, Health problems, Friendship, Social network

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<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>ADHD</td>
<td>Attention Deficit/Hyperactivity Disorder</td>
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<tr>
<td>ALMS1</td>
<td>The Alström syndrome gene</td>
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<tr>
<td>ANOVA</td>
<td>Analysis of Variance</td>
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<td>AS</td>
<td>Alström syndrome</td>
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<tr>
<td>ASD</td>
<td>Autism Spectrum Disorders</td>
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<td>ASI</td>
<td>The Alström Syndrome International</td>
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<tr>
<td>CI</td>
<td>Cochlear Implants</td>
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<tr>
<td>CSCT</td>
<td>Cognitive Spare Capacity Test</td>
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<tr>
<td>dB HL</td>
<td>Decibel Hearing level</td>
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<tr>
<td>EFs</td>
<td>Executive Functions</td>
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<tr>
<td>HI</td>
<td>Hearing Impairment</td>
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<tr>
<td>ICF</td>
<td>The International Classification of Functioning</td>
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<tr>
<td>ID</td>
<td>Intellectual Disability</td>
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<tr>
<td>LMBB</td>
<td>Laurence-Moon-Bardet-Biedl syndrome</td>
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<tr>
<td>LTM</td>
<td>Long-term memory</td>
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<tr>
<td>MANOVA</td>
<td>Multivariate Analyses of Variance</td>
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<td>MSNA</td>
<td>The Maastricht Social Network Analysis</td>
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<td>NHV</td>
<td>Normal Hearing and Vision</td>
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<tr>
<td>PhoWM</td>
<td>Phonological Working memory</td>
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<tr>
<td>PTA4</td>
<td>Pure Tone Average for four frequencies (0.5-4 kHz)</td>
</tr>
<tr>
<td>RP</td>
<td>Retinitis Pigmentosa</td>
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<tr>
<td>SLI</td>
<td>Specific Language Impairment</td>
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<td>SNI</td>
<td>The Social Network Inventory</td>
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<tr>
<td>ToM</td>
<td>Theory-of-mind</td>
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<td>USH</td>
<td>Usher syndrome</td>
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<td>USH1</td>
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<td>Usher syndrome type 2</td>
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<td>VA</td>
<td>Visual Acuity</td>
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<td>WAIS</td>
<td>The Wechsler Adult Intelligence Scale</td>
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<td>WHO</td>
<td>The World Health Organization</td>
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<tr>
<td>WMC</td>
<td>Working Memory Capacity</td>
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Included studies

The present thesis is based on the following four studies, which are referred to in the text by their roman numerals:


IV. Frölander, H. E., Möller, C., Marshall, J. D., Piacentini, H., & Lyxell, B. Theory-of-mind in young adults with Alström syndrome is affected by social relationships. In manuscript.

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3. SUMMARY OF THE STUDIES .............................................. 28
1. Introduction

The understanding of other humans’ emotional and intellectual life must be something absolutely fundamental (David Katz, born 1884).

This thesis is about young adults with Alström syndrome (AS). AS causes acquired deafblindness, a severe, progressive, combined auditory and visual impairment affecting daily life and self-reliance to a degree that full participation depends on help from others and society 127. Emphasis is placed on the emergence and expression of Theory-of-mind (ToM) in challenging conditions. ToM refers to the understanding of emotions and thoughts of other individuals 45, 55, 80, 133, 146. The challenge referred to is the deafblindness and, in addition, a high prevalence of additional health problems such as cardiomyopathy, endocrine disorders and metabolic dysfunctions, which are health problems that are often implicated in a shortened life expectancy. No previous research has focused on this issue in this population.

An understanding of the specific challenges for individuals with dual sensory loss requires a perspective that links biological, psychological and social elements to one another 22. The thesis focuses on the interaction between sensory prerequisites and individual capacity to compensate for the loss of sensory information by the use of cognitive skills. The phenotype of AS is portrayed in this respect, requiring a description of deafblindness in relation to biological, psychological, social and cultural perspectives. A specific focus on the interaction between functioning and disabling consequences is further required 123, 181. Comparisons with nondisabled populations are conducted to confirm whether ToM performance in individuals with AS diverges from performance by nondisabled individuals. Comparisons to other disabled populations with sensory loss enables examination of mechanisms of importance in the development of ToM in AS.

1.1. Thesis outline

This thesis begins with a definition of deafblindness and a description of its consequences for social participation. Then, the clinical features of AS are introduced, with a focus on the gradual loss of both hearing and vision. The secondary consequences of deafblindness will be investigated via a comparison to Usher syndrome (USH), another deafblind syndrome that differs from AS with respect to onset and degree of loss. Differences in ToM
will be briefly described and discussed. The possible compensatory role of
cognitive skills in communication challenged by dual sensory loss is
explored. In addition, the relationship between development of ToM and
the capacity and features of the social environment (i.e., the social network)
is described. The consequences of poor health in the development of ToM
are also emphasized. Finally, clinical applications and suggested future
studies are presented.

1.2. Deafblindness

Deafblindness is extremely heterogeneous, and different definitions of
deafblindness have been used, some following legal definitions of deafness
and blindness. Other definitions refer to the functional consequences of dual
sensory loss and include physical, social and attitudinal factors within the
environment. The most frequently used definition in the Nordic countries
states that deafblindness affects daily life and self-reliance to a degree that
full participation depends on help from others and from society. The
absence of an exact definition complicates an estimation of absolute
numbers, although the prevalence of deafblindness has been estimated to be
14/100 000. The causes are predominantly genetic, and more than 50
hereditary syndromes cause acquired deafblindness. Deafblindness can
be congenital (i.e., severe visual and hearing loss at birth) or acquired
(causing a progressive dual sensory loss later in life), as in the case of AS.
Severe sensory loss has a negative effect on the ability to develop
communicative and verbal skills. It has thus been
proposed that early severe hearing loss for children in hearing families leads
to poor social interaction, delaying ToM development, whereas native
signers with signing parents display a relatively normal ToM development.
Additionally, early visual loss has an effect and might cause a
delay in the development of ToM. In contrast to the cases of
individuals with Autism spectrum disorders (ASD), the development of
ToM might be delayed but does not differ in individuals with severe hearing
impairment or severe visual impairment. The combined effect of
deafblindness on development of ToM has not been previously studied.
1.3. Alström syndrome and Usher syndrome

AS is an autosomal, recessively inherited single-gene disorder addressing the ALMS1 gene. Both parents are of necessity carriers but do not exhibit features of the syndrome. AS has an incidence of less than one per million. However, AS is closely related to a group of other syndromes within the ciliopathy spectrum that often shares major features. The syndrome is named after the Swedish psychiatrist and geriatrician Carl-Henry Alström. In 1959, he described a group of patients with the clinical diagnosis of Laurence-Moon-Bardet-Biedl (LMBB) but without the severe cognitive dysfunction that is typical in LMBB. Despite similarities with the prevalence of retinitis pigmentosa and hearing loss, differences in clinical manifestations and endocrinological profiles and genetic differences were found. AS has a multi-systemic pathology, including a high incidence of additional multiple endocrine abnormalities, cardiomyopathy, pulmonary fibrosis, restrictive lung disease and progressive hepatic and renal failure leading to reduced life expectancy. AS has a mild sensorineural hearing loss, slowly progressing in the first decade, usually to moderate or severe loss in following decades. The severity is variable, and age of onset varies from infancy to adulthood. Otitis media is frequent, causing an additive conductive hearing loss. The medical care for the population is improving; with a prolonged life span, it is clear that the loss of hearing in patients over 30 years of age is profound, with a need for cochlear implants (CI). The progression of visual loss is faster than that of hearing loss. Although there is variability in age of onset, dysfunction is typically demonstrated within a few weeks after birth. Retinal dystrophy leads to retinitis pigmentosa (RP) and juvenile blindness in 90% of the cases by the age of 16. Cone dystrophy occurs first; hence, visual experience in early childhood primarily comes from rods, which are accountable for peripheral and night vision. Motor development is often delayed in AS, and repetitive motor mannerisms occur. Deficits in coordination balance and fine motor skills have been observed in addition to a language delay and atypical behavior such as lacking inhibition of irrelevant responses, extreme stubbornness and excessive
eating (Möller and Marshall, 2015, personal communication). A higher frequency of conditions along the autism spectrum disorder (3-4%), ranging from autism to milder forms such as Asperger syndrome and restricted, repetitive or stereotyped patterns of behavior, have been reported in AS.

Fig. 1 Symptoms in Alström syndrome

---

**Symptoms**

Eye
Ear
Balance
Heart
Lipids
Diabetes
Kidney
Liver
Teeth problems
Obesity
Pancreas
Usher syndrome (USH) is another autosomal, recessively inherited condition that causes loss of hearing and vision. USH is included in the empirical part of this thesis to examine more general consequences of dual sensory loss and to compare these consequences with individuals with AS. USH accounts for more than 50% of individuals with deafblindness. Due to a high degree of clinical heterogeneity in USH in sensory functioning, the present classification into three subtypes (USH1-3) was determined. Of these subtypes, individuals with USH2 display the most similarities to AS when sensory functions are addressed, implicating differences in both the rate of progression and degree of loss. Individuals with USH2 have a congenital non-progressive moderate-to-severe hearing loss. USH2 also includes RP, which leads to severe visual impairment. The type of RP in USH2 is, however, less aggressive and has a slower progression than the type in AS. In USH2, the onset of RP appears in early teenage years. The loss of peripheral vision is typically slow, and when the process stabilizes, there is a remaining central visual field of approximately 10 degrees. Individuals with USH2 do not have vestibular deficits or balance problems, deficits that are frequent in AS. No behavior patterns such as repetitive behavior have been reported within this population.

1.4. Theory-of-mind

The structure of the human brain reflects the demands of living in bonded social groups; development of ToM is indispensable to our species. ToM refers to specific emotional and cognitive skills molding a capacity to impute mental states to one’s self and to others. ToM is described as an innate biological ability that is activated and developed during interactions with the social environment.

Difficulties in ToM have been observed in individuals with Autism Spectrum Disorders (ASD). Other syndromal populations with atypical development such as individuals with Down’s syndrome, Fragile X syndrome, Williams syndrome, and CHARGE–syndrome display lower scores on ToM tests, which might indicate a biological explanation model. Explanations of deviances, however, cover biological, psychological and social levels.

An interplay between biological, psychological and social factors of importance in ToM development are inferred because both innate capacities to relate and social experience are required to develop knowledge about feelings and thoughts of other humans.
In contrast to theories underlining that ToM is innate, modularity theories suggest that ToM consists of serial modules triggered by the experience of social interplay. The formation of early social relationships is indispensable for further development of ToM, and variance in family patterns in particular contributes to differences. The importance of the establishment of an early parent-child relationship to develop ToM has been stressed. In particular, parental talk about desires promotes children’s talk about thinking, with an effect on ToM development.

During the first years of life, development of an implicit ToM is already performed, referring to a social-perceptual ability to attribute thoughts and feelings to behavior and action. Attention to other human’s faces and to their gestures and motions empowers development of an ability to predict events and to understand what another person will do next. Such an implicit understanding of behavior supports ToM development. Imitation, shared attention and empathy are fundamental social skills, further required for the development of an ability to reason about mental states.

An ability to understand that other humans might hold a false belief is an explicit social-cognitive form of ToM, indispensable in the development of a more advanced ability to understand the thoughts and feelings of others. This ability has largely been tested by the use of the false belief test and might be an indication of the understanding of mental states as a representation. Such an understanding is typically developed throughout preschool years around the age of four. An exclusive focus on false belief understanding has, however, lately been displaced by a broader perspective on the ability to impute mental states, affirming that development is triggered by the richness of the social environment. A noticeable account of ToM development is stimulation theory. According to this theory, ToM depends on self-awareness and the capacity to imagine and pretend. That capacity is developed in the same timespan as false belief understanding. Pretend play that involves a taking of different roles is reinforced by interplay with other children. Around the age of seven, an insight that another person understands something about someone or something else is developed. Such an ability is of importance to understand another individual’s reactions to a situation and the other individual’s reactions to the child’s actions.

Advanced ToM is one aspect of ToM that develops later in childhood and refers to the understanding of social deceptions (e.g., white lies and bluffs). Advanced ToM requires an ability to make context-appropriate
mental state references. Individuals with high functioning forms of autism do not display such complex mentalization ability \(^{16, 41, 72}\) and have problems with understanding indirect requests, sarcasm, jokes and metaphorical expressions. Advanced ToM is especially dependent on cultural stimulation and verbal understanding \(^ {26}\) but also requires focused attention and cognitive effort \(^ {63}\).

### 1.5. Cognitive functioning

Cognitive functions such as executive functions (EFs) and working memory (WM) are important for communication and for the development of ToM \(^ {45, 80, 84, 156, 188}\). No previous research on individuals with AS has explicitly examined cognitive functioning, verbal ability and communicative skills, despite frequent clinical observations of possible deficiencies in these aspects.

#### 1.5.1. Verbal ability

Language processing is a complex cognitive activity \(^ {12}\) involving a retrieval of language representations from long-term memory (LTM). Limitations in access to language and communication due to sensory loss in the first two years of life might cause a delayed development of language \(^ {67, 87, 100, 155}\).

Language entails several different skills such as lexical skills (e.g., expressive and receptive vocabulary), syntax (e.g., grammatical understanding and use) \(^ {9}\) and pragmatics (the use of language) \(^ {89, 161}\).

The development of spoken language is, among other things, dependent upon phonological skills such as the awareness of and sensitivity to the sound structure of language \(^ {4, 13, 131, 159}\). Verbal ability develops as the efficiency to retrieve and to use language representations in the semantic LTM develops \(^ {4, 131}\). Lexical skills also entail information access and processing of phonological representations \(^ {113}\). The pragmatic abilities of initiating, maintaining and terminating interaction are just as important as verbal lexical and syntactic abilities and thus are incorporated in a broad definition of language \(^ {97}\).

In the present thesis, the focus will be on aspects of verbal ability such as access and retrieval of semantic information and phonological representations in LTM.
1.5.2. Executive functions

EFs refer to top-down mental processes that promote concentration and the ability to focus attention. Top-down processes enable elaboration of ideas, planning of actions and assigning of options to handle unanticipated challenges. EFs are further of use in resisting temptations or acting impulsively. In addition, EFs enhance cognitive flexibility. There are three core aspects of EFs. One is to shift attention between different multiple tasks, operations or mental sets. A second aspect of EF refers to the updating of new incoming information in WM, at the same time replacing old irrelevant information. Inhibition or ignorance of irrelevant information and the suppression of prepotent responses is a third aspect of EFs. Behavioral control is another aspect of inhibition that refers to an ability to resist temptations and to avoid reacting impulsively. Poorer inhibitory control is associated with atypical behavior such as difficulties with regulating emotions and repetitive mannerisms.

EF is important for most communicative activities in disabled and nondisabled populations. The ability to understand speech in challenging conditions is dependent upon cognitive skills such as EFs. EF is also related to verbal ability in nondisabled populations. EF is to some extent also related to verbal ability in individuals with ASD. No previous research has focused on the specific contributions of EFs in the development of ToM in AS.

1.5.3. Working memory

WM refers to the capacity to hold and process information over a short period of time. The WM system includes four different components. The central executive is thought to be responsible for planning, coordination and execution of cognitive tasks in which WM is one involved component. The central executive is also proposed to have some storage capacity. The phonological store (PhoWM) holds auditory or auditory-related information active for a short period. The visuospatial store serves a similar role for visual and spatial information. The episodic buffer is proposed to bind old information (stored in LTM) with new, incoming information. WM develops over time and is fully developed by approximately 20 years of age. WM capacity (WMC) is predictive for a large number of cognitive activities including language comprehension and speech communication in a challenging listening situation due to hearing loss and/or the presence of noise.
The storage of phonological representations mediates the establishment of this specific representation in the LTM. Learning of new words is hence dependent upon PhoWM, and restrictions might be a reason for language deficits in, e.g., children with specific language impairment (SLI). Specific problems in PhoWM have also been demonstrated in children with Attention Deficit/Hyperactivity Disorder (ADHD). In addition, children with profound deafness and CI have poorer PhoWM capacity than age-matched hearing children. PhoWM within a group of deaf children with CI was found to be related to development of vocabulary and to development of grammar. A preference for oral communication in deaf children with CI was related to higher performance levels in the PhoWM span.

1.6. Social network

Social networks refer to the web of social relationships. Network data are defined by interlocutors and relationships within naturally occurring social clusters. Both quantitative descriptions such as number of relationships and qualitative data (e.g., quality of relationships) can be included. An egocentric perspective is often applied, with a specific individual in focus and related individuals grouped due to their specific role or function. One important function of a network is distribution of social capital (i.e., resources characterized by norms of reciprocity and social trust). Robust social networks positively affect health, employment and social inclusion. House (1981) defined different functions of the social network as provision of emotional support, services that assist needs, advice to addressed problems and information that is useful for self-evaluation. The social network can also be described by its structural features in terms of reciprocity or emotional closeness. The extent to which relationships exist in the context of organizational roles and whether equal powers are exerted are other important features of the network. Other aspects of importance are whether members of the network are demographically similar and whether they live in close proximity to the focal person.

Social support is transferred through the social network. In previous research on caretaking and support, the family constituted a primary focus. Peer relationships have also attracted interest in a supportive perspective. Bronfenbrenner argued for the importance of a larger social context to promote children’s development. Supportive functions of the network have also been studied in relation to disability. A social network focus can
enhance intervention planning for individuals with complex communication needs and for their communication partners. Individuals lacking opportunities to establish such ties might develop isolation. The risk of isolation is further increased in individuals with disability, despite an inclusive policy. Individuals with augmentative and alternative communication specifically face barriers. This statement also applies to individuals with visual loss. Social exclusion has also been reported in relation to individuals with acquired deafblindness.

1.7. ToM in relation to sensory capacity, cognition and social factors

Deafness and blindness might have a negative effect on communication and development of language (cf. 101, 102, 140). Early hearing loss for children in normal hearing families and early visual loss might lead to impoverished social interaction and might cause a delay in the development of ToM 134, 166.

Clinical observations of adult individuals with AS reveal a frequent presence of difficulty in understanding mental states. It is, thus, reasonable to assume that a dual sensory loss will have an effect on the development of ToM. Previous studies of individuals with hearing or visual loss underline that conscious mental processes might be required to gain sufficient information from the social environment, which is one prerequisite for the development of ToM. AS is a unique condition that might highlight cognitive mechanisms of importance for the development of ToM 133, 156, 177. Closeness to family members has proved to be important for the development of ToM 62, 94, 95, 168, as has range of social acquaintances 65, 132. Anecdotal data indicate a widespread loneliness that is not generally displayed in individuals with hearing loss or visual loss that could have an effect on the development of ToM. To facilitate the development of ToM in individuals with AS, it is necessary to consider biological aspects and both psychological and social components in the development of ToM.
2. METHODS

2.1. Methodological challenges

AS constitutes a small population, with an incidence of less than one per million, spread over a large geographical area105, which complicates any attempt to recruit research persons. Deafblindness restricts the number of research questions that can be posed. A small sample further declines the power of the statistical analyses. The population of AS is also very heterogeneous with respect to number of medical conditions. Onset of visual loss and hearing loss varies within the population. Type of educational setting and access to technical aids and healthcare support varies both within and between countries 106. To be able to include data beyond a single-case study level, it was necessary to collect data from outside Sweden. Thus, English-speaking individuals with AS, primarily from the US, participated in the studies. The tests used were all well established and have previously been frequently used in research. The tests were chosen to allow for comparisons of empirical patterns with other populations. The deafblindness also restricted the type of tests that could be used. That is, the tasks in the tests should be possible to perceive and understand with respect to the degree of participants’ dual sensory loss. Tests based on visual presentations were excluded for individuals with AS. The data were collected in a short period at two family and research conferences (2010 and 2013). At a similar event (2013), adults with USH were tested in Sweden. The small size of the AS population also makes participants in specific aspects easy to identify, a limitation that also restricts possibilities to present and publish results (e.g., about individual etiology, symptoms and personal traits).

In the empirical part, we divided the AS participants into subgroups based on a median-split, enabling more specific comparisons with the control group. Analysis on a subgroup level might highlight important mechanisms.

The genetic background of AS, the physiological dysfunctions, the diseases caused by the ALMS gene, and the connected disabilities have been studied in previous studies. Thus, the physical phenotype is fairly well described, whereas the mental phenotype is only anecdotally described. Behavioral traits such as difficulties to understand mental states, repetitive or stereotyped patterns of behavior and other neurological findings also have been reported at an anecdotal level105.
2.2. General aims

The general aims of this thesis were to explore and examine ToM in young adult individuals with AS and to examine whether and how ToM performance was related to sensory loss, to some cognitive skills and to the characteristics of the individuals’ social networks.

Specific aims in studies I-III were designed to examine ToM in individuals with AS, examine how ToM related to cognitive performance and to compare performance levels with populations of nondisabled individuals and individuals with USH. Study IV was designed to describe the size and content of individuals’ social networks and whether these characteristics were related to ToM, cognitive skills and the degree of deafblindness.
2.3. Participants

Study I included twelve adolescents and young adults with AS (six females) 16–37 years with a mean age of 27 years. A control group of 24 nondisabled individuals (12 females) was matched with respect to age and educational level. An initial analysis revealed a high degree of variability in ToM performance; to examine how ToM might relate to cognitive factors and factors connected to the disability, the AS group was divided into two groups by a median split based on their ToM performance.

Study II included the same 12 individuals (six females) with AS who took part in the first study and 13 individuals with USH2 (four females) 21–60 years with a mean age of 39 years. In addition, 33 nondisabled individuals were recruited of whom 24 individuals matched the AS group with respect to gender, age and educational level, and 10 individuals matched the USH group with respect to gender, age and educational level.

Study III included ten young individuals with AS (six females) 19–38 years with a mean age of 28 years. Seven of those took part in the first study. A control group of 20 nondisabled individuals was included, matched for gender, age and educational level. Similar to the first study, the participants in the AS group were divided by a median-split based on their ToM performance.

Study IV included the same ten young individuals with AS (six females) who participated in the third study. A reference group of 42 age-matched nondisabled individuals from the Maastricht Social Network Analysis (MSNa) was included to enable a comparison between nondisabled individuals and individuals with AS concerning quantitative aspects of the network. In addition, the same age and gender-matched ToM-tested nondisabled individuals from study III participated, chosen as a comparison to the group of AS individuals with better and poorer ToM performance.
Table 1. People with AS and USH included in the present thesis

<table>
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<th>AS study 1 Poorer ToM</th>
<th>USH2 study 2</th>
<th>AS study 3 &amp; 4</th>
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<td>Visual Field Mean (1-5, best eye)</td>
<td>4.70</td>
<td>4.67</td>
<td>4.83</td>
<td>3.54</td>
<td>4.75</td>
<td>4.33</td>
<td>4.89</td>
</tr>
<tr>
<td>Visual Acuity Mean (1.0-0.0, best eye)</td>
<td>0.04</td>
<td>0.04</td>
<td>0.02</td>
<td>0.45</td>
<td>0.03</td>
<td>0.04</td>
<td>0.03</td>
</tr>
<tr>
<td>Mean Discovered Hearing Loss (months)</td>
<td>8.9 (6.7)</td>
<td>5.8 (3.7)</td>
<td>12.4 (8.8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Discovered Visual Loss (months)</td>
<td>8.1 (13.4)</td>
<td>7.7 (4.3)</td>
<td>0.6 (1.3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2.4. Assessments

2.4.1. Hearing

Hearing impairment (HI) was assessed by pure tone audiometry, with a calculation of the average pure tone threshold for the best ear at frequencies of 0.5, 1.2, and 4 KHz (PTA4). The hearing tests used were either performed in standardized settings within 6 months and/or by audiometry performed at the time of testing. When audiometry was performed at the time of testing, an audiometer with earphones (Kuduawe Ltd) was used. The WHO grading of HI was used: 1 = mild, (PTA4 26-40 dBHL); 2 = moderate PTA4 (41–60 dBHL); 3 = severe, (61–80 dBHL), and 4 = profound, PTA4 (> 81 dBHL). In this thesis, the degree of hearing impairment was reported either by the use of the WHO scale \(^{181}\) or by the presentation of PTA4 values. All participants during the ToM and cognitive tests were fitted with bilateral hearing aids.
2.4.2. Visual acuity

Visual acuity (VA) of the best eye was measured using Snellen chart-based standard tests (0,0–1,0) in which normal visual acuity was denoted to be >0,8

2.4.3. Visual field

Visual field (VF) was measured by Goldmann perimetry, with categorization into five phenotypes: 1 = normal; 2 = presence of a partial or complete ring scotoma, the latter either extending or not extending into the periphery; 3 = concentric central field loss with a remaining peripheral island less than one-half of the field circumference; 4 = marked concentric loss (a visual field of less than 10 degrees); and 5 = no visual field, i.e., blindness.

2.4.4. Degree of deafblindness

In study I, we used a hearing impairment categorization according to the WHO recommendations, in which we used categories from mild to profound impairment. The scores of HI and visual impairment (visual acuity) in the first study were added to achieve a combined degree of deafblindness. Age of onset of sensory loss was obtained from the Alström International Questionnaire.

2.4.5. Vestibular functions

Data about vestibular functioning were retrieved from medical records, built on, e.g., bithermal-caloric tests, rotary tests, computerized dynamic posturography or Romberg’s tests. The vestibular function was categorized into normal function, hypofunction and vestibular areflexia.

2.4.6. Motor development, language, thinking and social behavior

ASI developed the questionnaire, “Alström syndrome questionnaire”, to be completed by a parent or another close associate together with the individual with AS. The questions were estimated to take about an hour to answer. The questionnaire included questions concerning social status, employment, education and schooling situations. The questionnaire also inquired whether health problems were generally observed in AS. If the answer was yes, a follow-up question inquired at what age AS was diagnosed.

Information about motor development, language, thinking and social behavior as a child under the age of ten and as an adolescent or adult (age
11–adult) were further obtained from responses in the questionnaire. The responses were categorized into five levels. The medical history was well documented, also focusing on functional aspects and developmental issues (Marshall and Möller 2014, Personal communication) 105, 106.

2.4.7. Theory-of-mind

Advanced ToM was measured by a set of eight social stories from Happé’s advanced test of ToM—the strange stories72, including examples of double bluff, persuasion, white lies and misunderstanding. In addition, eight matched physical control stories requiring a general reasoning ability were administered and scored on the basis of why an action had been performed. Eight unconnected sentences assessing an ability to recall were also administered. This shorter form of Happe’s test of advanced ToM has previously been used in functional imaging studies and neuropsychological studies 15, 60, 71, 72, 82, 179. The test took approximately 45 minutes to conduct.

2.4.8. Verbal ability

Verbal ability was assessed with tests of vocabulary. The AS group and the matched nondisabled control group were tested on the vocabulary subtest in the Wechsler Adult Intelligence Scale 175. Participants were asked to tell the meaning of words. Responses were matched to the general scoring principles and the sample responses to each item. The USH2 group and their matched nondisabled control group were tested on the Antonym Test, in which the participants were asked to identify the pair of antonyms among five visually displayed words 100, 158. Each of the vocabulary tests took 15–20 minutes to conduct.

2.4.9. Executive Functions

The EFs of updating and inhibition were measured using a shortened version of the Cognitive Spare Capacity Test (CSCT)116. Participants were asked to repeat a number of two-digit numbers. After each list, participants were asked to report particular list items depending on the condition. In the updating condition, participants were asked to report the first list item and the two highest numbers in the list. In the inhibition condition, participants were asked to report the two odd value items by a particular speaker. The EF test took approximately 15 minutes to conduct.


2.4.10. Working memory

General WMC was measured by a reading span test. Short three-word sentences were presented. After the presentation of each sentence, the individuals were asked to judge whether the sentence was absurd. After a series of sentences had been presented, the individuals were asked to randomly recall the first or the last word in every sentence. PhoWM was assessed using serial recall of non-word series with increasing lengths. Participants were asked to repeat each of the non-words after each series. Each of the WM tests took approximately 10 minutes to conduct.

2.4.11. Social network

Structured interviews were conducted with the Maastricht Social Network Analysis (mSNA) to measure the size of each participant’s social network. The reference group of nondisabled individuals was used to compare the size of the social network, listed as family members and acquaintances or as professionals/semiprofessionals. The Social Network Inventory (SNI), a sociometric method developed for small group studies, was used in addition to conduct structured interviews in which participants were asked to mention significant others in different environments. This inventory was used in addition because, aside from quantitative measurements, it also allowed qualitative measurements as estimations of the closeness to other individuals. The structured interviews took approximately 30 minutes to conduct.

2.5. Analysis

The designs of the studies were quasi-experimental, with an exploratory and descriptive focus. Individuals with deafblindness were matched to nondisabled individuals on background variables such as age, gender and educational level. To examine within-group differences and conduct specific comparisons with the nondisabled individuals, the population of AS and USH2 was divided into two groups by a median-split based on their performance on the strange stories test of ToM. Thus, the results were analyzed at three different levels, with comparisons at a group level, subgroup level and case-study level.

In study I, multivariate analyses of variance (MANOVA) and post hoc t-tests with Bonferroni correction were conducted to show group differences. Analyses were performed via a median-split of individuals with AS into a better and a poorer ToM performing group. This sub-division enabled a
description of characteristics of better versus poorer ToM performance with respect to WMC and verbal ability.

In study 2, a non-parametric Kruskal Wallis test was used to analyze differences between the two groups of deafblindness (AS and USH2) because the data were not normally distributed. Follow-up analyses of between-group differences were performed via a Mann-Whitney U test. The level of significance was adjusted, with the Bonferroni correction for multiple comparisons set to $p < 0.0167$. Analyses were also performed on two subgroups (regardless of syndrome), defined by their ToM performance. Individuals with deafblindness producing correct mental inferences within 1 SD of the mean of the control group ($n=12$) were compared with those whose production of correct mental inferences was below 1 SD below the mean of the control group ($n=13$).

In study 3, independent t-tests were performed to examine differences between the AS group and the nondisabled control group. Non-parametric Mann-Whitney tests were used to examine differences between both AS subgroups and between subgroups and the nondisabled control group. The subgroup of AS individuals producing correct mental references within 1 SD of the mean of the control group was compared with the control group. This comparison was done to determine whether the performance in this better ToM-performing subgroup in other domains also resembled that of the control group. The reminder of the group of individuals with AS was also compared with the control group to determine whether and how their performance differed in other domains (i.e., with respect to verbal and cognitive performance).

In study 4, one-way ANOVAs were used to examine differences between the AS group and the nondisabled control group. The AS group was divided into a better ToM-performing group and a poorer ToM-performing group. The better ToM-performing group consisted of AS individuals with a ToM performance within 1 SD of the mean of the nondisabled control group ($n=3$). The poorer ToM performing group consisted of AS individuals with a ToM performance poorer than 1 SD below the nondisabled control group mean ($n=7$). Both AS subgroups were specifically compared with the nondisabled group. Non-parametric Kruskal-Wallis tests were computed to examine differences between both AS subgroups or between the subgroups and the nondisabled group.

Spearman’s rho (non-parametric correlation) was also used in all four studies to evaluate interaction. The level of significance used was $p<0.05$ in all of the statistical analyses.
2.5.1. Ethical approval and considerations

The guidelines of the WMA Declarations of Helsinki, Ethical principles for medical research involving humans have been considered. The studies were approved by the regional ethics review Board of Uppsala – Örebro, Sweden and the Institutional Board of the Jackson Laboratory, USA. Signed informed consent was obtained from all participants. All participants were informed that participation in the study was confidential and voluntary. Analyses conducted in the studies at the subgroup level were connected to ethical issues and a need to protect the integrity of the participants. Demographic data were presented at a group level for the same reason.
3. SUMMARY OF THE STUDIES

Study I
Title: Theory-of-mind in adolescents and young adults with Alström syndrome.

The aim was to examine clinical observations revealing a higher frequency of deviations than a typical trend of development of ToM in AS. Possible factors contributing to ToM development such as verbal ability, WMC and onset and degree of sensory loss were assessed in relation to ToM performance.

The results demonstrated that individuals with AS performed at significantly lower levels in ToM tasks and displayed a higher degree of variability in performance than did the nondisabled control group. Individuals with AS and a relatively poor level of ToM performance produced fewer correct mental state inferences than did individuals with AS with relatively higher performance levels. AS individuals with relatively high performance levels made as many correct inferences in ToM tasks as the control group did, but their inferences often displayed a lower degree of exactitude (i.e., an incompleteness). Verbal ability and educational level but not WMC was correlated with ToM performance. Degree of deafblindness did not relate to ToM, but the time of onset of visual loss in contrast to hearing loss was correlated with ToM. The results were discussed with respect to how factors related to deafblindness and cognitive skills affected ToM.

Study II
Title: Theory-of-mind and cognitive function in adults with Usher or Alström syndrome.

The aim of this study was to investigate whether differences in visual loss and hearing loss had an effect on ToM. ToM was examined in adults with AS and USH2, and those adults were compared with nondisabled individuals. In addition, the ability to understand a logical outcome of a physical condition was examined.

The USH2 group outperformed the AS group in ToM tasks, but both the USH2 and AS groups demonstrated poorer performance levels than did the nondisabled group. Both groups also demonstrated poorer performance than did the nondisabled group in the physical condition. Variability within the AS group was related to verbal ability, and within the USH group, variability was related to WMC. Visual status, and to a minor extent level of hearing loss, was found to be related to ToM performance. The
prevalence of the additional physical diseases was not related to poorer ToM performance. The consequences of limited access to sensory information due to deafblindness were discussed with respect to both ToM and outcomes related to everyday situations.

**Study III**

Title: Theory-of-mind in individuals with Alström syndrome is related to executive functions, and verbal ability.

The aim of this study was to explore whether cognitive skills such as EFs and phoWM can account for differences in ToM performance in individuals with AS.

The AS group performed at a significantly lower level than did the control group in both the ToM task and the EF tasks. A significant correlation was observed between recall of non-words and EFs in the AS group. Updating, but not inhibition, correlated significantly with verbal ability, whereas both updating and inhibition were significantly related to the ability to initiate and sustain communication. Poorer performance in the ToM and EF tasks was related to language perseverance and to motor mannerisms independent of vestibular functioning. The AS group displayed a delayed ToM and reduced phonological WM, EF and verbal ability. The compensatory role of EFs to perceive and process information from the social environment when the interaction is challenged by deafblindness was discussed and related to ToM.

**Study IV**

Title: Theory-of-mind in young adults with Alström syndrome is affected by social relationships.

The aim of this study was to describe and examine the social networks of young adult individuals with AS and to examine quantitative network features (e.g., size) and qualitative features (e.g., closeness) related to ToM performance.

AS individuals with poorer ToM reported fewer friends than did AS individuals with better ToM, but both groups reported an equal amount of significant others. Proximity to others did not correlate with ToM. Reported frequency of pretend play in childhood correlated with both ToM performance and the ability to establish appropriate social relationships. Reported solitude in childhood related to inappropriate social responses and a poorer ToM in adulthood that in turn was connected to reported difficulties in focusing attention on others and understanding their thoughts. Individuals with AS displayed a reduced network of acquaintances relative to a nondisabled reference group. A large part of the
network of acquaintances consisted of professionals within the health care system and educational settings or semiprofessionals within disability organizations. Animals, primarily guide dogs, were also included in the social network. The role of deafblindness, childhood interaction and establishment of friendship in the development of advanced ToM were discussed.
4. DISCUSSION

The purpose of this thesis was to explore and examine ToM in young adults with AS and to examine whether and how ToM performance is related to some cognitive skills and to features of the social network.

The observations reported by families and professionals concerning difficulties for some individuals with AS in understanding the mental states of others were largely verified. We also observed that some of the individuals with AS reached performance levels in ToM tasks comparable to nondisabled individuals, although displaying a somewhat poorer rate of extended answers. Extended answers require an ability to completely understand and extensively refer to mental states, an ability that was seldom displayed among individuals with AS, even among those with higher ToM scores. AS individuals with a relatively poorer ToM referred to thoughts, feelings and desires less frequently to analyze the content of socially loaded stories. The less appropriate physical references associated with consequences (e.g., to obtain something) were instead more frequently used. This pattern of responses is also expressed frequently in individuals with high-functioning autism. The AS group differed from the nondisabled control group in both the mental and the physical conditions. The generally poor performance in the physical condition and lack of difference between individuals with higher and lower ToM performance in this respect might have been caused by a shared lack of sensory experience related to the dual sensory loss rather than to difficulties in reasoning. AS has not previously been reported as related to specific learning disabilities or intellectual disability (ID). General difficulties in reasoning would also have restricted participants’ ability to understand the thoughts of others at a more advanced level and are not compatible with the observation of ToM variance in the group of individuals with AS. The AS group was outperformed by the nondisabled control group in the EF and WM tasks and in verbal ability. ToM was predicted by EF and verbal ability but not by WM. Taken together, this performance indicates an interaction between ToM performance and cognitive and verbal abilities in the AS group. An interaction between ToM and verbal ability was not established in the USH group, indicating that a majority of the individuals in this group had sufficient verbal ability for reasoning in the mental condition. However, that complex WMC, which is important for development of language comprehension, related to ToM in the USH group emphasizes
the importance of cognitive skills in communication challenged by loss of hearing and vision.

4.1. Sensory loss and ToM

Our expectations based on previous studies on ToM in populations with either severe to profound hearing loss or severe visual loss to blindness\textsuperscript{115, 135, 166} were that individuals with AS would perform at a lower level on tests of advanced ToM than would nondisabled individuals. It was also expected that a less severe form of dual sensory loss, such as was displayed in the USH group, might be associated with a better ToM performance. These assumptions were largely verified. The ability to produce extended correct mental references was relatively poor in a significant number of individuals with AS and USH2. The majority of the individuals with USH2 did, however, display performance levels on ToM tasks comparable to nondisabled individuals, whereas a majority of the individuals with AS displayed a lower performance level. Degree of deafblindness did, however, not predict ToM variance in the AS group. The reason may be a relative within-group homogeneity in grade of sensory loss. The impact of sensory loss, in this group, was yet verified by the fact that an early age at which the first sign of visual impairment occurred related to a higher frequency of incorrect mental references. When the two groups with deafblindness were compared with the nondisabled control group using a stricter scoring criterion of the number of extended correct mental references, no significant difference between them emerged, thus also indicating possible consequences for ToM in milder forms of deafblindness.

4.2. Hearing loss, speech perception and ToM

A severe hearing loss is not fully compensated for by the use of hearing devices\textsuperscript{7, 126, 166}, which might cause a delay in the development in ToM\textsuperscript{136} because the individual lacks full access to spoken language. An effect on ToM development was expected in individuals with AS due to the progressive loss of hearing\textsuperscript{104}. However, neither degree nor the age of onset of hearing loss was related to ToM, possibly because the progress of hearing loss is relatively slow in AS. That slow progression provides some access to the hearing world and does not affect mental state understanding during the phase of early social interplay when implicit forms of ToM are formed and developed. The relatively slow progression of loss permits social interaction
and observation of others of importance to implicit development of ToM. The consequences of hearing loss during one of the most sensitive periods for the development of ToM (around the age of four) seems, despite frequent use of hearing aids to be more pronounced. At this age, the ability to understand that another person’s beliefs are based on knowledge and that mental states can differ from actuality is established. The relatively small differences between the high performing AS group and the USH2 group can be partly explained by the fact that individuals with USH2 have a moderate to severe HI at young ages, with permanent use of hearing aids.

The AS group was outperformed in the physical control stories by the nondisabled group. One reason for this outcome could be a less developed verbal ability than in an age-matched nondisabled control group. Severe hearing loss also affects daily life functioning negatively by restricting participation in social settings and might constitute one reason for lower performance levels in the physical control stories. Support for this assumption comes from a study of individuals with USH2 and USH1, in which individuals in the latter group who were congenitally deaf needed more overall support in daily life. This study highlights the consequences of hearing loss in everyday activities when vision is also poor. In the AS group, a mild hearing loss might actually be functionally “severe” without the ability to lip-read due to severe visual loss early in life.

### 4.3. ToM, visual loss and social interplay

The onsets of VI and ToM were related to one another in the AS group. The visual mode is important for early, general mental development. Children with AS encounter severe visual challenges early in life, and the sensory prerequisites for participation in social interplay are already negatively affected at this stage. Thus, a lack of visual experience from communicative and social stimuli might be one reason for the relationship between age of onsets of VI and ToM. Poor ToM might be caused by lack of a possibility to make judgments concerning other individuals’ mental states from their facial expressions. This type of judgment is important in early communication to establish implicit forms of ToM. This form of judgment also recruits other neural circuitries than explicit ToM and is not related to verbal ability. However, it might nonetheless constitute a platform for later development of advanced ToM.
The rapid visual dystrophy in AS might also be a part of the explanation for the difference in ToM between the AS group and the USH2 group. Development of ToM in USH2 is not affected because early RP has a pubertal onset in individuals with USH2. They have central vision in adulthood, although the visual field for smaller objects decreases \(^{102}\). The cone dysfunction in AS leads to an early loss of vision in the 2nd decade \(^{171},^{173}\). Thus, ToM development in USH2 is far less affected by visual loss in childhood and adolescence than in AS.

### 4.4. ToM, EF, WM, verbal ability and communication

Verbal ability is important for development of advanced ToM \(^{26}\). The demands on EF and WM \(^{63}\) might be further increased by the challenge of processing information with a dual sensory loss \(^{43}\), requiring focused attention and cognitive efforts \(^{63}\). In the present study, verbal ability and EF proved to be directly related to ToM, whereas WM displayed a more indirect role via the relationship with EF. The indirect relationship with WM might be an indication that a certain level of WMC is necessary to develop ToM but might not, beyond a critical level, lead to further improvement in ToM \(^{161}\).

Previous research has shown that the capacity to inhibit irrelevant information is important to initiate and sustain communication and might facilitate the development of mental references. This relationship has been previously demonstrated in populations with ASD \(^{109},^{128},^{185}\) and was found in individuals with AS in the present thesis.

The ability to update WM with incoming information and compare it with stored information in LTM correlated with verbal ability in the AS group. This relationship might suggest a mediating role for updating ability in vocabulary development, in turn promoting ToM.

Early language delay is frequently observed in individuals with AS. Odd rhythm of speech has also been reported in AS. The finding that inhibition of attention in general is related to inhibition of action \(^{64}\) supports the notion that both attentional difficulties and motor control difficulties (i.e. odd rhythm of speech) in AS, might be specifically related to poor inhibitory capacity. Such difficulties may have negative secondary consequences for verbal ability and then also for ToM development.
4.5. Biology and cognitive functions

Restrictions in inhibitory capacity have been established in a number of individuals with AS and might have contributed to the observed motor-mannerisms in AS that could not be explained by vestibular dysfunction, and the observed behavioral patterns \(^{104}\). This assumption is supported by the fact that biological influence on specifically behavioral inhibition has been reported \(^{107}\). AS is a genetic disorder with one gene detected thus far. The gene is very large, and many individuals have unique variations (mutations), which most likely explains the large heterogeneity in organ dysfunctions. The ALMS1 gene belongs to a group of ciliopathies \(^{106}\) in which neurocognitive impairments are frequently displayed \(^{90}\). One example is the closely related syndrome LMBB \(^{53, 78}\). Because the mutations causing AS are actively expressed in most organs, cerebellar anomalies have also been observed in individuals with AS. However, these findings are not consistent \(^{38}\), but individual cerebellar anomalies might have accounted for some of the EF deficits found in individuals with AS.

4.6. Social interaction and development of ToM

The reported problems in the AS group in understanding other individuals’ thoughts and interpreting their intentions correlated with a poorer ToM. ToM also correlated with reported frequency of pretend play in childhood. This correlation has previously been reported in various studies of nondisabled children \(^{91, 96}\) and stresses the importance of EFs to developing communicative skills. Such skills support interaction with other children and stimulate pretend play \(^{51, 52}\), in turn enhancing ToM development. The need of efficient EFs to communicate is increased by the challenge of sensory loss \(^{43}\). A reported preference in the AS group for solitary activities and a failure to develop peer relationships in childhood was accordingly related to relatively less pretend play and poorer ToM performance. Social isolation among deaf children is also related to poor ToM for similar reasons \(^{139}\). Because blind children have been reported to spend more time exploring the environment than engaging in pretend play, the development of ToM in this population for similar reasons might be delayed \(^{56}\). Verbal delay is frequent in AS and related to loss of hearing \(^{104}\), thus possibly affecting the development of pretend play in children with AS. A fast progression of visual loss early in life in AS was related to a poorer ToM capacity in adulthood, which might in turn be related to the significant
loss in one critical period for development of ToM around the age of four

4.7. Effect of friendship on development of advanced ToM

Individuals with AS reported significantly more contacts with professionals than age-matched nondisabled adults did, whereas the reported sizes of the networks of family members and acquaintances were significantly smaller. A similar pattern has been reported in other disabled populations (ASD and ID) 172. Individuals with physical disabilities in general display a wider social network than do individuals with developmental disabilities 98.

No relationship was observed between performance on ToM tasks and reported number of significant others or family-members. Additionally, performance in tasks tapping advanced ToM was not related to self-rated closeness to other individuals within the family, possibly because the individuals are adolescents or young adults, and friends become more important at this age 31. However, individuals with AS and relatively poor ToM reported fewer friends, which replicates results of studies including nondisabled individuals 94, 165 and deaf individuals, pointing to the interrelation between friendship and advanced ToM 139.

Friendship is dependent upon interpersonal competence and understanding of mental states 31, 37 but also upon social environments allowing encounters.

Many individuals with AS identified semiprofessionals (e.g., members of the Alström International board) or professionals, for example physicians and teachers, as members of their informal social networks. The same observation has been made in a group of individuals with developmental disabilities 75. Individuals with AS often attend boarding schools, and their health problems imply frequent contacts with the health care system 104, in which they frequently establish social relationships. In addition, a majority of the reported friends also belonged to ASI. Friendship relationships that primarily addressed professionals or semiprofessionals might imply a lack of equal relationships and a higher degree of formality, which could negatively affect the growth of an ability to cope with social situations 76, 110.
4.8. Conclusions

Early loss of vision in combination with a slower loss of hearing might in combination affect the development of ToM. Early loss of hearing is often associated with a delay in vocabulary development and thus with a negative effect on the development of ToM.

Early loss of vision leads to less exposure to social activities that facilitate development of ToM. Support of early interaction in the family and support to enhance play activities with other children already in preschool is important for establishment of ToM. In addition, the need for assistive technology and optimized social environments in adolescence and adulthood should be addressed to create possibilities for establishing and maintaining equal social relationships.

The present studies demonstrated a lower ToM performance level in AS compared with nondisabled individuals. Some individuals with AS could, however, reach levels comparable to nondisabled individuals. Similar patterns of results were observed for the cognitive and verbal tasks. A general decrease in ToM capacity is typical for individuals with ASD, and the threshold for verbal effect is markedly high. In the AS group, a significant within-group variance in ToM was displayed. This variability was highly dependent upon communicative skills, in which EFs had a mediating role.

The cognitive skills examined in this thesis can be modified with cognitive interventions at relatively young ages. However, the high degree of heterogeneity is a factor that must always be considered and adjusted to each individual level of functioning when interventions are being planned. Training of EF might be especially important because many individuals with AS are reported to display behavior in everyday life that might indicate less well functioning EFs.

4.9. Future research

The characteristics of deafblindness in AS complicate research. A main challenge is the within-group variance, which confounds between-group comparisons. However, the variance could also uncover patterns of interaction.

The recognized association between ToM and EFs in AS must be further elaborated and replicated. There might be different cognitive phenotypes dependent upon mutation sites in the gene, which might be possible to investigate in the future. In addition, neurological studies are required to
investigate the prevalence and character of specifically cerebellar anomalies in AS. Future research should also address phonological development and the specific role of EFs in the development of social participation in different adult populations with acquired deafblindness. The possibilities of supporting the social interaction between children with AS and other children should be further investigated, with a focus on implementation of assistive technology and methods to improve verbal ability and EFs.
5. Sammanfattning på Svenska/Swedish summary


Vid en jämförelse med ett annat dövblindrelaterat syndrom, Usher typ 2, med en generellt sett bättre förmåga att mentalisera, kunde synskärpa och synfält (som vid det syndromet bibehålls i högre grad i vuxen ålder) begripliggöra skillnaden i mentaliseringsförmåga mellan de två dövblindrelaterade syndromen. Att förmågan att mentalisera var
relaterad till verbal förmåga, lyfter fram hörselns betydelse, varvid bristande auditiva intryck på goda grunder antas medföra en försenad språkutveckling.

En nedsättning av både syn och hörsel har negativa konsekvenser för möjligheten att kommunicera. Av synnerlig betydelse är då kognitiva förmågor som de Exekutiva funktionerna, vilka understöder förmågan att styra uppmärksamheten 47. Eftersom utvecklingen av mentaliseringsförmåga baseras på erfarenheter utvunna vid socialt samspel kan förmågan att effektivt uppdatera arbetsminnet med ny information likväl som förmågan att avleda ovidkommande intryck, tankar eller associationer, kompensera för sensoriskt bortfall och skapa förutsättningar för att etablera en god mentaliseringsförmåga hos individer med AS.

Mentaliseringsförmågan visade sig också tydligt kopplad till de möjligheter till interaktion som det sociala nätverket medger. Anekdotiska data pekade på en utbredd ensamhet bland individer med AS. Resultaten indikerar omfattande konsekvenser av de hälso-problem som är förknippade med syndromet. Vänskapskretsen utgjordes i hög grad av vårdgivare samt företrädare för brukarorganisationer. Långt fler, än i andra jämförbara grupper med unga vuxna, bodde hemma hos sina föräldrar. Detta belyser generella svårigheter för människor med funktionhinder att knyta sociala kontakter utanför hemmet, i miljöer som inte är tillrättalagda 76, 110. En bättre förmåga att mentalisera visade sig vara relaterad till ett större nätverk av vänner och bekanta. De vänskapsrelationer som etablerats under uppväxt och tonår tycks stimulera framväxten av en mer avancerad mentaliseringsförmåga. Av det skälet är de yttre förutsättningarna, i form av tillgängliga och till individer med funktionshinder anpassade sociala arenor, av stor betydelse.

Implementering av metoder för att stimulera och utveckla Exekutiva funktioner 48, 169 hos individer med AS kan tillsammans med hörseltekniska hjälpmedel och anpassning av sociala miljöer underlätta kommunikation. Insatser via brukarorganisationer för att främja etablerande av sociala relationer rekommenderas för att skapa delaktighet.
6. Acknowledgments

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