



# An Urgent Call for an Evidence Based Management of Aggressive Behaviors in Autism Spectrum Disorder

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## ABSTRACT

### Background

Majority of children diagnosed with autism spectrum disorder (ASD) meet criteria for intellectual disability (ID). The prevalence of ASD has an increasing trend for unknown reasons; currently it is estimated to be approximately 1.5% in developed countries. The multifactorial etiology of ASD is still poorly understood. Persons with ASD have problems in social communication and interaction, and restrictive, repetitive patterns of behavior, interests and activities.

### Method

This paper describes the diagnostic and therapeutic challenges related to the management of neuropsychiatric disorders in intellectually disabled patients with ASD in clinical wards.

### Results

The most severe forms of behavioral disorders associated with ASD and ID include self-destructive behavior and/or aggression against other people or property. These symptoms require hospitalization, since in the most severe cases the behavioral symptoms do not respond to conventional non-pharmacological and pharmacological treatments.

### Conclusions

A need for multidisciplinary team work and new treatment options are evident. Because of the heterogeneity of this patient population, controlled, randomized clinical trials may not be sufficient to bring the much needed evidence based solutions to the challenges in clinical realm. Individually designed clinical trials are suggested in search for appropriate treatment protocols for the most severe cases of ASD related behavioral disorders.

### Keywords

Autism, Self-injury, Intellectual disability, Mental health

## Introduction

From clinical, scientific and an organizational perspective autism spectrum disorder (ASD) belongs to the most challenging co-morbidities in intellectual disabilities [1]. ASD is a range of conditions presenting with two types of symptoms: problems in social communication

and interaction, and restrictive, repetitive patterns of behavior, interests or activities. About 35-75% of children diagnosed with ASD meet criteria for ID, and since 1960 more than 30 epidemiological studies have shown ASD prevalence to have increased from 4.4 per 10 000 to 12.7 per 10 000 during the period 1992-2001

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[2]. The current prevalence is estimated to be at least 1.5% in developed countries [3].

Consensus on the reasons for the increased prevalence has not been reached so far: it has been speculated whether it is due to better diagnostics, changed definitions and terminology or whether it could be real. The challenges related to the management of this lifelong neurodevelopmental condition are further complicated by multifactorial etiology of ASD, which is still incompletely understood. Most likely both genetic and environmental factors contribute to ASD [3]. Lately it has become more and more clear that ASD is not a simple behavioral disorder (related to a relationship between a mother and a child as assumed earlier) but a multifactorial condition with immune dysfunction that affects one in 68 births in the United States and it has been suggested to be the fastest growing neurodevelopmental disability worldwide [4].

In spite of the plethora of numerous uncertainties related to causes and prevalence of ASD new interventions should be developed to prevent the patients (suffering from ASD related behavioral disorders) from injuring themselves and/or their caretakers seriously. For this we would need an intensive collaboration between basic researches, geneticists, immunologists, toxicologists, as well as treating physicians including neurologists, psychiatrists and other health professionals taking care of these patients. Development of the appropriate treatment protocols would require translational medicine and international efforts to find the right experts, who could tackle this challenge. This paper attempts to describe, from the clinician's perspective, why there is an urgent need for new interventions for the autism related behavioral disorders and what could be done to find efficient tools for clinicians to manage this patient group.

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### Clinical reality in the wards

The most severe forms of behavioral disorders associated with ASD and ID include self-destructive behavior such as banging the head on the wall, tearing of hair, nails and skin and aggressive behaviors (e.g. hitting, strangling, biting, kicking, tearing, breaking and throwing objects) towards other people or property. These symptoms place an individual or his or her caregivers at risk of serious physical harm. For example self-caused bleeding wounds can lead to significant anemia. Accordingly, the risk for

experiencing bone fractures, brain contusion and other physical injuries is everyday realm for both patients and their caregivers in the wards that are meant for the most severely disabled autistic children, adolescents and adults. Furthermore, aggressive behaviors can have significant financial consequences when furniture, windows or other property is destroyed and need a repair.

The most severe cases of ASD patients end up into the closed wards, where their symptoms are tried to minimize by arranging well-structured daily routines and by trying to find out the core causes of their undesired behavior. Occasionally, solving some underlying psychosocial problem suffices. It may also be helpful when the possible sensory hypersensitivities are acknowledged in their everyday life.

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### Diagnostic challenges

Consequently, behavioral interventions and individually tailored, structural daily activities are the first line treatment options but are rarely sufficient to those patients who need hospital care. In these cases the next step is to recheck the diagnosis and medication.

Mutual understanding among clinicians is that for most of the patients who enter the hospitals, thorough etiological evaluations have not revealed any specific cause or syndrome behind their ID and ASD. Single cases of Fragile-X or Smith-Magenis syndrome or anoxic brain injury may make an exception to this clinically observed rule. Additional examinations are, however, considered necessary case by case, since developmental disorders such as autism can be a feature of several underlying genetic syndromes [5] and may help in defining the right diagnosis and related comorbidities.

Intellectually disabled patients suffer commonly from medical comorbidities (incl. e.g. epilepsy, mood disorders) that occur in numerous different medical areas [5], which make diagnostics extremely challenging without multidisciplinary expertise. Furthermore, it is important for a clinician to keep in mind that problem behavior in developmental disorders may be a symptom of the underlying somatic disorder. One confounding diagnostic challenge is related to the prescribed medication because some of the prevailing behavioral symptoms may actually be caused by e.g. antiepileptic medication [6].

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**Current interventions**

Pertinent evidence-based clinical guidelines are largely missing; a common feature of the available guidelines is that they speak for the importance of multidisciplinary team assessment [7]. The usual treatments for ASD include antipsychotics, antidepressants, stimulants, mood stabilizers, anticonvulsants and often some form of behavioral therapy, including applied behavior analysis as well as sensory integration oriented occupational therapy and music therapy. The benefits of the commonly used pharmacotherapeutic interventions are uncertain as concluded in Cochrane reviews [8-11]. Furthermore, so far there are no specific treatment options for the characteristic restricted and repetitive behaviors in ASD, which have been suggested to be associated with neurocognitive deficits in flexible choice behavior [12].

Risperidon is the only antipsychotic medicine in Europe that has an official indication for a 6-week use in behavioral disorders related to IDs, but its use is hampered by adverse events [13] and a lack of evidence of its benefits in long-term use [14,15]. Some patients may respond to other experimental neuroleptics, like to clozapine most of which are prescribed off-label i.e. without an official indication of psychosis. According to the literature and clinical experience the benefits of psychotropic drugs are often modest and adverse reactions, some of which serious do occur in the long-term treatment [10,14].

Some individual patients have benefitted from a special diet and, therefore, research on the effect of diet and nutrition on autism has emerged during the past decades, but so far the conducted studies have been too small and short term to support nutritional supplements or dietary therapies for all children with ASD [16].

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**From experimental treatments towards evidence based personalized management of behavioral disorders in ASD**

Taken the heterogenic nature of patients with ASD it is hard to believe that the conventional randomized clinical trials would bring the much-needed evidence for the current clinical practices. There is some but not sufficient evidence from many different treatment options to be applicable to all ASD patients. In clinical terms this means simply that what benefits one patient does not necessarily benefit another. It might be possible to overcome this inevitable challenge by conducting individually designed clinical trials [17,18]. In this kind of single-case interventions each subject acts as his or her own control and an agreed end point(s) for efficacy is measured before and after the chosen experimental treatment. If the same intervention can be shown to lead to the same outcome several times in a row it cannot be considered as a coincidence. This approach requires naturally that all the possible nutritional deficiencies, somatic disorders and/or sensory hypersensitivities are excluded or treated/acknowledged in a meaningful way before an experimental intervention is started.

The most challenging part of such individualized study designs would be to choose the right experimental treatment on a case-by-case basis. A few (mainly pediatric) patients may respond to gluten- and casein-free diet [19]. In accordance, based on the positive results described in the medical literature [20] and on our own preliminary clinical experience electroconvulsive therapy could be considered as one potential option in some patients with ASD whose severe challenging behaviors are resistant to other treatments.

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