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Autosarcophagy: A Systematic Review of Psychological Correlates, with Genetic Propositions

Authors

Arumugam Subramanian Senthilkumar[1], Pichaachari Rathika[2*], Kaliyan Veeramuthu[3], Srinivasan Lakshmanan[4], Eswaran Sobana[5]

[1]Assistant Professor, Department of Psychiatry, Government Vellore Medical college Hospital, Vellore, Tamil Nadu, India
[2]Assistant Professor, Department of Psychiatry, GVMCH, Vellore, India
[3]Associate Professor & Head, Department of Psychiatry, GVMCH, Vellore, India
[4]Senior Resident, Department of Psychiatry, GVMCH, Vellore, India
[5]Senior Resident, Department of Psychiatry, GVMCH, Vellore, India
*Corresponding Author
Pichaachari Rathika

Abstract

Autosarcophagy (self-cannibalism) is rarely reported in the literature. Prognosis depends on the nature and severity of the primary cause or medical condition, more so in genetic disorders. Aggressive management can modify the outcomes preventing permanent disfigurement and disability. We did a qualitative systematic review on autosarcophagy, with prevalence of psychological correlates as the research question, and explored for specific patterns in gene loci of common syndromes of self-mutilation. Presence of psychosis, modes and parts ingested were the comparators studied. Analysis of clinical and psychosocial profile from all reports of "autosarcophagy/self-cannibalism" (eligibility) from PubMed database till December 2019 was done, along with documentation of two new cases. Out of 550 studies screened, eighteen (on 24 patients) were identified, wherein individual participant data was available for 85%. Documentations of autosarcophagy have increased to about six times since 2006 ($P<0.05$). More than three fourths of multiple attempts were by non-psychotic patients ($P<0.05$). Most non-psychotics preferred eating fingers, while more than one in five patients with psychosis preferred other organs. Paraesthesia and pain insensitivity were predominant in groups with and without psychosis respectively. Differences in all these other comparators were not significant. Impulsivity, obsessive compulsiveness, and aggressiveness were the commonest of all factors, in both groups. Targeting cumulative psychological factors from the onset may reduce frequency, relapse, insight and prognosis. Linkage and genetic recombinations were hypothesized from the adjacency of terminal gene loci of different chromosomes. The genomic analysis of the proposed linkage would help earlier diagnosis and intervention. Limitations include not evaluating other genes (of self-mutilation) of lesser scores.

Keywords: *autosarcophagy, self-cannibalism, Lesch-Nyhan syndrome, autism spectrum disorder, pain insensitivity, self-mutilation, terminal alleles, evolutionary genomics.*

Introduction

Autosarcophagy (ASP) or self-cannibalism, as a behavioural disorder has been rarely reported in literature so far, as only few patients have had qualified in the literal meaning, "eating one's own flesh." Erysichthon from Greek mythology and Jörmungandr from Norse mythology were the first known with ASP, while Sembiyan and Porkaipandyan from prehistoric South India were known for grotesque self-mutilation. ASP was first reported by Richard von Krafft-Ebing in a patient with paraphilia in 1886.

Nomenclature

At least three terms have been used synonymously over the past 135 years to denote eating parts of one's own body. Autophagy, autophagia, auto-cannibalism and self-cannibalism have been consistently and overwhelmingly used in literature to denote specific intracellular phenomena (of lysosomes and apoptosis), and tissue mechanisms observed in host defense, cancer, dementia, nutrition and muscle-related catabolism. The authors propose the use of "autosarcophagy," a seldom used term, instead of the confounding terms above.

The syndrome

As a syndrome it comprises of an idea, urge or impulse, and the act of procurement and ingestion, complemented by repetitiveness, gratification or assuagement and a lack of remorse. It may have multiple instigating factors like impulsivity, disinhibition, psychomotor agitation, irritability and compulsive biting –the last as a counter to resist another obsessive urge and to alleviate bodily pain or dysphoria from guilt, rejection or boredom. Frustration from isolation and pain insensitivity, and hyperorality-related stereotypical, pseudofunctional or habitual biting, are the usual driving forces.[1] ASP may also be a punitive, abhorrently violating, or body-modifying behaviour. Instant and temporary relief from distress, guilt, bewilderment and perplexity –arising from bodily or sexual preoccupations, disorganized and delusional thoughts, depersonalization, and auditory, visual and tactile hallucinations, may be the motive in patients with psychosis, substance intoxication and borderline personality disorder.[2,3]

There is a lack of consensus on how to conceptualize ASP. The phenomenon should clearly include the triad of voluntariness, self-mutilation and swallowing with or without chewing. Stereotypical biting behaviour is included, while forced self-cannibalism as in reports from military prisons, detention and refugee camps, in the background of a civil war, coup d'état and ethnic genocide, is not.[4] Inadvertent acts as in cases of biting and swallowing automatisms in complex partial seizures, and partial auto-amputation of tongue from dystonia of masticatory muscles,[5,6] do not qualify, so does an accidental aspiration and swallowing,[2] and spitting out after chewing. Nail biting, skin picking, swallowing hair, nipping at the skin of lips, nail flanks and buccal mucosa, chewing peeled off dead skin (of pustules, scabs and exfoliates from rashes) and drinking one's own blood (from a preexisting wound) and urine, cannot be considered as true autosarcophagy. ASP may be related to other problematic body-focused repetitive behaviours like trichotillomania.

Rationale for the review study was that the psychosocial and possible genetic correlates of ASP have not been explored so far, especially as they apparently varied in the presence of psychosis.

Aims and Objectives

To do a qualitative systematic review on the prevalence of psychological correlates in the documented cases of autosarcophagy of the world, with the documentation of two new cases with different clinical phenotypes, and then explore the patterns of possible genetic causes.

Materials and Methods

We searched PubMed and PubMed Central databases for all reports on ASP published till December 2019, using the search queries of "self-cannibalism"(SC), "autophagia" (AP), "autosarcophagy" (ASP), "autocannibalism"(AC)

and "biting, eating/nibbling and self-mutilation" (in title and text fields) as the eligibility for inclusion into this study.

Exclusion criteria included incidents of self-biting but without mention of "eat" or "nibble" or "swallow," and hence not considered as autosarcophagous.

Relevant studies from the search results were then reviewed systematically (fig. 1), and sociodemographic, clinical and psychological correlates were analysed for their patients along with the new case reports of ASP in a female child with autism spectrum disorder, and a male child with Lesch-Nyhan syndrome, from the department of psychiatry, Government Vellore Medical College. The Genecards database[44] was searched for genes related to ASP, AC, SC and AP, and none were found. Top self-mutilation gene and disorders were tabulated, along with symptoms and clinical synopsis, and analysed to arrive at possible new genetic propositions. Institutional ethical committee approval was obtained.

Statistical analysis was done using SSPS software version 20.0. Descriptive statistics including frequency and mean/standard deviation were used. P value <0.05 was taken as significant.

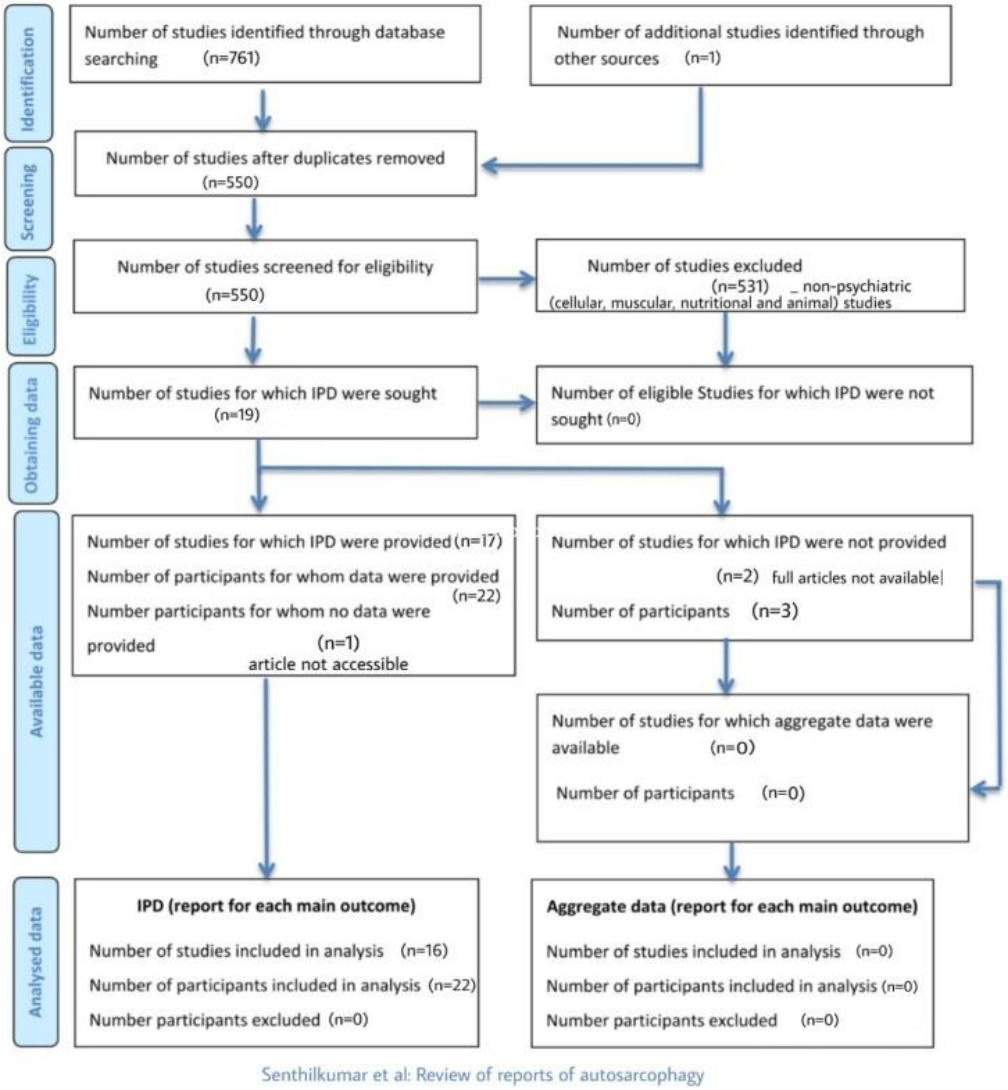

Fig. 1: Protocol followed for identification and selection of cases of autosarcophagy for the systematic review.

Results

Report of cases

Case 1: A seven year old girl was brought by her parents for complaints of deliberately picking at both her cheeks and eating the skin with soft tissue, for the past six months. She had sat up at six months, and walked at 10 months, but now was tripping frequently while running. She spoke two-word sentences. She seldom made eye contact or played with her peers. Her mother complained of her not being as smart as her four year old brother. General and neurologic examinations were normal. Partially healed wounds with surrounding hyperpigmentation were noted on both cheeks. She could not attribute specific reasons for her behaviour. Her IQ score (by Binet-Kamat Test) was 71 and VSMS social quotient score was 75, which was borderline; her CARS score was 39. A diagnosis of autism spectrum disorder (ASD) was made. Inpatient admission proved her self-mutilating behaviour, and child abuse was ruled out. She improved in a few days with minimal antipsychotic dose.

Case 2: A four year old male child born out of second degree consanguineous marriage was brought by father with complaints of self-destructive biting of his fingers, with delayed developmental milestones and presence of spastic posturing in the extremities. The first born male child had died after similar complaints; the mother had a second trimester abortion.

Fig. 2: Finger auto-amputations due to autosarcophagy in a case of Lesch-Nyhan syndrome.

On clinical examination, neither minor physical anomalies nor any abnormality in major systems was detected. Complete amputation of the second and third fingers of both hands (fig.2), dyskinetic movements and dystonia were noted. Though physical examination and a social worker inquiry ruled out child abuse, chronic parental neglect was apparent. Serum uric acid level was 45.8mg/dl and urinary uric acid level was 78mg/dl. Echocardiogram ruled out congenital heart conditions. IQ score in BKT showed a score of 51, and VSMS score was 57. Plain MRI brain showed minimal diffuse cerebral atrophy. Blood hypoxanthine phosphoribosyl transferase enzyme level was found to be just about 3.4% of normal levels, and was being evaluated for a HPRT1 mutation. With the triad of hyperuricemia, neurological, and cognitive and behavioural signs present, the child was formally diagnosed with Lesch-Nyhan Syndrome (LNS).[8] He was managed with physical restraint, sodium valproate and diazepam. Self-biting stopped during hospital stay and was discharged as the wound started healing.

Review of cases of Autosarcophagy (self-cannibalism) from literature

Out of 550 studies screened (fig.1) with search queries in PubMed and PubMed Central databases, 18 of them with 24 cases were identified (table 3). The search was exhaustive. Individual Patient Data(IPD) including sociodemographic and clinical details (table 4-6) was obtained for 22 patients(84.6%). About 46% used the term AP, 38.5% used SC, 23.1% used ASP, 11.5% used AC and 7.7% used "biting, nibbling/eating and self-mutilation" in the descriptions.

Mean age of all patients was 34.433+/-6.8 years (table 1). Mean age of males (36.6+/-5.5 years) among patients with available demographic data was higher than that of females (30.4+/-8.4 years), with p value being not significant. Peak incidences were noted among the children, young adults and the elderly; about 20% were children, 5% were in the late teens, 20% in the twenties, 15% in the thirties, 5% in the forties and 35% in their

fifties/sixties. Mean age of patients with psychosis (38.4+/-4.8 years) was higher than that of those without psychosis (32.3+/-6.6 years), with *P* value being not significant.

About 65% were males and 35% females; about 57.1% were males among patients with psychosis, compared to 69.2% in non-psychotic patients. The difference observed was statistically not significant. While geographic distribution of the incidences reported appear sporadic, no cases have yet been documented in South America and Africa.

Table 1: Socio-demographic profile and psychosis

	Male	**Female**	**Total**	**Statistic**	***P* value**
Age	**n=13**	**n=7**	**n**	t_0	
Mean	36.615	30.381	20	0.641 df=18	0.529 NS
s.e.m.	5.526	8.413			
s.d.	19.141	20.607			
Median	34.0	28.0			
Range	4.0-68.0	1.67-56.0			
Psychosis	**Male, n=13 (%)**	**Female, n=7 (%)**	**Total n=20**	χ^2	***P* value**
Present	4 (57.1%)	3 (42.9%)	7	0.002	0.961 NS
Absent	9 (69.2%)	4 (30.8%)	13		
Psychosis	**Fewer attempts n(%)**	**Multiple attempts n(%)**	**Total n=22**	χ^2	***P* value**
Present	3 (42.9%)	4 (57.1%)	7	4.202	0.040* Sig
Absent	1 (6.67%)	14 (93.3%)	15		

Eleven (42.3%) of the cases have been reported from the US, five (19.2%) from the East Mediterranean countries and four (15.3%) from the North European countries. Others include three Indians, two Australasians and a Japanese. Possible analogy or stylization with the individual's native, archetypal modelling in a mythological background (Greek and Norse) and/or punitive culture bound syndromes (North American and Tamil) is arguable. Though the first case was documented in 1886, further reports were regular at two per decade over the latter half of twentieth century. But since then cases are on the rise, with about 17 over the past 13 years, about six times more ($P<0.05$).

Eighteen (81.8%) patients had frequent (more than two) attempts, and two (9.1%) each had done for the first and second time. Seven (31.8%) patients were documented as psychotic. Stressors and emotional responses dominated mutilating behaviour in others (68.2%), including one who had deliberately and systematically scarified her skin by ASP and split her tongue for “beautification." None had diagnoses of malingering or factitious disorder.

Majority (72.7%, 16) had eaten their fingers, while 27.3%(6) dwelled upon with small to large areas of skin and soft tissue; one each had eaten parts of their palate and pinnae/penis (table 2). About 73.3% of patients who had eaten their fingers, and 57.1% of those who ate skin and soft tissue, had no psychosis. The difference observed was statistically not significant. While in 44.4% of the instances patients with psychosis had eaten their fingers, in 33.3% they had ate parts of skin and soft tissue, and in 22.2% other parts (pinnae and part of penis). Patients without psychosis had eaten their fingers in 68.8% of instances, parts of skin and soft tissue in 25% and other parts (palate) in 6.3% of instances.

About 72.7%(16) of the patients procured the flesh by biting, 22.7%(5) by cutting and 4.5%(1) by picking. About 31.3% of those who procured flesh by biting themselves, and 40% of those who had cut themselves, were diagnosed with psychosis. The difference was statistically not significant. About 71.4% of patients with psychosis and about 78.6% of non-psychotic patients had procured by self-biting.

Three fourths of those with less number of attempts, i.e. with earlier documentations were psychotic. About 77.8% (14 of 18) patients who had multiple attempts were non-psychotics. Mean duration between the onset of clinical symptoms and self-mutilating behaviour was 2.4 years +/- 7 months, among the 14 with relevant details. Mean duration between the onset of self-mutilating behaviour and presentation for treatment is 9 years +/- 2 months. About seven (43.75%) out of the 16 adults were unmarried during presentation.

Common stressors included social isolation (n=7, 31.8%), paralysis and bed/home-bound (9,40.9%), anaesthesia/hypoaesthesia in body parts(6,27.3%), financial conflicts(3,13.7%), and stereotypical behavioural disturbances as in IDD(3,13.7%). Other

causes included family conflicts(3,13.7%), schizophrenia(3), depressive disorders(2,9.1%), alcohol and nicotine dependence(2), peripheral neuropathy(2), orthopaedic conditions(2), primary impulse control disorder(1,4.6%), paraphilia(1), and autism spectrum disorder(1).

Six patients (27.3%) each had pain insensitivity and paraesthesia/hyperaesthesia. About 43% of patients with psychosis had abnormal or high pain sensitivity.

Table 2: Autosarcophagy attributes and psychosis

	Psychosis present	**No psychosis**	**Total n**	**Statistic**	***P* value**
Age	**n=7**	**n=13**	**n=20**	**t_0**	
Mean	38.428	32.282	20	0.632 df=18	0.535 NS
s.e.m.	4.750	6.599			
s.d.	11.636	22.859			
Median	35.0	28.0			
Range	19.0-51.0	1.67-68.0			
Location (>1 part in some cases)	**n=9 (%)**	**n=16 (%)**	**Total n=25 (>1 part in some cases)**	**χ^2**	***P* value**
Fingers	4 (26.7%)	11 (73.3%)	15	4.828	0.305 NS
Skin & soft tissue	3 (42.9%)	4 (57.1%)	7		
palate	0 (0)	1 (100%)	1		
pinnae	1 (100%)	0 (0)	1		
penis	1 (100%)	0 (0)	1		
Pain sensitivity	**n=7, (%)**	**n=15, (%)**	**Total n=22**	**χ^2**	***P* value**
Insensitivity	0 (0%)	6 (40%)	6	4.023	0.134 NS
No abnormality	4 (57.1%)	6 (40%)	10		
Paraesth-esia/hyper-aesthesia	3 (42.9%)	3 (20%)	6		
Procure-ment	**n=7 (%)**	**n=15 (%)**	**Total n=22**	**χ^2**	***P* value**
Biting	5 (31.3%)	11 (68.7%)	16	0.623	0.732 NS
Cutting	2 (40%)	3 (60%)	5		
Picking	0 (0%)	1 (100%)	1		

Among non-psychotic patients about 40% had insensitivity and 20% had abnormal/high pain sensitivity, with no statistically significant difference between the two groups.

Impulsivity was the commonest of myriad psychological factors seen in 86.4% of patients, followed by obsessive-compulsiveness in 36.4%, aggressiveness(31.8%), distress(27.3%), stereotypy (27.3%), pain insensitivity (22.7%), restlessness (22.7%), countering irritant(18.2%), gratification (9.1%) and reacting to delusions(9.1%).

Table 3**:** List of all autosarcophagy cases, documented as "self- cannibalism"(SC), "autophagia"(AP), "autosarcophagy"(ASP), "autocannibalism"(AC) and "biting, eating/nibbling and self-mutilation"(B/ N/E/SM).

Author	Place of report	Year	Journal in which reported	Age /Sex	Term used: AP /ASP/SC/AC	Location /flesh part
Basyuni S & Quinnell T[9]	UK	2017	Sleep Medicine		SC, ASP	*fingers*
Benecke M[10]	Cologne, Germany	1999	Am J Forensic Med Pathol	28/F	SC, AP	large skin patch
Comarr AE & Feld M[11]	California, US	1964	Am J Surg		AC	fingers
Dahlin *et al*1[12]	Florida, US	1985	Paraplegia	31/M	B/ N/E/SM	fingers
Dahlin *et al*2[12]	Florida, US	1985	Paraplegia	35/M	B/ N/E/SM	fingers
Frost FS *et al*1[13]	Ohio, US	2008	J Spinal Cord Med	45/M	AP	fingers
Frost FS *et al*2[13]	Ohio, US	2008	J Spinal Cord Med	55/M	AP	fingers
Frost FS *et al*3[13]	Ohio, US	2008	J Spinal Cord Med	68/M	AP	fingers
Frost FS *et al*4[13]	Ohio, US	2008	J Spinal Cord Med	56/F	AP	finger
Frost FS *et al*5[13]	Ohio, US	2008	J Spinal Cord Med	51/F	AP	fingers
Harris AP *et al*[14]	Rhode Island, US	2017	J Orthopedic	50/F	AP	fingers
Ito Y *et al*[15]	Japan	2010	Rinsho Shinkeigaku	19/F	AP	fingers
Koops E & Püschel K[16]	Hamburg, Germany	1990	Arch Kriminol	51/M	AP	ears, penis
von Krafft-Ebing[17]	Stuttgart, Germany	1886	Verlag von Ferdinand Enke	23/M	AP	Skin over arm, abdomen, thigh
Libbon R *et al*[18]	Colorado, US	2015	J Nerv Ment Dis	29/M	SC	*finger*
Michopoulos I *et al*[19]	Athens, Greece	2012	J Nerv Ment Dis	66/M	AP	fingers
Mikellides AP1[20]	Cyprus	1950	Cyp Med J		SC, ASP	
Mikellides AP2[20]	Cyprus	1950	Cyp Med J		SC, ASP	
Mintz IL[21]	US	1964	Am J Psychiatry		AC, ASP	
Monasterio E & Prince C [22]	New Zealand	2011	Australas Psy	28/M	SC	finger
de Moore GM & Clement M[23]	Australia	2006	Aust NZ J Psy		SC	
Singer M & Schorr L[24]	Israel	2019	J Am Acad Orthop Surg Glob Res Rev.	1yr 8mo/F	AP	finger
Veeramuthu K *et al*1	Vellore, India	2019	this article	7/F	ASP, SC	cheeks
Veeramuthu K *et al*2	Vellore, India	2019	this article	4/M	ASP, SC	fingers
Verma R *et al*[25]	New Delhi, India	2014	J Pediatr NeuroSci	7/M	A C	face
Yilmaz A *et al*[26]	Turkey	2014	West J Emerg Med	34/M	SC	thigh

Table 4: Clinical and psychiatric findings in cases of autosarcophagy

Author	Location of lesion	Mode of harvest of flesh and consumption	First time /Frequent	Psychiatric diagnosis	General medical diagnosis	Immediate neuro/psychological factors
Basyuni S & Quinnell T	*fingers*	*Biting and eating*	recurrent		Obstructive sleep apnoea, tetraplegia	Impulsivity, possibly obsessiveness and pain insensitivity
Benecke M	Skin	Cutting skin, intent to scarify, splitting tongue	recurrent, 5	"non-psychotic"; Culture body modification to "western civilization"		Novelty seeking, gratifying tending towards modern/urban/westernized identity, Obsessive compulsiveness
Comarr Ae & Feld M	Fingers of both hands	Biting and eating	recurrent	"aggressive hostility towards paralyzed and anaesthetic extremities"	Tetraplegia	Aggression, probably punishing the hands, which had turned faithless and unheeding towards him, possible impulsivity; pain insensitivity
Dahlin *et al*1	Partial autoamputation of right 2nd finger (2 1/2 phalanges) and 4th finger (distal phalanx)	Nibbling, chewing	recurrent	Mixed anxiety and depression	Spinal cord injury	Restlessness, impulsivity, frustration, aggression
Dahlin *et al*2	2 1/2 phalanges of right 2nd finger and 2 phalanges of right 3rd, 4th and 5th fingers; near total autoamputations of 2nd, 4th and 5th fingers on the left hand	Eating, nibbling	recurrent	Depressive neurosis, narcissistic traits, not concerned -not considering SM as a problem, Past history of severe self neglect and elevated self-esteem	Spinal cord injury, multiple surgeries for contractures and pain syndrome, bladder dysfunction, bedsores, ischial osteomyelitis,	Increasing frustration towards multiple recurrent complications, impulsivity, aggression
Frost FS *et al*1	Distal phalanges in both hands	biting	recurrent	Recurrent DSH	Tetraplegia, traumatic spinal cord injury	Pain insensitive, impulse dyscontrol initially, stereotypical later
Frost FS *et al*2	Distal phalanges In both hands	biting	recurrent	Alcohol and nicotine dependence syndrome	traumatic tetraplegia, chronic tracheostomy	Pain insensitive, frustration and increased impulsivity secondary to distress about multiple disabilities (motor, sensory, vocal and respiratory), restlessness, stereotypical later
Frost FS *et al*3	All phalanges in both hands	biting	recurrent		Traumatic tetraparesis	Pain insensitive, impulse dyscontrol initially, stereotypical later

Table 5: Clinical and psychiatric findings in cases of autosarcophagy, *contd.*

Author	Location of lesion	Mode of harvest of flesh and consumption	First time/Frequent	Psychiatric diagnosis	General medical diagnosis	Immediate neuro/psychological factors
Frost *et al*4	fingers	biting	recurrent		Traumatic tetraplegia, tendon transfer surgery, paraesthesia extremities	Irritant (abnormal sensations) related, impulse dyscontrol, repetitiveness as in OCD spectrum disorders
Frost *et al*5	Soft tissue of both forearms, and fingers	Gnawing and biting	recurrent	Possible organic psychosis as post-operative sequelae (in retrospect)	Traumatic tetraparesis, pain syndrome, bilateral cingulate gyrectomy	Hyperesthesia+; irritant (pain syndrome) related, impulse dyscontrol, secondary to distress about pain; post-surgically, probably stereotypical
Harris *et al*	Right hand fingers	Biting as bits and chewing	recurrent	Psychosis NOS	Right 2nd finger osteomyelitis, pyogenic flexor tenosynovitis, end stage renal disease, dialysis dependent, renal transplant recipient, HCV positive, hyperparathyroidism	irritant-related, impulse dyscontrol
Ito *et al*	*fingers*	Nibbing and chewing	recurrent	Schizophrenia	anti-NMDA receptor encephalitis, dyskinesia, recent seizure, Antenatal 2nd trimester	Probable restlessness, Impulsiveness, obsessiveness
Koops E & Püschel K	Pinna of both ears, and partial amputation of penis	Cutting and chewing ear pinna and penis	first self-injurious behaviour	Paranoid schizophrenia		Aggression, impulsiveness, bizarre delusions, restlessness
von Krafft-Ebing	Skin over arm, abdomen, thigh	Cutting with knife and scissors, and "masticating"	recurrent	Fetichism with cutis feminae, with obsessive (impulse) and schizotypal-like features; autophagy for instant orgasm and ejaculation		Sexually gratifying, obsessiveness
Libbon *et al*	*finger*	*Biting and eating*	recurrent, 2nd	Psychosis, Polysubstance abuse		Aggression, impulsivity, restlessness, resulting in bizarre countermeasures in dealing paranoid ideations and substance craving
Michopoulos I	Distal phalanges in both hands	biting	recurrent	Impulse control disorder NOS	Diabetic peripheral neuropathy, cerebral atrophy (CT)	Impulsivity, obsessive compulsive spectrum

Table 6: Clinical and psychiatric findings in cases of autosarcophagy, *contd*.

Author	Location of lesion	Mode of harvest of flesh and consumption	First time/Frequent	Psychiatric diagnosis	General medical diagnosis	Immediate neuro/ psychological factors
Monasterio E & Prince C	One finger	Amputation and eating	1st	"non-psychotic," ?possible body dysmorphic disorder		Impulsiveness, probably obsessiveness
Singer M & Schorr L	Distal phalange of fifth finger on the right hand	biting	recurrent		Hypoesthesia from partial ulnar nerve injury, from supracondylar humerus fracture	Impulsivity, frustration
Veeramuthu *et al*1	Skin with soft tissue of cheeks	Picking and eating	recurrent	Autism spectrum disorder, borderline intelligence		Stereotypical, impulse dyscontrol
Veeramuthu *et al*2	2nd& 3rd fingers, both hands	Biting and chewing	recurrent	Moderate intellectual disability	Lesch-Nyhan syndrome	Aggression, obsessive compulsiveness, impulsivity
Verma R	Upper lip, philtrum, anterior part of palate	Biting and chewing	recurrent	Intellectual disability, behavioural disorder		Aggressive, impulse dyscontrol, stereotypical
Yilmaz *et al*	Thigh skin patch with soft tissue	Cut laceration, ingestion	recurrent2nd	Schizophrenia, multiple DSH	prisoner	Bizarre delusion/ disorganized behaviour

Table 7: List of prominent genetic disorders with self-mutilation

Gene [44]	Protein	Loci	Disorder	Medical/Neurological features	Psychiatric features[44]
NTRK1	Neurotrophic Receptor Tyrosine Kinase 1	1q23.1	Congenital Insensitivity to Pain with Anhidrosis,	Pain and temperature insensitivity, anhidrosis, autonomic dysfunction, Osteomyelitis, skin ulcers,	Irritability, self-mutilation, intellectual disability, emotional lability, rage, hyperactivity
HPRT1	Hypoxanthine Phosphoribosyl transferase 1	Xq26.2-q26.3	Lesch-Nyhan Syndrome, Kelley-Seegmiller Syndrome	Hyperuricemia, choreoathetosis	mental retardation, and compulsive self-mutilation
MECP2	methyl-CpG binding protein	Xq28 (subtelomeric)	Rett syndrome	Microcephaly, seizure, scoliosis	Poor language and communication, stereotypies -hand wringing, clapping, biting hands, girls exclusive

Table 8: List of prominent genetic disorders with self-mutilation, *contd.*

Gene [44]	Protein	Loci	Disorder	Medical/Neurological features	Psychiatric features[44]
NAA10	N alpha acetyl transferase 10	Xq28-ter	Ogden syndrome	Congenital heart disease, dysphagia, arrhythmia, dysmorphic facies, cerebral dysgenesis, short neck, scoliosis, aged appearance, neurodegenerative conditions	Hand biting, IDD, hypotonia, self-hugging, unmotivated laughter, aggressivity, stereotypical behaviour
RAI1	Retinoic acid 1 induced transcription factor	17p11.2 microdeletion	Smith-Magenis syndrome	Scoliosis, short stature, pain insensitivity, hoarseness of voice, square face, flat mid-facies, deep-set eyes	Biting, hitting, skin picking, repetitive self-hugging, ADHD features, aggression, altered sleep pattern, mild/mod IDD, language deficits
NAT8L	N-acetyl transaminase 8 like	4pter-16.3	N-acetyl aspartate deficiency Canavan disease	Truncal ataxia, seizure, microcephaly, inguinal hernia	Self-mutilation, ADHD features, stereotypical behaviour, hyperorality, developmental delay
EHMT1	Euchromatic histone lysine methyltransferase 1	9q34.3-ter	Kleefstra syndrome, autism spectrum disorder	Renal cyst, genital defects, arrhythmia, short stature, epilepsy, congenital heart disease, abnormal facies, hearing difficulty	self-mutilation, ADHD like and autism like features
TCF4	Transcription factor 4	18q21.2	Pitt-Hopkins syndrome	Tented upper lip, wide shallow palate, anteverted nares, aphasia, cyanotic apnoea, myopia, seizure, bulbous caudate nuclei, hypoplastic rostral and splenial corpus callosum	Autism spectrum features, aggressive outbursts, anxiety, hand biting, stereotypic hand or head movements, mod/severe IDD, night terrors
INPP5E	Inositol polyphosphate 5phosphatase E	9q34.3-ter	Joubert syndrome	Macrocephaly, ataxia, hypotonia, protruding tongue, anteverted nostrils, oculomotor apraxia, retinal disease, cerebellar hypoplasia	self-mutilation, aggression, attention deficit, intellectual disability
PHYH	Phytanyl CoA 2 hydroxylase	10pter-11.3	Refsum disease	Ataxia, intentional tremors, nystagmus, hypotonia,	self-mutilation, developmental delay
RDPA	Phytanyl CoA hydroxylase with pipecolic acidemia	10pter-11.2	Adult Refsum disease	Neurological deficits, ataxia, peripheral neuropathy, sensorineural hearing loss, retinitis pigmentosa	self-mutilation
FMR1	Fragile X Mental Retardation 1 Protein	Xq27.3	Fragile X Syndrome	Elongated face, large ears, hyperextensible digits, flat feet, macroorchidism, hypotonia, recurrent otitis media, seizures	Intellectual disability, autistic features, cluttered speech, stereotypic hand flapping, occasional self-injurious behaviour

Discussion

Discussion of the cases

There was considerable variation in phenotype and severity between the two cases. Differential diagnoses for primarily self-mutilating behaviour include childhood disintegrative disorders including Rett syndrome, Smith-Magenis syndrome, Joubert syndrome, Refsum disease and Prader-Willi syndrome. Other conditions like fragile X syndrome, tuberous sclerosis, congenital rubella, predominantly compulsive obsessive compulsive disorder and Tourette's syndrome that may also mimic such a presentation.

Autism first elaborated by Kanner, includes the triad of poor social interaction, language and communication, and restricted interests and

repetitive behaviour. Stereotypical behaviour, misdirected aggression and borderline intelligence are known to be contributory to the self-mutilating behaviour in children with ASD. Behavioural modification through negative reinforcement and extinction, and antipsychotics in minimal doses usually help prevent permanent disfigurement and disability.

In the second case, other causes of hyperuricemia like gout, congenital heart disease (with hypoxia and polycythemia), haemolytic anaemia, haematological malignancies, bronchial asthma, acute gastroenteritis (rotavirus), antiepileptics and immunosuppressants[7] were ruled out. Lesch-Nyhan disease, is an X-linked disorder of purine metabolism presenting with hyperuricemia, mental retardation, involuntary movements, and self-destructive behaviour, and results from decreased activity of the hypoxanthine-guanine phosphoribosyl transferase (HPRT1) enzyme due to mutations in the HPRT1 gene. Variable HPRT enzyme activity is inversely proportional to clinical severity.[7] But genetic loci linkage seems to be consistent with sharing of common phenotypic features, even within the same family.[27,42] The chewing and eating acts may have been aided by the minimal ossification of phalanges (which just start by three years of age).

ASP behaviour could have been instigated and driven by impulsivity and pursued as a stereotypical behaviour possibly from comorbid ADHD and autism spectrum symptoms. Treatment includes use of allopurinol, S-adenosyl methionine, anti-anxiety and mood stabilisers, physical restraints and deep brain stimulation. Though sodium valproate is known to increase uric acid levels, excessive impulsivity and movement disorders may warrant its use, if benefits outweigh risk, under close monitoring.[7] Average life time is generallly found to be 30 to 40 years.

Discussion for the systematic review of ASP cases

We found no review studies so far on ASP and genetic correlations of self-mutilation. MRI studies showed inconsistent findings like changes in basal ganglia, amygdala, basal forebrain and amygdala, and polymicrogyria in median frontal and temporo-occipital areas in patients with self-mutilation. Self-cannibalism occurring in different clinical conditions almost all of which were genetic disorders was studied.

The review showed that the cases have been progressively on the rise over the past few decades –about six times in the past 13 years. Frequencies among patients with psychosis and non-psychotic patients were comparable. More than three fourths of multiple attempts were by non-psychotic patients. Most non-psychotics preferred eating fingers, while more than one in five patients with psychosis had preferred specific parts of body. Paraesthesia and pain insensitivity were predominant in patients with psychosis and non-psychotic patients respectively. Impulsivity, obsessive compulsiveness, and aggressiveness were the commonest of all factors.

According to Matorin and Ruiz, psychotic patients with bizarre modes of self-mutilation like autoamputation, enucleation and castration among others, may have subjective symbolic import with the delusions of implausible or mystic content.[28]

In non-psychotic patients, emotional numbing is encountered in acute life threatening events, PTSD-like phenomenas, and chronic traumatizing histories.[29] This along with passive influence experiences disassembles the sense of integration of self increasing normalization of the frequenting dissociative states of mind. Simeon and Loewenstein[29] have detailed that chronic depersonalization, emotional numbing, and a sense of detachment from self, fosters risky and self-mutilating behaviour. Numerous studies including those by Kluft RP, Lewis et al, and Loewenstein RJ, have documented association between self-mutilation and dissociation.[30,31,32] They may even be the attempts to break through profound states of numbing and depersonalization.[29] Dissociation also increases reliving phenomenon and predisposes to recurrent traumatization, setting up a vicious cycle of evermore alienation of self and higher risk of self-mutilation. Borderline, histrionic and anankastic traits and mixed personality disorders

appear as primary determinants in self-mutilating behaviour.[28] Release of tension, externalizing internal agony, and reassuring oneself with pain against the dissociative numbness, are usual psychological reasonings in personality disorders.

Treatment

Promptly addressing the self-mutilating behaviour at the first presentation is vital in healing injuries, minimizing permanent disability, and preventing further relapses. The evidence for effective medications in reducing self-cannibalism in developmental disabilities are limited so far, more so if it is associated with genetic conditions.

Various studies document successful management of self-mutilating behaviour with physical restraints, negative reinforcements, systematic desensitization and extinction.[32,33,34]

Identification of environmental protective factors helps useful intervention models in the management.[32,33] Restraints include hand braces, protective gear for fingers and lips, and orthotics for teeth and jaws. Reinforcements include using fine water mist on the face, combined with a pre-recorded or loud call of "No!" at a biting attempt, and a clear verbal praise for a consecutive stop response.[35] Iwata et al had shown that differential reinforcement, combined with response interruption techniques, produce reductions in self-harming behaviour and increase in useful goal-directed motor performance (instruction following and toy play).[36] Regular tracking by self-recording, aversive response substitution, and individualized relaxation therapy help complete healing and permanent recession from mutilating behaviour.[37]

Appropriate training of the caregivers to morally support and constantly encourage the patient to persevere therapy is essential.[32,33]

Most disorders show better results with antipsychotics, topiramate and N-acetyl cysteine. Drugs targeting the psychological correlates like impulse dyscontrol, aggression and obsessiveness/perseveration, may improve the abnormal behaviour.

Many enter second and third decades of life with severe disability. In India, disability certification under the head of "chronic neurological conditions with mental illness," could make them eligible for monetary, transport and other aids from the state.[38]

Legal intervention may be needed if the psychiatric evaluation points to factitious disorder –which often shares similar psychological attributes, insofar as the intent is persistent and motivation high for gains.[39]

Probable genetic coordinates in LNV and ASD

Decreased serotonergic and increased dopaminergic activity is implicated in self-mutilating and self-cannibalistic behaviour.[40,41] ASD favourites include 22q11 microdeletion and duplication, 15q13, and SHANK3 mutations; 8p21 and 9qter mutations code both for ASD and self-mutilation. Disruption of PTCHD locus on Xp22.11 both code for ASD and IDD.

In general, similar clinical LNS phenotypes arise from similar HPRT1 gene mutations in Xq26.2-26.3, with minimal variations.[42,43]

Involvement of multiple terminal gene loci on different chromosomes[44] with possible evolutionary linkage, or ectopic recombinations in the chromatin state, is proposed below in view of significantly diverse clinical phenotypes with respect to ASP.

Propositions

Studies show that the intensity of genetic preponderance precludes the response and symptom-related prognosis of these disorders.

Genetic recombination with ectopic gene conversion (paralogous sequences) leads to repairs maintaining the integrity of genomic DNA, and forms distinctive haploids contributing to genetic diversity.[45] We explored for possible relationship between the loci identified for self-mutilation,[44] and to evaluate other related dynamics of genetic causes.

1. The terminal genes with shared conditions – similar to those listed in table 7 and 8 where seven out of the top ten involve terminal

alleles, implicate either overt ectopic recombinations or an evolutionary continuity between the terminal loci between two different chromosomes, sharing proteins of similar or related functions, involved in similar diseases or disorders. Since many of these recombinations are non-homologous "isofunctional," we propose that specific chromosomes must have been lying contiguous in the same particular order, either in the chromatin form or at some point in the past during human evolution. Examples of such serial arrangement between parts of chromatin of interphase corresponding to 22qter and 19qter, 3qter and 17qter, and 15qter and 10qter in the chromosomes of the metaphase of mitosis, are graphically represented in figure 3.

2. Acetyl serotonin OMT(-like) gene at Xpter and platelet activating factor gene Xq26/28, together with Xq26.3 of LNS are related to serotonin which is implicated in aggressive behaviour. These are likely to be inherited together as linked genes (X-linked recessive) though chances of recombination are limited due to proximity.[44]

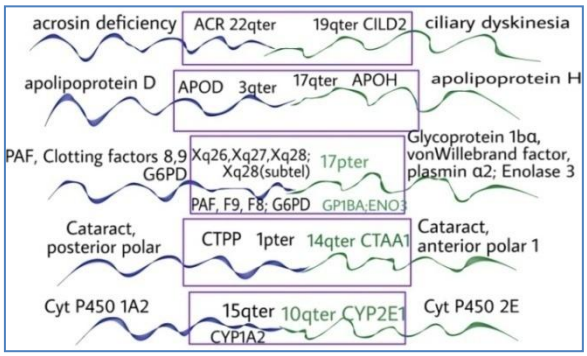

Fig. 3: Proposed contiguity of isofunctional terminal genes of would-be chromosomes.

3. Some chromosomes like 17 and X have two or more different loci for similar or closely related conditions, apart from few possibly linked genes. For example, glycogen storage diseases 2 and 13 have loci at 17pter and 17q25.2, colour and night blindness have loci at Xq28 and Xp11.23, as also the 5-HT/PAF genes mentioned above. Such close intrachromosomal paralogous sequences (on the opposite arms of same chromosomes) of related genes with probable shared ancestry, therefore suggest either a highly probable lemma of recombinant gametes with the original cross involved genes in repulsion phase –thereafter being regularly inherited in larger proportions as a single dominant allele (Ab or aB), or another possibility of being originally ring chromosomes, and both at some point of evolution of life getting through to the human genome. They could also be due to being possibly ring-shaped in the chromatin during the interphase, but then the two distant genes would be actually more closer and smaller centiMorgans backwards, making fewer cross over events occurring between them and hence fewer recombinant chromosomes.[45] Hence the evolutionary one-time recombination is a more plausible postulate.

4. It is more than obvious that many homologous crossover recombinations of flanking regions of Xq26-28 determine the Lesch-Nyhan, Ogden, Rett, Börjeson-Forssman-Lehmann, Fragile X syndromes and a few non-eponymous syndromes of intellectual disability.

As distances approach 50 cM it is difficult to determine if two genes are linked on the same chromosome.[45] Therefore, other mapping techniques must be used to determine the linkage relationship among distantly associated genes.

Conclusions

Autosarcophagy is a self-destructive and debilitating phenomenon that causes permanent disability. Prominent psychosocial factors are treatable and/or modifiable with drugs, psychotherapy and appropriate care giving. With the varying phenotypes in ASP-related syndromes, genomic analysis of the associated loci posits a possible linkage between them, more apparent with terminal alleles. Study of such inter-relationships is

vital as conditions with non-homologous and novel mutations are most challenging.

Such studies can help in expected self-mutilating behaviour, early diagnosis and intervention, treatment options, and prognosis-oriented approach.

Limitations

The complete list of all conditions featuring self-mutilating behaviour could not be assessed for correlation of more common genetic attributes. Further delineation of genetic sequences related to autosarcophagy and other self-mutilations can provide additional insight and guidance during genetic counselling for grave syndromes like LNS.

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