



Review article

Self-injurious behavior

Sylvia Huisman^{a,b,*}, Paul Mulder^c, Janneke Kuijk^d, Myrthe Kerstholt^b, Agnies van Eeghen^{a,d}, Arnold Leenders^a, Ingrid van Balkom^c, Chris Oliver^e, Sigrid Piening^c, Raoul Hennekam^a

^a Department of Pediatrics, Academic Medical Center, University of Amsterdam, Meibergdreef 9, 1105 AZ Amsterdam, the Netherlands

^b Prinsenvestiging, Kwadijkpark 8, 1444 JE Purmerend, the Netherlands

^c Jonx Department of Youth Mental Health, Lentis Psychiatric Institute, Laan Corpus Den Hoorn 102, 9728 JR Groningen, the Netherlands

^d De Hartenkamp Groep, Richard Holkade 24, 2033 PZ Haarlem, the Netherlands

^e Cerebra Centre for Neurodevelopmental Disorders, School of Psychology, University of Birmingham, B15 2TT Birmingham, United Kingdom



ARTICLE INFO

Keywords:

Self-injurious behavior
Intellectual disability
Genes
Genetic syndromes
Angelman syndrome
Cornelia de Lange Syndrome
Cri du Chat Syndrome
Down syndrome
Fragile X syndrome
Lesch-Nyhan syndrome
Lowe syndrome
Prader-Willi syndrome
Rett syndrome
Smith-Magenis syndrome
Tuberous Sclerosis Syndrome
Williams-Beuren syndrome
Somatic factors
Pain
Interdisciplinary study

ABSTRACT

Self-injurious behavior (SIB) is a relatively common behavior in individuals with intellectual disabilities (ID). Severe SIB can be devastating and potentially life-threatening.

There is increasing attention for somatic substrates of behavior in genetic syndromes, and growing evidence of an association between pain and discomfort with SIB in people with ID and genetic syndromes.

In this review on SIB phenomenology in people with ID in general and in twelve genetic syndromes, we summarize different SIB characteristics across these etiologically distinct entities and identify influencing factors. We demonstrate that the prevalence of SIB in several well-known genetic intellectual disability syndromes is noticeably higher than in individuals with ID in general, and that characteristics such as age of onset and topographies differ widely across syndromes. Each syndrome is caused by a mutation in a different gene, and this allows detection of several pathways that lead to SIB. Studying these with the behavioral consequences as a specific aim will be an important step toward targeted early interventions and prevention.

1. Introduction

Self-injurious behavior (SIB) is a relatively common behavior in individuals with intellectual disabilities (ID). Severe SIB can be devastating and potentially life-threatening (Fig. 1), and is associated with compromised mental health in parents and caregivers, high service needs and excessive health care costs (Wulffaert et al., 2009; Hassiotis et al., 2008; Ruddick et al., 2015; Felce et al., 1998).

While there is abundant scientific interest in SIB in behavioral sciences, only limited attention is paid to SIB in medical sciences, despite increasing attention for somatic substrates of other behavior and evidence of an association between pain and discomfort with SIB (Brunner et al., 1993; Tint et al., 1994; Kishino et al., 1997; Breau et al., 2003; Symons et al., 2009; Symons, 2011; Diaz-Stransky and Tierney, 2012; Rosell and Siever, 2015; Wink et al., 2015). Studying specific genetic

syndromes, with different molecular or metabolic etiologies, may show different characteristics of SIB depending on etiology, allowing various pathways leading to SIB to be discovered.

In this review we highlight twelve genetic syndromes in which sufficient phenomenological data are available: Angelman Syndrome (AS), Cornelia de Lange Syndrome (CdLS), Cri du Chat Syndrome (CdCS), Down Syndrome (DS), fragile X Syndrome (fraX), Lesch-Nyhan Syndrome (LNS), Lowe syndrome (LS), Prader-Willi Syndrome (PWS), Rett Syndrome (Rett), Smith-Magenis Syndrome (SMS), Tuberous Sclerosis Syndrome (TSC), and Williams-Beuren Syndrome (WBS).

The paper is based on a review of the literature concerning SIB studies with detailed analysis of phenomenology. Information regarding review methods and individual studies can be found in the Supplemental Materials.

* Corresponding author at: Department of Pediatrics, H7–228, Academic Medical Center, Meibergdreef 9, 1105 AZ Amsterdam, the Netherlands.
E-mail address: s.a.huisman@amc.uva.nl (S. Huisman).



Fig. 1. Individual with Cornelia de Lange Syndrome at 7, 21 and 38 years of age. Self-injurious behavior started before 7 years of age and deteriorated during puberty and adolescence. Hitting and head banging resulted in permanent sensory loss due to bilateral blindness, bilateral ear deformations and hearing impairments.

2. Conceptualization and definition

The term SIB was introduced by Tate and Baroff in 1966, to replace earlier labels such as masochism, auto-aggression, self-aggression and self-destructive behavior. Tate and Baroff stated that the term SIB did not imply an attempt to destroy, nor did it suggest aggression. It simply meant behavior that produces physical injury to the individual's own body (Tate and Baroff, 1966).

Subsequently, numerous authors have used variations of this definition (Table 1). The main elements in definitions were: self-initiated; directed towards the body; involves specific forms and body parts; contains repetition; can be chronometrically or chronographically quantified (frequency, duration, intensity); and its effects or extent of tissue damage can be classified. Disqualifiers are intent of suicide or sexual arousal. Hence, we propose to define SIB as non-accidental behavior resulting in demonstrable, self-inflicted physical injury, without intent of suicide or sexual arousal. Typically the behavior is repetitive and persistent.

3. SIB prevalence

In this review twelve genetic syndromes are highlighted in which sufficient data were available: Angelman Syndrome (AS), Cornelia de Lange Syndrome (CdLS), Cri du Chat Syndrome (CdCS), Down Syndrome (DS), fragile X Syndrome (fraX), Lesch-Nyhan Syndrome (LNS), Lowe syndrome (LS), Prader-Willi Syndrome (PWS), Rett Syndrome (Rett), Smith-Magenis Syndrome (SMS), Tuberous Sclerosis Syndrome (TSC), and Williams-Beuren Syndrome (WBS).

The paper is based on a review of the literature concerning SIB studies with detailed analysis of phenomenology. Detailed information regarding review methods and individual studies can be found in the Supplemental Materials.

SIB prevalence rates within and across genetic syndromes heavily depend on the methodology employed, i.e. definition, recruitment, sample characteristics and etiological diagnoses of ID. In populations of people with ID of unknown etiology, not stratified for age or levels of functioning, the prevalence of SIB in a non-residential care setting is ~30%, irrespective of age and level of cognitive functioning versus 41% in a residential care setting (Lowe et al., 2007; Harris, 1993; Limdqvist, 2013; Oliver et al., 2012; Taylor et al., 2011; Saloviita, 2000). If autism spectrum disorders (ASD) are present the prevalence rises markedly, varying from 42% to 70% (Buono et al., 2010; Eden et al., 2014). In a number of specific syndromes prevalence figures can differ strikingly from prevalence rates in individuals with ID in general, and can be very high (Fig. 2a). Highest prevalence rates have been reported in LNS, SMS, PWS, CdCS and CdLS.

SIB has also been reported in a number of other genetic syndromes such as chromosome imbalances and non-genetically determined

entities including teratogenic entities such as rubella encephalopathy and Fetal Alcohol Syndrome (May et al., 1981; Pace et al., 1986; Prasher et al., 1995; Engelen et al., 1999; Hoch et al., 2013; Plaisancie et al., 2014). The divergent prevalence figures for the twelve selected genetic syndromes and other entities advocate to organize early intervention, assessment and treatment strategies that are syndrome sensitive.

4. SIB phenomenology

4.1. Age of onset

Generally SIB starts in early childhood: 50% of individuals showed SIB before 3 years of age, 70% before 7 years of age up to 90% before 10 years of age; percentage rates in larger genetic syndrome studies vary from 12% < 1 year, 63% < 4 and 93% < 11 years of age in fraX, versus 72% < 7 years of age in DS, and 73–91% < 7 years of age in PWS (Wigren and Heimann, 2001; Buono et al., 2005; Buono et al., 2010; Symons et al., 2010). Wide variation exists as in individual cases age of onset may occur in the first year of life, or SIB may first become manifest in adulthood. Case series in individuals with ID of unknown origin and in individuals with ASD demonstrated similar rates, but in the different syndromes median ages of onset vary widely (Fig. 2b). Rates may be prone to selection bias and can be over-estimations, especially in small case series. Conversely, age of onset, may be underestimated when outcomes like physical damage is a criterion, and identifying SIB in childhood is difficult as behavior like self-hitting and even head banging may sometimes be judged as age appropriate behavior and is seen in typical development.

4.2. Course of SIB

Figures about the course of SIB are sparse. SIB has been reported as persistent in 62% over 2 years, in 71% over 7 years and in 84% over 18 years (Taylor et al., 2011; Emerson et al., 2001; Cooper et al., 2009; Oliver and Richards, 2015a). Long-term persistence of SIB is more likely with early onset and head directed self-injury (Emerson et al., 2001). SIB present at 20 years of age or older has an 84% chance to be chronic (Taylor et al., 2011). The relative risk of SIB increases until 30–40 years of age and starts to decrease after the age of 50 (Davies and Oliver, 2013).

4.3. Severity

Severity of SIB is determined by a combination of characteristics: chronography (frequency, duration), topography (form, localization, number), and physical damage. Both in research and patient care quantifying severity comprehensively is informative for comparisons of

Table 1
Main Definitions of Self-Injurious Behavior Used in Literature.

Author	Body object ^a	Individual subject ^b	Recurrence ^c	Topography ^d	Chronometrics ^e	Effects severity ^f	Exclusion ^g
Tate and Baroff (1966)	Behavior which produces physical injury to the individual's own body, i.e. relatively repetitive self-hitting; series of responses that are repetitive and sometimes rhythmic	X	X	X			
Bechman (1972)	Behavior of individuals who inflict physical damage and, perhaps, pain upon themselves	X				X	
Carr (1977)	Behavior that involves any of a number of behaviors by which the individual produces physical damage to his or her own body. Some individuals engage scratching, biting, or head banging to the point at which bleeding occurs and sutures are required. Others may engage in self-inflicted punching, face slapping, or pinching, thereby producing swellings and bruises over large areas of their bodies	X		X		X	
Solnick et al. (1977)	Any repetitive making and breaking of contact between one part of the body and another. Some of these contacts quite forceful, producing bruises and scars	X	X			X	
Mizuno et al. (1979)	Aggressiveness toward oneself	X					
Pace et al. (1986)	Behavior that results in physical injury to the individual's own body; in general, it is chronic and repetitious, occurring at frequencies ranging from several times per week to hundreds of times per hour over a sustained period of time	X	X		X		
Oliver (1988)	Non-accidental behavior initiated by an individual which directly results in physical harm; it can lead to sensory impairments, brain damage and other disability	X				X	X
Winchel and Stanley (1991)	The commission of deliberate harm to one's own body. The injury is done to oneself, without the aid of another person, and the injury is severe enough for tissue damage (such as scarring) to result. Acts that are committed with conscious suicidal intent or are associated with sexual arousal are excluded	X				X	X
Baumeister et al. (1993)	Acts that result in physical injury to a person's own body. In particular, SIB usually refers to acts that are repetitive, sometimes rhythmic, as acts which would likely produce immediate pain in the absence of some sensory impairment, and acts which occur in certain clinical populations with diminished intelligence	X	X			X	
Saloviita (2000)	A large group of differing behaviors which are usually highly repetitive, and which result in direct physical harm or tissue damage to the person himself, e.g. head-banging, or slapping, scratching, or biting of oneself	X	X	X		X	
Schroeder et al. (2001)	Acts directed toward one's self that result in tissue damage	X				X	
Ross Collins and Cornish (2002)	Behavior that causes demonstrable damage to one's own body, including hitting the head with a hand or other body part; self-biting; hitting the head with or against objects; and hair pulling	X		X		X	
Wisely et al. (2002)	Any behavior, initiated by the individual, which directly results in physical harm to that individual, including bruising, lacerations, bleeding, bone fractures and breakages, and other tissue damage	X				X	
Kahng et al. (2002)	A response that produces physical injury to the individual's own body	X				X	
Baghdadi et al. (2003)	Aggressive behaviors directed towards one's self but they can have varying onset, duration, topographies	X		X	X		
Moss et al. (2005)/ Hall et al. (2008)	Non-accidental behaviors which produce temporary marks or reddening of the skin or cause bruising, bleeding or other temporary or permanent tissue damage (self-biting, head banging, head punching or slapping, removing hair, self-scratching, body hitting, eye poking or pressing)	X		X		X	X
Oliver et al. (2006)	Non-accidental body-to-body contact behaviors that may have resulted in tissue damage, such as hand-biting, face-hitting, and body-picking	X		X		X	X
Staley et al. (2008)	Behavior that results in physical injury to one's own body	X				X	
Danquah et al. (2008)	Any behavior, initiated by the individual, which directly results in physical harm to that individual, including bruising, lacerations, bleeding, bone fractures and breakages, and other tissue damage	X				X	
Richman (2008)	An act directed towards oneself that results in tissue damage	X				X	
Langthorne and McGill (2008)	Behaviors, such as head-hitting or scratching, that people direct towards themselves and that results in tissue damage	X		X		X	
Cooper et al. (2009)	A. The general diagnostic criteria for problem behavior are met. B. Self-injury sufficient to cause tissue damage, such as bruising, scarring, tissue loss and dysfunction, must have occurred during most weeks of the preceding six month period, e.g. ranging from skin-picking/scratching, hair-pulling, face slapping, to biting hands, lips, and other body parts, rectal/genital poking, eye-poking, and head-banging. C. The self-injurious behavior is not a deliberate suicide attempt	X	X	X	X	X	X

(continued on next page)

Table 1 (continued)

Author	Body object ^a	Individual subject ^b	Recurrence ^c	Topography ^d	Chronometrics ^e	Effects severity ^f	Exclusion ^g
Buono et al. (2010)	Represents behavioral characteristics that can damage body tissue. Behavior that produces immediate or cumulative physical damages to one's own body, self-biting, head banging, self scratching; disturbance caused by stereotyped movements, ie voluntary, repetitive, stereotyped, non-functional	X	X	X	X	X	
Wachtel and Dhossche (2010)	Any self directed action resulting in bodily harm; can include multiple topographies, like head banging, self-hitting, etc directed at any body surface. Frequency and intensity varies widely, but may reach extreme levels of complications	X		X	X	X	
Taylor et al. (2011)	Repeated, self-inflicted, non-accidental injury producing bruising, bleeding, or other temporary or permanent tissue damage, and repetitive behaviors that had the potential to do so if preventive measures were not taken	X	X			X	X
Limeres et al. (2013)	Behavioral disturbance consisting of deliberate destruction of or damage to body tissues, not associated with a conscious intent to commit suicide. Characteristics: socially unacceptable, direct, repetitive, mild or moderate damage. Most common forms: cuts, burns, scratches, blunt injury, bites, and interference with wound healing. Most frequently affected regions are head, hands, and neck	X	X	X		X	X
Medeiros et al. (2013)	Self-directed behavior that causes or has the potential to cause physical damage, occurs repeatedly in idiosyncratic form, including banging head or body with other body parts or objects, self-biting, self-scratching, self-pinching, gouging body cavities with fingers, and self-hair pulling	X	X	X		X	
Tureck et al. (2013)	Behavior or set of behaviors that can result in injury to the person's body and that occurs repetitively	X	X			X	
Wolff et al. (2013)	Particularly troubling form of repetitive motor behavior that involves purposeful and repeated patterns of self-inflicted bodily injury without intent of suicide	X	X			X	X
Proposed definition	Non-accidental behavior resulting in demonstrable, self-inflicted physical injury, without intent of suicide or sexual arousal. Typically the behavior is repetitive and persistent.	X	X	X	X	X	X

^a Body object: the behavior is directed towards the body; physical target.

^b Individual subject: actor exhibits the behavior to oneself; self-directed.

^c Recurrence: reiteration, repetition.

^d Topography: compromised body site/location of action, i.e. head to body, body to body, head to object, body to object; e.g. head-banging.

^e Chronometrics (frequency, duration, temporal distribution, intensity): acts per time unit/rate, per unit area/impact force.

^f Effects severity: severity of the effects/extent of tissue damage (description/classification).

^g Exclusion: conditions disqualified, i.e. without intent of suicide.

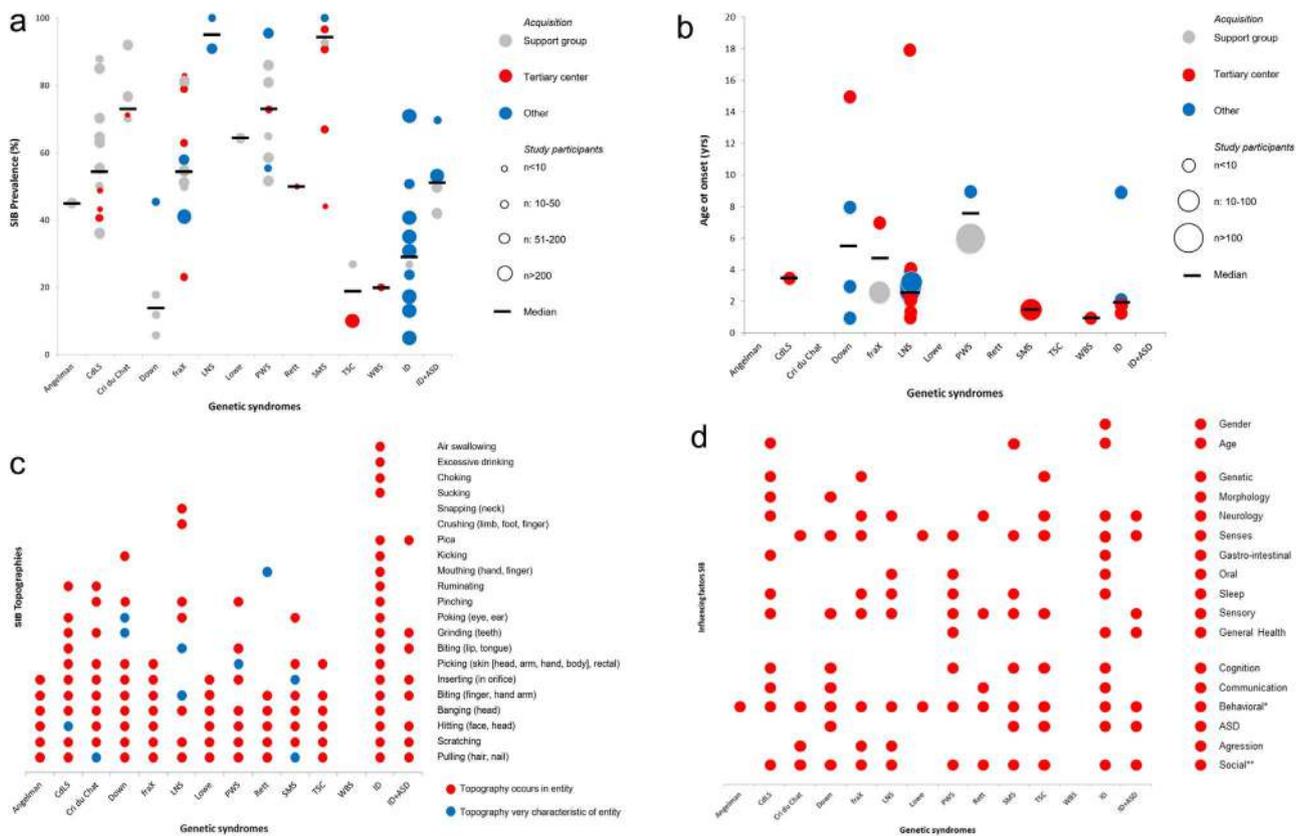


Fig. 2. Phenomenology of SIB in selected genetic syndromes, in ID of unknown origin and those with ID of unknown origin and ASD: (a) Prevalence. (b) Age of onset. (c) Topographies. Some topographies have been indicated as being very characteristic for syndromes: this is based on the literature review and personal experiences but could not be determined statistically due to small numbers. (d) Influencing factors.

Subscripts for Fig. 2d:

*Behavioral: i.e. stereotypy, repetitive, compulsive, impulsive behavior, hyperactivity, distractibility, anxiety, prolonged distress, nervousness, mood, affect, tantrums, disturbing inter-personal behaviors.

**Social: social contact, adult attention, ignoring, demand avoidance, automatic reinforcement, thwarting, boredom, solitude, being teased, frustration, change of routine, changes environment, length of institutionalization.

studies.

4.3.1. Chronography

Chronographic parameters (frequency, duration, intensity) can objectively quantify clinical severity and the effectiveness of interventions. These are parameters typically more accurately presented in case reports but less so in studies of larger cohorts. Therefore only limited data are available.

In general ID population studies SIB occurs occasionally in 27% and frequently in 14% (Saloviita, 2000); and every 30 min in 18%, hourly in 11%, daily in 43%, weekly in 19%, monthly in 8% and yearly in 1%, respectively (Saloviita, 2000; Griffin et al., 1987). In various syndromes this can be markedly different: for instance in LNS SIB is typically almost continuously present and may even occur during sleep, without changing over time.

4.3.2. Topography

There are many forms of SIB involving divergent body sites, which are referred to as topographies. The most common forms are pulling (hair or nails), scratching, hitting, banging and biting. When hitting oneself a part of the body is typically used as the ‘instrument’ to hit, but objects can be used as well. Other common forms are inserting in orifice, picking, grinding, poking (eyes or ears), pinching and ruminating. Less common forms are mouthing, pica, crushing, snapping (neck), excessive drinking and air swallowing, sucking and choking (Fig. 2c). These less common forms can also occur without the other characteristics of SIB and this behavior should not always be considered SIB. The

most commonly involved body parts are the head, the hands and fingers. SIB remains confined to a single body part in 28%–46% of individuals, but involvement of several body parts frequently occurs, particularly in CdLS and SMS (Hall et al., 2001; Taylor et al., 2011; Petty et al., 2014).

4.3.3. Physical damage

Physical damage as result of SIB is one of the main reasons for serious concerns of the caregivers, and for medical consultation. The physician needs not only to qualify but also to objectively quantify clinical severity, both to indicate immediate medical interventions and to judge the effectiveness of interventions. Although medical evaluation of physical damage is obligatory, very limited data have been reported on specific physical damage due to SIB. In seven of the twelve selected genetic syndromes in this review no data on severity of physical damage are provided. Detailed information on physical consequences in the remaining five syndromes has been best described in case reports. The Challenging Behavior Interview provides a four point Likert scale item on physical injury and the Self-Injury Trauma scale scores physical consequences in a subjective and time-consuming way, but otherwise there is no instrument available to the physician for scoring physical damage (Iwata et al., 1990; Oliver et al., 2003). Hence, we have designed a relatively simple scoring system for the physician defining the degree of severity based on the physical consequences of SIB and providing guidance on the need for further medical measures:

- (relatively) mild: indicating non-permanent, minor tissue damage

- such as scratches, abrasion, bruises, temporary reddening of the skin, teeth marks;
2. moderate: indicating non-permanent, marked tissue damage or function loss, such as deep fissures, fractures, large scars and ulcerations;
 3. severe: indicating permanent tissue loss, loss of sensory function (deafness; blindness), loss of neurological function (brain damage) and life-threatening consequences.

Since there are only small series that report information on tissue damage and function loss, it proved not to be possible to present results across genetic syndromes in a figure. We can only state reliably based on available literature and personal extensive experiences that severe tissue damage is commonly prominent in LNS and CdLS. The frequent use of constraints in both syndromes is an indirect indication of the SIB severity.

4.4. Factors influencing SIB

A main issue in managing SIB is to assess and define factors predisposing, evoking and maintaining SIB as they indicate potential intervention strategies. These factors may be personal (gender; age), somatic (including genetic, neurobiological and medical conditions) and behavioral (including operant learning) in nature. Physicians in charge of SIB patients have a role that is complementary to that of the behavioral specialist, to evaluate health and functioning, paying specific attention to (painful) physical conditions which may lead to SIB. Behavioral specialists have a key role in assessing cognitive, adaptive and communicative abilities of SIB patients, in evaluating psychopathology that might be related to SIB and in performing a functional behavioral assessment.

4.4.1. Somatic

Somatic influencing factors of SIB in genetic syndromes (Fig. 2d) are subdivided in: genetic mutation, morphology, neurology, senses, gastro-intestinal, oral/dental, sleep, sensory and general health.

Larger numbers of different somatic influencing factors are reported in studies in individuals with ID of unknown origin, and also in CdLS and fraX. Senses (visual and hearing impairments) and other sensory (pain and tactile sense) problems are reported most across the various entities. However, most publications on SIB fail to report on even basic physical examinations by physicians who might evaluate potential physical causes of SIB, such as constipation, gastro-esophageal reflux disease (GERD)/esophagitis, intestinal obstruction, dental problems, urinary tract infection, otitis media, sinusitis, presence of a foreign body, or fracture. Information on visual and hearing abilities is needed due to their high prevalence in individuals with ID, and their influence on adaptive and communicative abilities.

Furthermore, SIB is known to occur very frequently in several specific genetic syndromes and to occur in most of these genetic entities more frequently than in a population with ID of unknown origin (Fig. 2a). In the present analyses of studies on SIB the number of individuals in whom no or only partly genetic and metabolic diagnostic studies have been performed was remarkably high, which hampers optimal use of the knowledge of behavior in such entities, including the somatic substrates of behavior (Table 2).

4.4.2. Behavioral

Behavioral factors influencing SIB are presented in Fig. 2d and for the overview divided in 2 categories: developmental (i.e. cognitive, communicative and adaptive abilities) and behavioral (intrapersonal and interpersonal). Intrapersonal characteristics include: stereotypy, repetitive, compulsive, impulsive behaviors, hyperactivity, distractibility, anxiety, and mood. Interpersonal behavioral characteristics encompass social contact and environmental dimensions such as adult attention, ignoring, demand avoidance, solitude, change of routine,

changes to environment, institutionalization. ASD and aggression are presented separately. However, ASD as a distinctive etiology is problematic because ASD can be difficult to classify in these entities and symptoms of adaptive impairments and repetitive and stereotyped behaviors are also clustered within developmental and behavioral factors. These characteristics influence behavior dysregulation and operant learning, and hence possible leads for behavioral interventions.

5. Discussion

SIB can be a devastating problem. It is devastating for the individuals who harm themselves, and who may experience a significant physical and psychological distress due to their SIB. It is devastating for the parents who see progressive damage to the one they love and who feel they cannot offer the protection they want to offer as a parent. It is devastating to caregivers who may feel ineffective and can experience this as a failure of their care.

Patients with SIB visit their general practitioners, pediatricians, child psychiatrists and pediatric neurologists, and later in life their internists, psychiatrists and even surgeons. Managing SIB can be a huge challenge for physicians.

SIB is common in individuals with intellectual disabilities, often starts in early childhood and can aggravate into a destructive and persistent problem if interdisciplinary assessment and interventions are not applied. Accurate and detailed information on SIB characteristics such as chronography, topography and resulting physical damage may offer clues for the physician to the causes of pain or distress, either in the past or present, which may play a crucial role in the development and maintenance of SIB.

There is need for careful interdisciplinary evaluation of every patient who shows SIB. SIB should not be seen as a diagnosis, but as a symptom of an underlying problem. The physician must be alert to symptoms of underlying pain and discomfort as medical conditions causing or prolonging SIB may go unrecognized, undiagnosed and untreated, specifically due to the impaired communications skills in patients with ID. A comprehensive medical evaluation is particularly valuable as frequent medical conditions like constipation, GERD, otitis media, dental problems, presence of a foreign body, or fracture, have excellent treatment options.

Until now several theoretical models for SIB have been proposed, varying from neurobiological (including genetic and neurochemical), medical (pain and discomfort) and behavioral or operant learning models. There is growing evidence for an integrated biological and behavioral model in which genotypic-phenotypic characteristics and operant learning principles are complementary and lead to effective interventions (Oliver and Richards, 2015b; Minshawi et al., 2015). Understanding the interactions between all these influencing factors needs longitudinal studies in which phenotyping the SIB characteristics and personal (developmental and behavioral) characteristics, the physical signs and symptoms of patients demonstrating SIB, and genotyping the same individuals, will be essential.

This review demonstrates that the prevalence of SIB in several well-known genetic ID syndromes is noticeably higher than in individuals with ID in general and that characteristics such as age of onset and topographies differ widely across syndromes, each caused by a different gene with a different action when mutated. Pathogenetic mechanisms behind these differences remain to be elucidated. It may be many different pathways can cause SIB. One may also hypothesize that these genes may have more than one action, one causing the syndrome and another causing SIB. Studying these multifunctional, ‘moonlighting’ proteins may show a common pathway to SIB (Jeffery, 2015). Comprehensive phenotype – genotype studies and functional analyses will be an important step towards targeted early interventions and effective prevention.

Table 2
Summary of a Literature Review of SIB in Genetic Syndromes.

Syndrome	Study Characteristics										Somatic Aspects			Self-Injurious Behavior			
	Design ^a		Acquisition			Participants		Confirmed diagnosis ^b		Physical examination ^c		Prevalence (%)		Age of onset (yr)		Characteristic topography	
	n	case-control	cohort	cross-sectional	case series	support group	specialized centers	combination	other	not mentioned	M/F	molec/metabolic	clinical	full	limited		median
Angelman	1	-	-	1	-	1	-	-	-	-	58/46	-	-	1	1	45.1	-
CdLS	17	4	-	8	5	10	3	4	-	-	353/445*	1	4	4	7	55.3	3.5
Cri du Chat	4	-	-	3	1	3	-	-	1	-	65/83	2	-	1	2	73.9	-
Down	21	5	1	1	14	3	5	-	7	6	156/139	4	2	2	6	15.0	5.5
fraX	13	6	-	4	3	4	4	4	1	-	2949/1199*	11	1	1	6	54.8	4.8
LMS	30	1	-	2	27	-	22	1	6	1	166/3	20	-	9	9	95.5	2.6
Lowe	1	-	-	1	-	1	-	-	-	-	56/0	-	-	-	1	64.3	-
PWS	24	4	-	11	9	10	8	2	4	-	532/556*	15	1	3	9	73.0	7.5
Rett	6	2	-	1	3	1	4	-	1	-	0/119	-	2	-	3	50.0	-
SMS	10	2	-	5	3	2	3	4	-	1	105/128	9	-	3	2	94.8	1.5
TSC	5	2	-	-	3	1	3	-	1	-	20/20*	1	1	1	4	18.5	-
WBS	1	-	-	-	1	-	1	-	-	-	7/3	1	-	-	1	20.0	1
ID	46	5	5	13	23	1	11	9	21	4	8710/6498*	-	-	2	16	28.9	1.9
ID + ASD	4	3	-	1	-	2	-	-	2	-	505/103	-	-	2	2	51.5	-

* Total n is larger than M + F due to missing gender data, when no data are available, sections are empty.

^a Study design: Case-control study: observational, analytical, sampling based on outcome; Cross sectional study: observational, analytical, cross sectional; Cohort study: observational, analytical, sampling based on exposure; Case report/series: observational, descriptive, no comparison group, no hypothesis testing.

^b Confirmation by either metabolic, cytogenetic or molecular studies; clinical confirmation scored positive if performed by expert.

^c Physical exams: Full: personal examination by physician, includes laboratory or imaging investigations; Limited: no full examination, e.g. health questionnaire.

Acknowledgement

We thank the family of the individual shown in Fig. 1 for allowing us to show the pictures of their son.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.neubiorev.2017.02.027>.

References

- Bachman, J.A., 1972. Self-injurious behavior: a behavioral analysis. *J. Abnorm. Psychol.* 80, 211–224.
- Baghdadi, A., Pascal, C., Grisi, S., Aussilloux, C., 2003. Risk factors for self-injurious behaviours among 222 young children with autistic disorders. *J. Intellect. Disabil. Res.* 47, 622–627.
- Baumeister, A.A., Todd, M.E., Sevin, J.A., 1993. Efficacy and specificity of pharmacological therapies for behavioral disorders in persons with mental retardation. *Clin. Neuropharmacol.* 16, 271–294.
- Breaux, L.M., Camfield, C.S., Symons, F.J., Bodfish, J.W., Mackay, A., Finley, G.A., McGrath, P.J., 2003. Relation between pain and self-injurious behavior in nonverbal children with severe cognitive impairments. *J. Pediatr.* 142, 498–503.
- Brunner, H.G., Nelen, M., Breakefield, X.O., Ropers, H.H., van Oost, B.A., 1993. Abnormal behavior associated with a point mutation in the structural gene for monoamine oxidase a. *Science* 262, 578–580.
- Buono, S., Palmigiano, M., Scannella, F., Occhipinti, P., Greco, D., 2005. Self-injury and Prader-Willi syndrome. *J. Policy Pract. Intellect. Disabil.* 256–259 (Brief Research Report).
- Buono, S., Scannella, F., Palmigiano, M.B., 2010. Self-injurious behavior: a comparison between Prader-Willi syndrome: down syndrome and autism. *Life Span Disabil.* 187–201.
- Carr, E.G., 1977. The motivation of self-injurious behavior: a review of some hypotheses. *Psychol. Bull.* 84, 800–816.
- Cooper, S.A., Smiley, E., Allan, L.M., Jackson, A., Finlayson, J., Mantry, D., Morrison, J., 2009. Adults with intellectual disabilities: prevalence, incidence and remission of self-injurious behaviour, and related factors. *J. Intellect. Disabil. Res.* 53, 200–216.
- Danquah, A., Limb, K., Chapman, M., 2008. An investigation of factors predictive of continued self-injurious behaviour in an intellectual disability service. *J. Appl. Res. Intellect. Disabil. epub*.
- Davies, L., Oliver, C., 2013. The age related prevalence of aggression and self-injury in persons with an intellectual disability: a review. *Res. Dev. Disabil.* 34.
- Diaz-Stransky, A., Tierney, E., 2012. Cognitive and behavioral aspects of Smith-Lemli-Opitz syndrome. *Am. J. Med. Genet. Part C: Semin. Med. Genet.* 160C, 295–300.
- Eden, K.E., de Vries, P.J., Moss, J., Richards, C., Oliver, C., 2014. Self-injury and aggression in tuberous sclerosis complex: cross syndrome comparison and associated risk markers. *J. Neurodev. Disord.* 6, 10.
- Emerson, E., Kiernan, C., Alborz, A., Reeves, D., Mason, H., Swarbrick, R., Mason, L., Hatton, C., 2001. Predicting the persistence of severe self-injurious behavior. *Res. Dev. Disabil.* 22, 67–75.
- Engelen, J.J.M., De Die-Smulders, C.E.M., Vos, P.T.H., Meers, L.E.C., Albrechts, J.C.M., Hamers, A.J.H., 1999. Characterization of a partial trisomy 16q with FISH. Report of a patient and review of the literature. *Ann. Genet.* 42, 101–104.
- Felce, D., Lowe, K., Perry, J., Baxter, H., Jones, E., Hallman, A., Beecham, J., 1998. Service support to people in Wales with severe intellectual disability and the most severe challenging behaviours: processes, outcomes and costs. *J. Intellect. Disabil. Res.* (October), 42.
- Griffin, J.C., Ricketts, R.W., Williams, D.E., Locke, B.J., Altmeyer, B.K., Stark, M.T., 1987. A community survey of self-injurious behavior among developmentally disabled children and adolescents. *Hosp. Commun. Psychiatry* 38, 959–963.
- Hall, S., Oliver, C., Murphy, G., 2001. Early development of self-injurious behavior: an empirical study. *Am. J. Ment. Retard.* 106, 189–199.
- Hall, S.S., Arron, K., Sloneem, J., Oliver, C., 2008. Health and sleep problems in Cornelia de Lange Syndrome: a case control study. *J. Intellect. Disabil. Res.* 52, 458–468.
- Harris, P., 1993. The nature and extent of aggressive behaviour amongst people with learning difficulties (mental handicap) in a single health district. *J. Intellect. Disabil. Res.* 37 (Pt 3), 221–242.
- Hassiotis, A., Parkes, C., Jones, L., Fitzgerald, B., Romeo, R., 2008. Individual characteristics and service expenditure on challenging behaviour for adults with intellectual disabilities. *J. Appl. Res. Intellect. Disabil.* 21.
- Hoch, J., Symons, F., Sng, S., 2013. Sequential analysis of autonomic arousal and self-injurious behavior. *Am. J. Intellect. Dev. Disabil.* 118, 435–446.
- Iwata, B.A., Pace, G.M., Kissel, R.C., Nau, P.A., Farber, J.M., 1990. The Self-Injury Trauma (SIT) Scale: a method for quantifying surface tissue damage caused by self-injurious behavior. *J. Appl. Behav. Anal.* 23, 99–110.
- Jeffery, C.J., 2015. Why study moonlighting proteins? *Front. Genet.* 6, 211.
- Kahng, S., Iwata, B.A., Lewin, A.B., 2002. Behavioral treatment of self-injury, 1964 to 2000. *Am. J. Ment. Retard.* 212–221.
- Kishino, T., Lalonde, M., Wagstaff, J., 1997. UBE3A/E6-AP mutations cause Angelman syndrome. *Nat. Genet.* 15, 70–73.
- Langthorne, P., McGill, P., 2008. Functional analysis of the early development of self-injurious behavior: incorporating gene-environment interactions. *Am. J. Ment. Retard.* 113, 403–417.
- Limdvqvist, L.O., 2013. Prevalence and risk markers of behavior problems among adults with intellectual disabilities: a total population study in Orebro County, Sweden. *Res. Dev. Disabil.* 34, 1346–1356.
- Limeres, J., Feijoo, J.F., Baluja, F., Seoane, J.M., Diniz, M., Diz, P., 2013. Oral self-injury. *An update. Dent Traumatol.* 29, 8–14.
- Lowe, K., Allen, D., Jones, E., Brophy, S., Moore, K., James, W., 2007. Challenging behaviours: prevalence and topographies. *J. Intellect. Disabil. Res.* 51, 625–636.
- May, A.E., Gilbert, T., Ostler, E., 1981. Self-injurious behaviour: a case study. *Br. J. Mental Subnormal. Dec-D82*.
- Medeiros, K., Curby, T.W., Bernstein, A., Rohahn, J., Schroeder, S.R., 2013. The progression of severe behavior disorder in young children with intellectual and developmental disabilities. *Res. Dev. Disabil.* 34, 3639–3647.
- Minshawi, N., Hurwitz, S., Morriss, D., McDougle, C., 2015. Multidisciplinary assessment and treatment of self-injurious behavior in autism spectrum disorder and intellectual disability: integration of psychological and biological theory and approach. *J. Autism Dev. Disord.* 45, 1541–1568.
- Mizuno, T., Ohta, R., Kodama, K., et al., 1979. Self-mutilation and sleep stage in the Lesch-Nyhan syndrome. *Brain Dev.* 1, 121–125.
- Moss, J., Oliver, C., Hall, S., Arron, K., Sloneem, J., Petty, J., 2005. The association between environmental events and self-injurious behaviour in Cornelia de Lange syndrome. *J. Intellect. Disabil. Res.* 49, 269–277.
- Oliver, C., 1988. Self-injurious behaviour in people with a mental handicap. *Curr. Opin Psychiatry* 1, 567–571.
- Oliver, C., Arron, K., Hall, S., Sloneem, J., Forman, D., McClintock, K., 2006. Effects of Social Context on Social Interaction and Self-Injurious Behavior in Cornelia de Lange Syndrome. *Am. J. Ment. Retard.* 184–192.
- Oliver, C., Richards, C., 2015a. Practitioner review: self-injurious behaviour in children with developmental delay. *J. Child Psychol. Psychiatry* 56.
- Oliver, C., Richards, C., 2015b. Practitioner Review: self-injurious behaviour in children with developmental delay. *J. Child Psychol. Psychiatry* 56, 1042–1054.
- Oliver, C., McClintock, K., Hall, S., Smith, M., Dagnan, D., Stenfort-Kroese, B., 2003. Assessing the severity of challenging behaviour: psychometric properties of the challenging behaviour interview. *J. Appl. Res. Intellect. Disabil.* 16, 53–61.
- Oliver, C., Petty, J., Ruddick, L., Bacarese-Hamilton, M., 2012. The association between repetitive, self-injurious and aggressive behavior in children with severe intellectual disability. *J. Autism Dev. Disord.* 42, 910–919.
- Pace, G.M., Iwata, B.A., Edwards, G.L., McCosh, K.C., 1986. Stimulus fading and transfer in the treatment of self-restraint and self-injurious behavior. *J. Appl. Behav. Anal.* 381–389.
- Petty, J.L., Bacarese-Hamilton, M., Davies, L.E., Oliver, C., 2014. Correlates of self-injurious, aggressive and destructive behaviour in children under five who are at risk of developmental delay. *Res. Dev. Disabil.* 35, 36–45.
- Plaisancie, J., Bouneau, L., Cances, C., Garnier, C., Benesteanu, J., Leonard, S., Bourrouillou, G., Calvas, P., Vigouroux, A., Julia, S., Bieth, E., 2014. Distal 10q monosomy: new evidence for a neurobehavioral condition? *Eur. J. Med. Genet.* 57, 47–53.
- Prasher, V.P., Roberts, E., Norman, A., Butler, A.C., Krishnan, V.H.R., McMullan, D.J., 1995. Partial trisomy 22 (q11.2-q13.1) as a result of duplication and pericentric inversion. *J. Med. Genet.* 32, 306–308.
- Richman, D.M., 2008. Early intervention and prevention of self-injurious behaviour exhibited by young children with developmental disabilities. *J. Intellect. Disabil. Res.* 52, 3–17.
- Ross Collins, M.S., Cornish, K., 2002. A survey of the prevalence of stereotypy, self-injury and aggression in children and young adults with Cri du Chat syndrome. *J. Intellect. Disabil. Res.* 46, 133–140.
- Rosell, D.R., Siever, L.J., 2015. The neurobiology of aggression and violence. *CNS Spectr.* 20, 254–279.
- Ruddick, L., Davies, L., Bacarese-Hamilton, M., Oliver, C., 2015. Self-injurious, aggressive and destructive behaviour in children with severe intellectual disability: prevalence, service need and service receipt in the UK. *Res. Dev. Disabil.* 45–45, 307–315.
- Saloviita, T., 2000. The structure and correlates of self-injurious behavior in an institutional setting. *Res. Dev. Disabil.* 21, 501–511.
- Schroeder, S.R., Oster-Granite, M.L., Berkson, G., et al., 2001. Self-injurious behavior: gene-brain-behavior relationships. *Ment. Retard. Dev. Disabil. Res. Rev.* 7, 3–12.
- Solnick, J.V., Rincover, A., Peterson, C.R., 1977. Some determinants of the reinforcing and punishing effects of timeout. *J. Appl. Behav. Anal.* 10, 415–424.
- Staley, B.A., Montenegro, M.A., Major, P., et al., 2008. Self-injurious behavior and tuberous sclerosis complex: frequency and possible associations in a population of 257 patients. *Epilepsy Behav.* 13, 650–653.
- Symons, F.J., Harper, V.N., McGrath, P.J., Breaux, L.M., Bodfish, J.W., 2009. Evidence of increased non-verbal behavioral signs of pain in adults with neurodevelopmental disorders and chronic self-injury. *Res. Dev. Disabil.* 30, 521–528.
- Symons, F.J., Byiers, B.J., Raspa, M., Bishop, E., Bailey, D.B., 2010. Self-injurious behavior and fragile X syndrome: findings from the national fragile X survey. *Am. J. Intellect. Dev. Disabil.* 115, 473–481.
- Symons, F.J., 2011. Self-injurious behavior in neurodevelopmental disorders: relevance of nociceptive and immune mechanisms. *Neurosci. Biobehav. Rev.* 35, 1266–1274.
- Tate, B.G., Baroff, G.S., 1966. Aversive control of self-injurious behavior in a psychotic boy. *Behav. Res. Ther.* 4, 281–287.
- Taylor, L., Oliver, C., Murphy, G., 2011. The chronicity of self-injurious behaviour: a long-term follow-up of a total population study. *J. Appl. Res. Intellect. Disabil.* 25, 107–117.
- Tint, G.S., Irons, M., Elias, E.R., Batta, A.K., Frieden, R., Chen, T.S., Salen, G., 1994. Defective cholesterol biosynthesis associated with the Smith-Lemli-Opitz syndrome.

- New Engl. J. Med. 330, 107–113.
- Tureck, K., Matson, J.L., Beighley, J.S., 2013. An investigation of self-injurious behaviors in adults with severe intellectual disabilities. *Res. Dev. Disabil.* 34, 2469–2474.
- Wachtel, L.E., Dhossche, D.M., 2010. Self-injury in autism as an alternate sign of catatonia: Implications for electroconvulsive therapy. *Med. Hypotheses* 75, 111–114.
- Winchel, R.M., Stanley, M., 1991. Self-injurious behavior: a review of the behavior and biology of self-mutilation. *Am. J. Psychiatry* 148, 306–317.
- Wigren, M., Heimann, M., 2001. Excessive picking in Prader-Willi syndrome: a pilot study of phenomenological aspects and comorbid symptoms. *Int. J. Disabil. Dev. Educ.* 129–142.
- Wink, L.K., Fitzpatrick, S., Shaffer, R., Melnyk, S., Begtrup, A.H., Fox, E., Schaefer, T.L., Mathieu-Frasier, L., Ray, B., Lahiri, D., Horn, P.A., Erickson, C.A., 2015. The neurobehavioral and molecular phenotype of Angelman Syndrome. *Am. J. Med. Genet. A* 167, 2623–2628.
- Wisely, J., Hare, D.J., Fernandez-Ford, L., 2002. A study of the topography and nature of self-injurious behaviour in people with learning disabilities. *J. Learn. Disabil.* 6.
- Wolff, J.J., Hazlett, H.C., Lightbody, A.A., Reiss, A.L., Piven, J., 2013. Repetitive and self-injurious behaviors: associations with caudate volume in autism and fragile X syndrome. *J. Neurodev. Disord.* 5, 12.
- Wulffaert, J., van Berckelaer-Onnes, I., Kroonenberg, P., Scholte, E., Bhuiyan, Z., Hennekam, R., 2009. Simultaneous analysis of the behavioural phenotype, physical factors, and parenting stress in people with Cornelia de Lange syndrome. *J. Intellect. Disabil. Res.* 53, 604–619.