



(REVIEW ARTICLE)



A review on Angelman syndrome

Swathi Krishna KV ^{1,*}, Vasunoori Anitha ², Vasunoori Hemalatha ², Vinukonda Aravindh ², Yalakapalli Poojasree ² and Yarraballi Suneel kumar ²

¹ Department of Pharmaceutics, Saastra College of Pharmaceutical Education & Research, Near Varigonda Jwalamukhi Temple, Muthukur Raod, Kakupalli, Nellore-524 311 Andhra Pradesh, India.

² Saastra College of Pharmaceutical Education & Research, Near Varigonda Jwalamukhi Temple, Muthukur Raod, Kakupalli, Nellore-524 311 Andhra Pradesh, India.

World Journal of Advanced Research and Reviews, 2023, 17(03), 070–086

Publication history: Received on 06 January 2023; revised on 25 February 2023; accepted on 27 February 2023

Article DOI: <https://doi.org/10.30574/wjarr.2023.17.3.0282>

Abstract

"Angelman syndrome" AS seems to be a neurodevelopmental illness for whom significant aspects were learning impairment, total absence like presentation, convulsions, and a character trait behavior resume. Its behavior includes the delighted public persona, easily angered amusement, hard time concentrating, and hyper motoric actions, swearing like things, disruptive behavior, and an attachment such as liquid. Developmental problems and delicate dysphoric includes, along with incoordination and other mobility disruptions, have been extra functionality in essential people with the condition. And so is resulting from short invocation of something like the tubulin nutrient ubiquitin E3A (ube3a) mutation, which shows parental bonding. There are four single-molecule classrooms upon as, and somegenotype-phenotype collinearity has popped up. More than stays to be acknowledged about why issues like E6-AP and its nutrient merchandise like UBE3A end up in its noticed neurobehavioral deficit spending. Research like animal studies has allegedly involved UBE3A along with experience-dependent synapses redeveloping. Its pharmacogenetic facets include Angelman disorder, its basic biomolecular tenets, and access to basic service methods. And so is one neurobehavioral disorder that is characterized while also a severely impaired handicap, engine failure to thrive, communication difficulties, impulsiveness, but also ordinary epileptic fits. And so is attributable to interruption of prenately conveyed but also generationally ingrained UBE3A, which also lossless encoding the ubiquitin secondments. Four methods in the production of its gene encoding UBE3A non - functional were also acknowledged, the most typical of which would be the deactivation of such motherly love human chromosome 15q11-q13. Amazingly, redundancy with the same human chromosome is amongst the few best-described continual chromosomal mutations linked to asperger's syndrome disease, cropping up along >1–2 Percentage among all situations like autism diagnosis. While outcome morphological characteristics of something like the central nervous system and communication like neurons projected numbers are mainly standard in animal studies, primary operating deficiencies were also discovered just at a standard like discussion training. Also, they impeded developmental processes like learning, memory, and neurogenesis circuit design. Offers similar promote confidence a significant involvement such as proteolysis protein ligase E3A along synapses advancement, its operations to dysfunction like tubulin transcription factor E3A results samples pathogenic mechanisms along living beings poor job performance did understand. but even so, current attempts have also shown keep promising through trying to restore continues to function interrupted into it as mouse model, reactivating keep hoping how the effectiveness of treatment's management strategic plan could be discovered.

Keywords: Angelman Disorders' AS;' Chromosomes 15q11-13; UBE3A; Imprinting

* Corresponding author: Swathi Krishna KV

1. Introduction

Harry Angelman, the English professor of pediatrics, primarily characterized one such situation through 1965 because he mentioned three children. It was known as "puppet children" because of their unexpected grip stance, jerking motions, and distinctive feature movement patterns. Addison said intellectual disabilities impairment, unavailable monologue, and spates like unnecessary amusement. The phenotypic expression has been explained within fifty years since the entire study, and the causative agents of such illness are defined just like dysfunction like ube3a. It is single-molecule pathogenic as to how UBE3A condition can lead towards this phenotypic expression seems to be starting to something that is clearly stated. How much continues to follow is just a characterization like in our modern understanding of the diagnostic and therapeutic as well as single-molecule facets [1].

The Angelman disorder seems to be multiple genetic diseases that disproportionately impact the central nervous. Essential characteristics of this situation include postponed evolution, mental retardation, extreme language disorder, and troubles with action and rebalancing. Disrupted advancement will become visible by six months, full twelve months, and other clinical manifestations typically appear from birth to age. Often these young individuals both have reoccurring epileptic fits as well as a tiny head surface area.

Children with Angelman disorder generally have a joyful, enthusiastic public persona for a visit, regularly laughing, laughing, and hand-flapping moves. Impulsivity, as well as a limited attention span, have been frequent. Important children also have terrible insomnia and wish for less snoozing because of regular[2].

1.1. History

Angelman disorder was first characterized in published research in 1965 by dr. Harry Angelman, a British physician. This same character trait research results like Angelman disorder are still not ordinarily evident in newborns, and treatment of both diseases is frequently created among both 1 to 4 years AGE [3].

The disease is now named after dr. Harry Angelman first revealed its disorder in 1965.

Feature-specific help describes this same disease, including [4]:

- Developmentals delay
- Intellectuals disability
- Severe monologue impairment
- Problems with mobility as well as balancing act (ataxia)
- Recurrent epileptic fits (epilepsy)
- Delighted public persona as for regularly attending laughter
- A slight underbite surface area (microcephaly)

Often, there too, are gastrointestinal, rheumatology, and eye issues. Impulsiveness, as well as a hard time concentrating, have been prevalent.

Infants usually function sometimes when newborns and sometimes have trying to feed troubles during the first months after birth. Additionally, they demonstrate developmental problems between six and twelve months. Epilepsy almost always initiates in both centuries two and three.

The illness outcome from transcriptional silencing of the specific gene ube3a that gives guidance such as attempting to make someone nutrient the said plays a significant role in nervous system development of both the central nervous.

They have specialized treatment for just that. This same concentrate-like diagnosis is really to start reducing epilepsy and nervousness, but also gastrointestinal problems and enhance bedtime. Epileptic fits might well be treated with prescription drugs and nutritional treatments. Sleeping problems could be treated, as well as prescription drugs and behavior modification. Physiological, employment and presentation treatments must also help speed up and happen as long as they are usually required. Many individuals might enjoy implementing behavioral assessment and modification [5].

1.2. Definition

Angelman disorder was generally known as 'happy puppet disorder' because of the infant's sunshine viewpoint and spastic movements [6]. It has become started calling Angelman disorder now since Harry Angelman, this same general practitioner who was the one who asked to investigate this same symptomatology in 1965. Important diagnosis and treatment have been decided between the centuries of two and four yrs old.

Angelman disorder is a genetic condition brought on by an issue with the UBE3A genotype through genetic code 15. Individuals with Angelman disorder either are omitted a replica of that genotype, or even the replicate they have doesn't operate effectively.

Common characteristics include intellectual impairment, deferred statements, no presentation, jerky having to walk design, and delighted body language.

There is no remedy. However, the infant could take pleasure in psychotherapy, which includes physiotherapy, special needs, and behavior modification.

1.3. Clinical Characteristics [7]

- Usually pregnant mothers but also newborn background, standard smaller head about as developing, neither any field of study newborn defects
- Delayed accomplishments like expected developmental besides the age of 6 of between twelve months, finally categorized just like extreme, instead of lack of skills
- Speech impairments, as for bare minimum to the no utilization utterances; language comprehension skill sets but also nonverbal signals skill sets better just as receptive and expressive skills
- Movements and balancing act disease, generally incoordination like functional mobility OR trembling mobility of limbs
- Behavioral individuality along with any combo like visit regular laughter OR smiling, noticeable pleased public persona, excitatory, and hyper motoric actions.

2. Behavioural Characteristics



Figure 1 Behaviour and Appearance of AS

These same behavioral traits of that AS have been trying to strike, so it is these, and it almost always stimulates healthcare professionals to think about its treatment. They may be displayed over all patient populations regardless of the type [8], like a biological chromosomal anomaly. Convulsions like easily agitated laughing started within several weeks after birth. Almost all clients have been pleased but also big grins regularly. Laughing is frequently prompted, but the stimulation often is negligible, and laughing could be unnecessary. Impulsiveness and sleep disruption have been frequent throughout adolescence and, therefore, can present substantial control issues. These same sleep problems could be improved while also behavioral therapy for adherence to the tough time for bed training regime than by using circadian rhythms, which would be efficacious in about 50Percentage of sick people. Twelve members of

Angelman disorder adore liquid and have a keen interest in reflective materials, PVC, and party poppers. People experience being in the business of someone else and sitting watching, particularly comic relief dry wit. As for advancement into the adult years, its actions have become calmer, and the intensity timeframe tends to increase. Its socially adept temperament continues unabated, and apoplectic fits like laughing might well happen. A few grown-ups seem to have a natural inclination to complete physical aggression, particularly infuriated due to poor communication skills. Figure 1.

2.1. Natural history [9]

Labor and childbirth are frequently unremarkable; however, the babies measure 250 - 300 gms just under their sister and brother through the median. They may frequently be glum newborns, but trying to feed issues are a principal reason, such as big worry. Jerking motions are becoming evident in the first few months, and engine postponement is apparent while also nine months like time of life. Epilepsy initiates over one year and continues to be a problem for seven or eight decades. Once they reduce along recurrence or may completely stop altogether, impulsive behavior and insomnia, which are frequent through adolescence, improve over time. Its facial characteristics are still not generally evident through childhood, even though they transform during the first five years of living. Vocabulary doesn't establish; often, these people undergo just one or two or more words, regardless of experiencing a proper understanding of straightforward instructions and paragraphs. A few sick people could converse utilizing shorthand gesture recognition and other expressions. Critical patients remain ambulatory in and out of later life unless they keep cell phones to stop atrophied muscles from creating osmotic pressure on arms and legs. Overall, health is sweet. Orthopedic takes place through 10 Percentage clients. It is a childish kind of infertility, obvious well before the age of five years, so although liberal, especially during teenage years. Cardiovascular and respiratory troubles might very well originate whether this is left unchecked.

2.2. Seizures in Angelman Syndrome

Grand mal seizures happen in 80 Percentage of sick people. Time of life, sometimes when emergence tends to vary between one and five centuries. This same immediate result of both epileptic seizures seems to be paroxysmal seizures through childhood. Through adolescence, a wide range of epilepsy can be noticed, starting from antinociceptive epilepsy, nontypical missed days, paroxysmal, tonic-clonic, and myoclonic seizures, but also elixir epilepsy complete epilepsy. Utter lack of prestige, as well as tonic-clonic conditions, could also happen. Previous reports recommended one lowering recurrence like grand mal seizures for maturity level, so further follow this up shows that even though there could be a comparatively steady-state time frame throughout late adolescence and early adolescence, numerous grown-ups have psychotic symptoms, notably unusual missed days and seizures usually [10]. Its epileptic seizures, like Angelman disorder, have been difficult to regulate as for antipsychotics, particularly throughout adolescence. The most straightforward substances were sugar and salt, although combined therapy for clobazam or other anti-depressants. Benzodiazepine does have some detrimental impacts. Through grown-ups, the sample used in this study also is efficient. Encounter with both modern prescription medications is so very severely restricted.

2.3. Angelman Syndrome in Adults

Its phenotypic expression, like Angelman disorder, is indeed a developing one that only keeps changing as for process into the adult years. Adolescence happens at such a regular time. Hence, there are typical secondary sex characteristics and character traits. Skincare routine character traits throughout grown-ups are so much more declared, as well as the characterized mandible feebler, responded by pointing neck, macrostomia, or an influential bottom lip. Eyes pop more profoundly established, and thin corneas have been noticed in some sick people. Portability significantly reduces since body part was formerly growth like thoracolumbar kyphosis, as well as an overall unwillingness complete take a stroll. A few of those patients experience atrophied muscles, so in those with limited movement, incoordination becomes less pretty evident. Numerous sick people are becoming overweight, and oropharyngeal reflux could occur, and it can be severe. Despite the challenges, an excellent life quality seems to be sustained into the adult years, and even the percentage of the patient's life cycle isn't reduced [11]. Figure 2



Figure 2 Man With AS

3. Natural History and Medical Problems

3.1. Gastrointestinal issues and oral-motor behaviors

Supposed feed troubles were also typical but not commonly severe and typically showed up slightly earlier difficulty throughout trying to suck and swallow. Language movement may well be indisciplined for ramming and broad sweeping oral-motor counter-reformation. There could be distress beginning to try to suck and maintain breastfeeding, and formula feeding might very well verify simple and easy. Standard throwing up may be perceived even though equation prejudice and gastroesophageal reflux [12]. Extremely rarely, drastic share more information reflux might very well undergo surgery just like youngsters were also primarily known regarding trying to put all of that in their jaws. Throughout young infants, arm slurping seems to be expected. Later, often these explorative games would be by intranasal deception and chomping. So many, not all, have language protuberance but also salivating, but others have invagination that's also primarily perceptible during amusement.

3.2. Hyperactive behaviors and sleep problems

Difficulty sleeping has been expected, especially during an ordinary evening at home trying to wake up but also slightly earlier starting to wake up. Significantly reduced need for a nap and unusual snooze/wake periods was also a character trait of that. Primarily, only those young kids with it also had elements like impulsive behavior; males and females are similarly affected. Babies and children may very well have neverending exercise, accountable and transparent fingers, and gadgets of their tongue, trying to move because after complete attribute item [13]. A hard time concentrating seems to be displayed throughout most. A few of those behavior patterns might very well recommend some autistic spectrum concern. Although socializing is usually decent, archetypical behavior patterns include queueing up like gadgets and the sense of wonder for rotating object-based and flashing headlamps occasionally happen.

3.3. Hypopigmentation and ocular albinism

Also, when brought on by the massive removal, eyes and skin erythema could happen and therefore is thought to be due complete haploinsufficiency of both the oca2 genotype, placed close to ube3a. This same oca2 gene provides instructions for making someone nutrient significant through phosphorylation and various metabolic-related developments like color within hair and skin, but instead irides [14]. In certain youngsters, too, one such erythema can become so drastic that a sort of early - onset has been accused. Also, when it seems to be brought on by other biological mutations, normal eyes, and skin pigment have been seen. Not that all, even though kids, as for deleted comments of both the oca2 genotype, were also evidently depigmented, but it may have only comparatively paler skin coloring than both families.

3.4. Language and developmental impairment

Speech disorders seem to be serious. Acceptable, using just one or two or more words in such a consistent way has been unique. Language comprehension abilities are more progressed because of verbal ability skills. Influential older individuals have been allowed to converse while also trying to point, including using expressions and information exchange planks. The ordinary conversation somehow doesn't establish in even high-functioning autistic individuals

people. Efficient effluent utilization gesture recognition doesn't take place. Intellectual capabilities were also profoundly influenced. Precise neurodevelopment going to test has been difficult due to difficulty in paying awareness, impulsivity, and total absence like a monologue. Personality assessment trying to push means that this same topmost neurodevelopment possibility would be in the 24- 30-day variety. Individual people with difficulty regulating epileptic fits will be more intoxicated. However, as for coherent intervention and prevention as well as stimuli, the kid's display continued to improve growth.

3.5. Mouse Models of Angelman Syndrome

Mouse model as for patriarchal up just that copy of the gene 7 seemed to be first revealed as little more than a framework because as, and though a known today radiation-induced deactivation and it appears to lack that both p genomic regions but also ube3a could still be used to provide mother and newborn de-efficiency regarding ube3a. These designs involve significant areas like cursor genetic code 7c and might affect many loci. Humans managed to produce one undefined mutagenesis through ube3a through genetic manipulation and located the said motherly love efficiency mouse model display neither any distinguishable utterance of both the genomic regions through neuronal cells nor just in neurologic pork intercellular. This same maternal love efficiency mouse model illustrates diesel engine failure to thrive, transcriptional epilepsy, a deformity through differentiated instruction, and glutamatergic ltp. Context-specific worry reinforcing seems to be a cognitive processing behavior pattern suspected of being involved through mammal brain-lesion studies implicate learning and memory operation. LTP appears to be an electroencephalography sociological phenomenon through which stimulus like postsynaptic nerve fibers tends to increase its force-like interconnection between receptor activation neurotransmitters such as days or even weeks and therefore is commonly considered as just a form like neurons in the brain elastic-plastic that's also meaningful versus memory and learning. ltp is usually taken into account this same best overall presidential contender cell membrane framework, just that memory and education. Its deformity along ltp, which is quite influential in just as a mouse model, symbolizes its first scientific proof for just an involvement like constitutive activation along placental mammal ltp [15]. Among people with asthma, someone much-studied physical model for such mechanistic mechanisms as cognitive processing, ubiquitin-dependent proteasome has been accused of being involved with synapse changes that occur through lengthy enablement.

Nevertheless, it seems unclear whether e6-ap plays an explicit or implicit role in determining ltp. Because rats have standard neuroanatomical but regular baseline synapses transmitting, its deficiency through ltp might reflect some principal chromosomal anomaly. Just like rats have had an increase in abundant supply like cytosolic p53 along reticular formation cellular and some adult neurogenesis, that also means that e6-ap helps regulate its ample supply like p53 straight through vitro systems thru all the developmental conditions.

3.6. Pathogenesis of Angelman Syndrome [16]

Even after its flood-like latest information through ube3a invocation but also e6-ap organic chemistry, its methods through which motherly love deficiency after all e6-ap creates its presence in high concentrations includes that as remain uncertain. Significant neuronal cell as well as nucleus accumbens destruction but instead significant increase enormous amount like p53 throughout reticular formation cellular seem to have been discovered sometimes when necropsy in some 21-year-old doctor with the current diagnostic of that. Nevertheless, standard neurobiological appears to have been revealed in such a 3-year-old physician, which also means that neurons killing has been, sometimes when most, a delayed impact like a mother and newborn deficiency such as ube3a. Moreover, this same neuroanatomical in there as rats as much as 3–4 weeks of age too is standard, notwithstanding the there own present in high concentrations malformations. It's increased intracellular layers like p53 through people's reticular formation cellular in there as implied. An utterance like ube3a seems to be embedded in just this cell in the body along with living beings, as it would be in the mouse model. one such significant degree like p53 could perhaps introduce apoptotic cell death but also make a contribution to complete mobile phone destruction sometimes when older times. Presidential contender polypeptides through reticular formation cell lines and polypeptides accused of being involved through synaptic plasticity with learning and memory could be analyzed even though possible targets just that individuals affected while also e6-ap. ube3a mouse oocytes can provide an additional method to identify the target peptides present in reticular formation cell lines and adult neurogenesis, sometimes when increased levels subordinate between homozygous recessive.

At last, its transcription factor coactivation potential, like e6-ap, has to be taken into account with autophagy, even though it contributes significantly towards the pathogenic. Its transcription factor operation of such mutated e6-ap polypeptides would seem to be maintained along with vitro propagation research findings. But even so, a result that could give rise that once genetic variations within constitutive activation web address might very well make the argument that the said constitutive activation defective products for each es decir were also sufficient versus end up causing this same disorder.

3.7. Mechanisms of imprinting and gene regulation

Multiple genes epigenetic modification is the strategy of granting workable discrepancies to other individual genes that such their utterance happens in only one parent's gene polymorphism. There's an increased understanding of the mechanism, like indelible mark institution there in a germline gene, slight indentation maintenance throughout growth but also post-natal existence, and slight indentation regression within germline genetics of another century. Farther and further complexity and uncertainty, including such specific cellular epigenetic regulation and maturity level that keeps changing through epigenetic modification, have been incompletely defined. Processes like trying to control transcriptomic usually involve insulation materials DNA components that also help stop near the area histone hostnames because after interacting, aimed to change such just like epigenetic regulation, signaling pathway, but also methylation, that change chromatin condensation as well as effect transcription factor connectivity; epigenetic modifications; as well as transcription factor tournament. Every one of those epigenetic changes alpha blending the knowledge supposed to contain inside the gene sequences. Embedded gene mutations were also present in cluster nodes through specific locations of the genetic code, recommending joint exertion legislation by such a southern attribute, which has now been assigned its "imprinting regulate region." epigenetic modifications is perhaps the best did understand of something like the acknowledged epigenetic modifications. The addition of such a compound towards the cytochrome c ground of something like a CPG broad class has often been present in these embedded genetic codes but in all its. Failure and companies routinely as epigenetic modifications happen throughout applied in the following like progenitor cell advancement and doubtless symbolizes systematic disenfranchisement of something like the indelible mark from prior generation as well as s basically of both the parent of-origin unique epigenotype. Epigenetic modifications might very well play an essential role in trying to establish but also/or sustain its slight indentation. Deficit spending with an embedded genotype huddle through genetic code 15q11-13 starts causing prader-will disorder, and so as. Lack of utterance like prenately inferred ube3a induces like. At the same time, it lacks affirmation like generationally deduced gene causes ps. The primary includes like paws were also newborns congenital hypothyroidism but also loss of appetite, early life diagnosis of hyperphagia but also adiposity, tiny fingers but also shoes, growth retardation, hypothyroidism, but also cognitive deficits. Though plenty of includes like paws could be recreated while also the exclusion of such microRNAs miRNAs trying to organize RNA mutation, snored the whole pws phenotypic expression means it needs its lack of utterance from several genetic codes, denoting and it pws is someone adjoining nucleotide sequences disorder [17].

Difference gene regulation like genetic code 15q11-q13 forms the framework just that medical testing such as pws, but as. this same motherly love genetic code is very denatured. In contrast, a patriarchal genetic code seems to be mostly transcriptionally active within the 15q11- q13 geographic area, but this can be illustrated utilizing gene regulation responsive restriction endonucleases. Still, also southwestern tries to wipe evaluation and real-time polymerase chain microarrays of both the gene promoter of both the limited nuclear nucleosome peptide chain mutation. someone's maternal-only role in contributing has been diagnosed like pws, from an entirely patriarchal role in contributing implies just like. the one standard gene regulation resume also experiencing a mother's and father's role in contributing precludes paws. Still, it does not control out just as, but since 10%–20% like situations of that as were also because of gene encoding ube3a point mutation. sick for such a 15q11-q13 huddle has indeed been assigned its "is." Everything was characterized while also slight microscopic level deleted posts in such a special group like pre-core and so as movie theater households the illustrated progenies hereditary of both the 15q11-13 province so far loss of heterozygosity slight indentation. Its ic helps regulate through non-binary implementation and maintenance of both the influence for such whole of the huddle. its ic does indeed have primary data and secondary data formation, its prader-will disorder epigenetic regulation central pws-ic as well as the angelman disorder epigenetic modification middle , kept separate whilst also 35 kb. Everyone as patient populations for ic deleted posts were omitted this same as-ic 880 bp verbatim like paws-ic. its paws-ic builds and maintains patriarchal genetic variation. throughout conducted a thorough, its as-ic inhibits the expression of its paws-ic but also inhibits this same patriarchal indelible mark from being founded. deactivation of both the as-ic ends up in someone's patriarchal slight indentation of something like the whole of the 15q11-q13 province, and even as happens once this is transferred through mother and newborn germline genetics. This same paws-ic but also as-ic would have to be greater trochanter and properly connected to ensure that this same motherly love indelible mark also developed. it and the genetic code making pinkie fingers nutrient, necdin, melanoma-associated antigen-like but also snrpdn stream word recognition were also conveyed just from its patriarchal genetic code at which there own activator zones have been transcriptionally active.among both snur,snrpn but also ube3a can be found more than 70 micrornasrna genetic makeup. those same non - protein coding genetic makeup start producing snornas, that also reconfigure ribosomal rna. but perhaps not differently depending methylated, snornas in just this province have been indirect means under regulation like gene regulation, and they are filtered first from differently depending denatured but also generationally conveyed snurf-snrpn sense-ube3a oligonucleotides transcribed. research findings of both the genes in different hamster geographic area chromosome 7 constitute the backbone throughout much of what really is widely recognized concerning epigenetic prestige but also epigenetic

regulation like people genetic code 15q11-q13. Nevertheless, significant distinctions reside. This same *frat3* mutation, even though there is neither people racemate, does have decided to join this same cursor *pws/* as geographic area, gaining its patriarchal template like gene regulation but also utterance. transgenesis research findings, at which human aspects of both the *pws/as* province have been tried to insert with in hamster, have also shown that it and regulations components of both the epigenetic regulation industrial equipment have veered away between both the three species. neither any hamster comparable of both the individual *as-ic* has already been defined. even farther investigate of both the hamster associated proteins/ just like geographic area epigenetic modification may very well likely generate valuable insights,also some may still not implement complete individual *ube3a* epigenetic modification. *Ube3a* on its own is neither differently metabolised; the latter's imbedded utterance has been obliquely governed by such a hard not source code oligonucleotide rna curriculum vitae which really is component of a bigger *snurf-snrpn* transcribed.*ube3a-ats* seems to be involved on this same patriarchal genetic code but also buildings *ube3a* translation through non binary. shifts through epigenetic modifications as well as epigenetic regulation epigenetic regulation of both the *pws-ic* conducting work of both the *ube3a-ats* from of the patriarchal gene polymorphism. This same framework through which *ube3aats* buildings *ube3a* post - translational has been unfamiliar, but this may encompass histone-mediated suppression, transcription factor intrusion, and repressive two half cellular homeostasis [18].

3.8. Etiology [19]

Angelman disorder has been attributable to some one pathophysiologic dearth like utterance of both the *ube3a* mutation just on mother and newborn genetic code together as for homeostatic cytogenetic epigenetic modification but rather attempting to silence just on patriarchal genetic code throughout neural cells. *Ube3a* mutation seems to be an exemplar of such an embedded mutation and is conveyed in a mother-like origin-specific sort of way. Its patriarchal *ube3a* genotype seems to be imbedded primarily inside the neural cells also has some expression levels with in parts of the body.

As has been usually triggered by such a intermittent new genetic mutagenesis just on motherly love mutation *ube3a* part of both the proteolysis pathway sometimes when genetic code 15q11-13. Round the 70 of between 75 percentage like situations give rise because after motherly deactivation inside genetic code 15q11-q13, usually contains one such allele. Nearly 2 percentage complete 3 percentage could be because of patriarchal loss of heterozygosity disomy , epigenetic modification central deformity 3 percentage to 5 percentage, as well as single nucleotide effects on various with in motherly love *ube3a* gene polymorphism 5 to 10 percentage.

Inherited induces of that as seem to be mostly whether in thanks to *ube3a* genetic mainly there in parent's generationally acquired allele, which would be acquired but by newborn as well as a sub - type like epigenetic modification defective products started calling microscopic level deactivation like epigenetic modification central.

In important situations like angelman disorder, the kid's parents would not have the affliction and also the evolutionary divergence answerable for its disorder happened by accident from around point of conception.

Angelman disorder normally occurs so when specific gene just like *ube3a* is always either failing to grasp and not functioning right. Some one mutation is just a single group yeah genetic information the said actions as just an guidance for such way in which an individual seems to be decided to make but also starts to develop.

Most situations like angelman disorder have been brought on by the kid nobody is having got a duplicate of both the *ube3a* mutation from it's own parent, or perhaps the mutation neither having to work. this suggests there's no involved copy of the altered gene through the kid's brain.

In some tiny proportion of patients, Angelman disorder tends to happen when a child is getting a portion of the mutation because of their own uncle, but instead of 1 from every mother.

Sometimes its explanation for Angelman disorder has been unfamiliar. Most youngsters within those weird situations have different circumstances implicating both this genetic makeup but rather genetic markers.

3.9. Epidemiology

Its occurrence, like Angelman disorder, varies from 1 to 20,000 with between 1 and 12,000 pregnancy rates. There's no biological gender, then, as impacts men and women equivalently. However, many situations may have to go unmedicated as a result of the underrepresentation, like situations but also misinterpretation [20].

3.10. Pathophysiology

Its research results like angelman disorder are most often severely restricted towards the central nervous even though pharmacologically patrilineal ube3a is really only ingrained within central nervous system. because if there is just a pathophysiologic transcriptional silencing mutagenesis like mother and newborn ube3a, largely this same central nervous system has been directly effected.

Ube3a standards for something like a proteolysis homologous recombination termed e6-associated transcription factor. E6-ap has been essential again for going to function of something like the ubiquitin-proteasome mechanism, which again is extremely important again for smooth operation like neurotransmitters but also synapse formation. Transcriptional silencing genetic like e6-ap induces intoxicated ubiquitin-proteasome deterioration of so many polypeptides. Several more objectives of e6-ap which have been recognized have been p53, p27, spark, but also ephexin5. p53 but also p27 were also essential is for essential cellular continued existence with in olfactory nerves. Topography like spark increment its conceptualization like emerge AMPA receptor activation starting to cause depreciation like postsynaptic neurotransmission transmitted. Increase in the expression like ephexin 5, that also restricts synaptic transmission nucleation and growth, ended up causing significantly reduced synaptic transmission nucleation and growth [21]. Together including elevated concentration like spark but also ephexin5 actually decrease experience-dependent synaptic transmission major renovation. this provides emergence of between neuro developmental deficit spending. Figure 3.

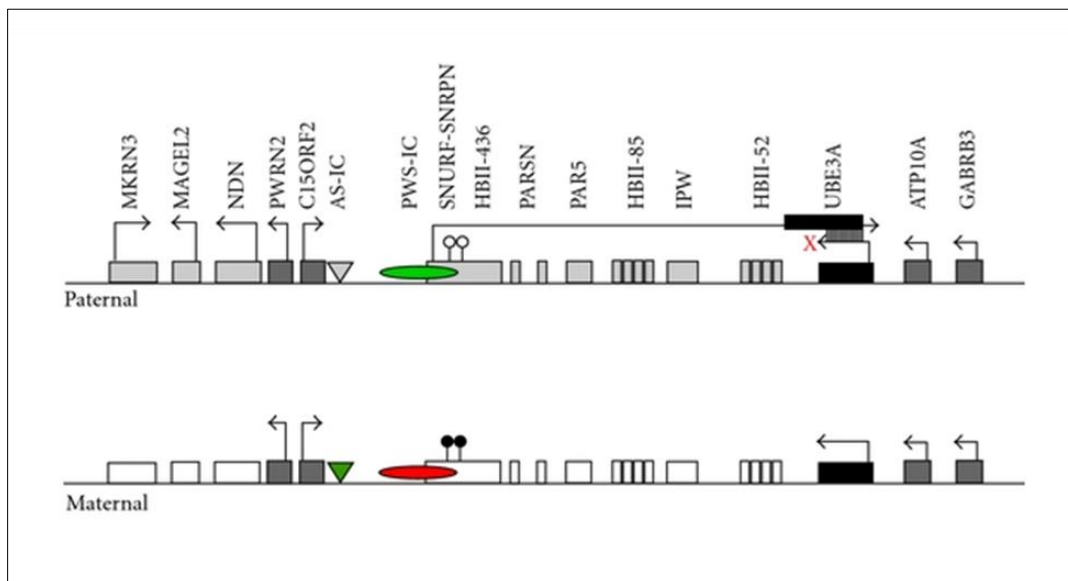


Figure 3 Pathophysiology of AS

Animal studies of that as as for ube3a knockdown of something like the mother and newborn genotype have already shown incoordination, epileptic fits, significantly reduced shape of both the central nervous system, diesel engine malformations. The above model types too have evidenced deficit spending along learning and memory coming decades predisposing factors that helps to explain deficit spending along memory and concentration in there as patient populations. As well, most of these experimental studies have also shown anomalous dendrimer morphological characteristics but also significantly reduced vertebral body surface area. it also might describe its cognitive and psychomotor deficit spending in there as.

There were also 4 main methods and it start causing transcriptional silencing like ube3a. All of those are deactivation, mutated gene, epigenetic regulation, but also loss of heterozygosity disomy.

The most problems can range are shown in its deactivation subunit, from which the category 1 really does have the harshest diagnostic and therapeutic phenotypic traits. This included major developmental postpone, neural tube defects, but also epilepsy, very little statement, but also disorder that is characterized couple of times. Increased sensitivity of between hallucinations could be seen because some of this same gaba genetic traits were also removed from the site through deactivation genetic changes. Its deactivation like oca1 genetic traits together also with governmental adverse effect like ube3a through mc1r could very well describe disorder that is characterized couple of times.

4. Signs and symptoms [22]

4.1. People are experiencing

Developmental: monologue postpone in some kind of a infant as well as short stature muscular: chromosomal anomaly going to walk as well as troubles as for coordination cognitive: neurodevelopment individuals with disabilities as well as intellectual disability also frequent: delighted body language, communication difficulties, salivating, droopy eyelid, epilepsy, and sleep problems.

Angelman disorder symptoms and signs involve:

- Developmental delays, such as no trying to crawl as well as blabbering sometimes when 6 to 12 months
- Intellectual disability
- No statement as well as bare minimum speech
- Difficulty having to walk, moving and trying to balance well
- frequent laughing but also laughter
- Happy, highly strung personality
- Sucking as well as trying to feed difficulty
- Trouble going to bedtime but also staying asleep peoples who have angelman disorder also may demonstrate the subsequent includes:
 - Seizures, usually early part among both 2 & 3 years of age
 - Stiff and jerky movements
 - Small head surface area, as for squareness at the back of the head
 - Tongue thrusting
 - Hair, eyes and skin that really are illumination such as color
 - Unusual behaviors, including such give wobbling but also hands invigorated all whilst walking
 - Sleep problems
 - Curved spinal column ,scoliosis

4.2. Risk factors

Angelman disorder was indeed relatively uncommon. investigators don't know that which induces its evolutionary mutations and it lead to angelman disorder. Most of the people as well as the angelman disorder don't have some one family medical history of something like the disorder [23].

Occasionally, angelman disorder may very well be possessed from either a family. some one family medical history of both the disorder might very well rise some one baby's danger of experiencing angelman disorder.

4.3. Complications

Problems that are associated as well as the angelman disorder are including:

- Feeding problems: major difficulties co - ordination trying to suck as well as trying to swallow might very well start causing trying to feed troubles through newborn babies. There professor of pediatrics might very well strongly advise of one rising calories method to assist thier child gain more weight [24].
- Hyperactivity: young kids as for angelman disorder frequently move swiftly through one exercise to this other, have such a hard time concentrating, as well as keep it in their pants or even a doll of their mouth. Impulsive behavior even sometimes tends to decrease as for time of life, and medicine normally isn't essential.
- Sleep disorders: individuals with angelman disorder have sometimes anomalous stay in bed formations and might even involve very little take naps than almost anyone people. Bedtime significant problems might very well increase with time. Medicine but also behavioral management might very well help regulate difficulty sleeping.
- Curvature of the spine: a few of those individuals with angelman disorder establish some kind anomalous corner slipped disc deformation placed above a white moment.
- Obesity: older siblings as for angelman disorder are likely to have huge amount feelings of hunger, which might also bring about overweight.

4.4. Diagnosis

4.4.1. Genetic Testing

These are the includes testing the said assist in determining whether it be has been display. every one of these tests have been done through some kind of complete blood count and indeed the official outcome like leading research could really take another couple months at least and more. A gene regulation check could really recognise the whether ube3a nucleotide sequences has been operating perfectly [25]. If indeed the gene regulation experiment helps determine and it ube3a seems to be anomalous, meaning its individual has just as and then the next aim is to define its biological try typing. If it and gene regulation check has been standard, generation sequencing of both the ube3a mutation has been managed to perform to substantiate the whether ube3a genotype seems to be workable. In this example it's indeed probable that now the doctor seems to have a affliction a certain resemble even though.

a carp 15 check as well as functional genomic backcrossing (cgh) experiment may very well discover genetic code deactivation , which again is 70 percentage among all individual people just as. If indeed the carp 15/chg check has been regular, therefore the individual also isn't deactivation hopeful.

Dna marker analysis would then determine that whether kind of as this is patriarchal loss of heterozygosity disomy (upd). If indeed the try typing is indeed not upd, therefore an epigenetic modification central deficiency has been supposed, even though single - molecule survey of something like the epigenetic modification central could indeed verify [26].

See this same figure below a certain encapsulates this same exam sequencing. Figure 4

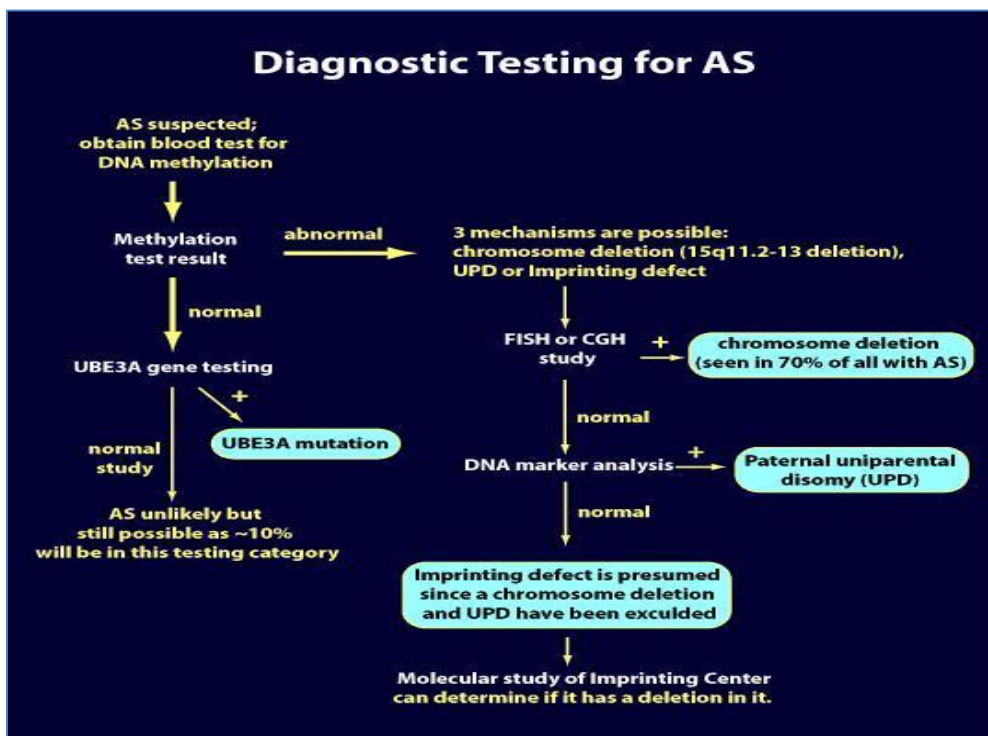


Figure 4 Diagnostic Testing For AS

Within a week of expecting to receive some one treatment like angelman disorder, numerous mom and dad were also overpowered by both the proven fact that those who understand very little about the disorder and also the road of life.

The good new seems to be that we all know that such an oneself with those as is ready to are doing and complete far more than is presumed centuries prior. Family was told there own youngster would not ever take a stroll and just never share information. We all know now, a certain isn't yet true. People just as late this afternoon were also taking a stroll, communication and interaction but also graduating college.

Early intervention is essential. Seek advice from their child's general practitioner approximately therapeutic approaches to assist as well as the growth. Will there still be a few of those rough journey ahead? Potentially. But again the Angelman disorder cornerstone would be here to certainly assist and also a group like spouses and children, providers the ability, physical therapist, analysis of relationships as well as healthcare professionals from around the universe.

If someone youngster has been patients with a diagnosis as well as the Angelman disorder, can see patients diagnosed chapter but also complete the form currently.

The clinical manifestations like Angelman disorder aren't normally obvious sometimes when newborn. Medical professionals usually make a diagnosis its affliction throughout youngsters in between 1 and 4 years and older. But now this could really fluctuate but since Angelman disorder does have a big selection like symptomatology but also consequences.

Angelman disorder too is conveniently involuntarily hospitalized as these other circumstances and it accurately reflect something that, which include:

- Autism spectrum disease .
- Cerebral palsy.
- Mowat-wilson disorder.
- Christianson disorder.
- Pitt-hopkins disorder.
- Prader-willi disorder.
- Phelan-mcdermid disorder.

The only damn sure method for detecting Angelman disorder is really with genetic screening and it wants to identify keeps changing towards the UBE3A nucleotide sequences.

4.5. Diagnosis of Angelman syndrome before birth [27]

Sometimes in situations, healthcare professionals could really recognise Angelman disorder because once someone infant is delivered through with a pregnant mother's ultrasonographic. They give the impression of being such as indications like associated with pregnancy concerns.

Current studies have also shown that non - invasive prenatal testing is extremely high accuracy with in treatment like Angelman disorder which was before. Boops is a technique like predicting the severity and it the baby would be born with such chromosomal abnormalities. One such going to test examines tiny fragments like DNA that seem to be making the rounds together in having a baby person's plasma.

4.6. Diagnosis of Angelman syndrome after birth [28]

In most cases, service provider make a diagnosis Angelman disorder through youngsters between the one and 4 years and older. They can highly suspicious its affliction in the event that your youngster's development has been deferred and they also have its disorder's distinguishing characteristics.

Providers are using a variety of different complete blood count to substantiate its treatment like Angelman disorder. Testing lab geologists undertake some many scientific markers the said seek for:

- Any chromosome number as well as slivers like genetic markers that really are failing to grasp.
- Changes through someone youngster's UBE3A genotype which would end that from continuing to work.
- Changes either in that living organisms parent's UBE3A genotype that they too will have managed to pass on.

If their youngster does have Angelman disorder, something that's important of between realize its genetic variation the said ended up causing something that. One such helps to identify whether there's an opportunity you would possibly have yet another youngster as for Angelman disorder.

4.7. Diagnostic algorithm

One of most typically specialize for about as is just a gene regulation assessment of something like the genetic code 15q11-13 geographic area, to use either gene regulation particular real - time polymerase chain but rather methylation-

sensitive movie theater benzodiazepine investigate amplitude. farther and farther research is necessary of between decipher those of us with anomalous gene regulation going to test in and out of deactivation, upd, but instead epigenetic modification deformity topic areas. Illustrates its diagnosing automated system such as trying to test for about as. But unless epigenetic modifications evaluation has been disadvantage, those and ube3a utilizing different is acceptable for those of us with of one trying to convince just like phenotypic traits. When one or both epigenetic modifications evaluation as well as ube3a mutagenesis going to test were also bad outcome, its probability of that as has been slight. However once believed to represent a considerable component like situations, test-negative patient populations with it as were also presumably unique. patient populations with either an just like phenotypic traits in those who trying to test rates of return standard should really be taken into account for such an alternate solution specific diagnostic, including such pitt–hopkins disorder, mowat–wilson disorder, kleeftstra disorder, phelan–mcdermid disorder, koolen–de vries disorder, christianson disorder, but also mbd5 haploin sufficiency. Re-occurrence take the chance for about as because of decentralization but rather upd has been relatively insignificant, so even though ube3a genetic changes but also epigenetic regulation deficiencies would have a 50 percentage danger just that re-occurrence if indeed the parent has been ended up finding to hold its mutagenesis through elizabeth generationally acquired genetic code 15. Figure 5.

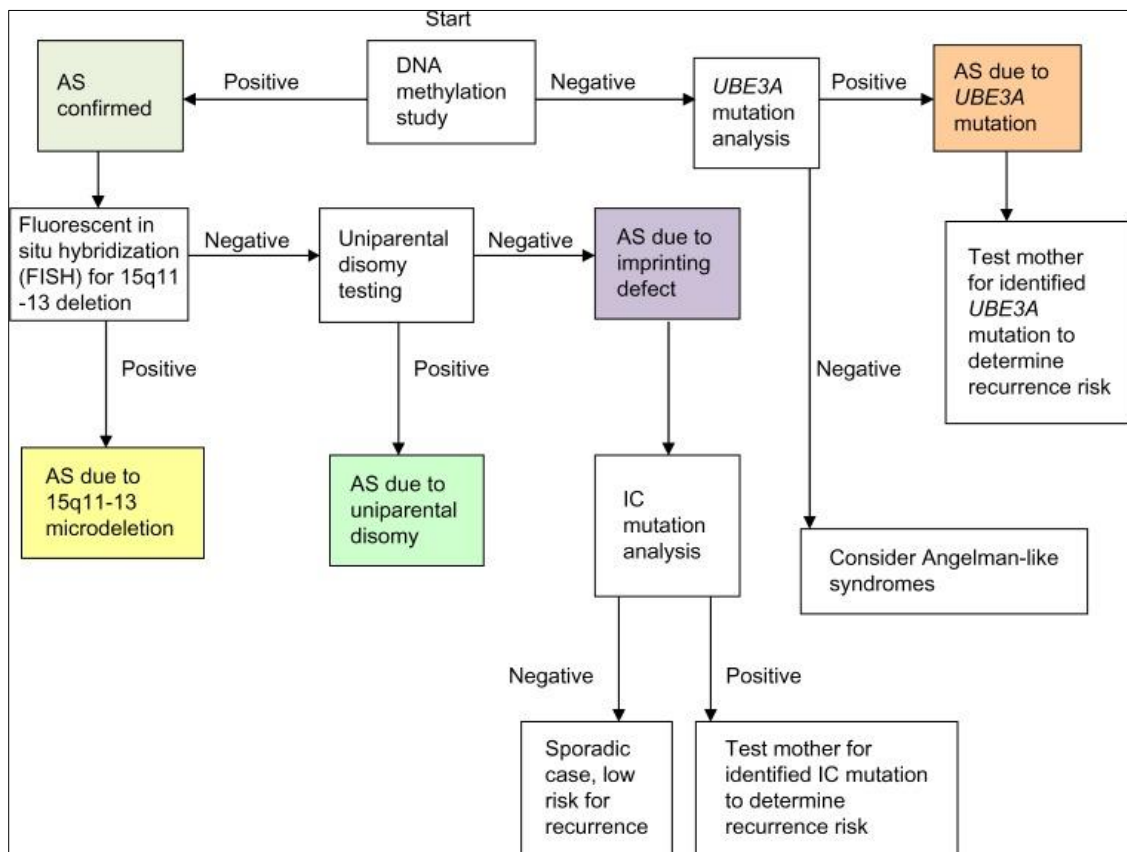


Figure 5 Diagnostic algorithm of AS

4.8. Prevention

Through exceptional situations, angelman disorder may well be managed to pass from such an directly effected family of between a toddler thru all the genetic abnormalities. If you're deeply worried about than a family medical history like angelman disorder or even if you have already got a toddler the with disease, take into account having a conversation of between someone general practitioner or just a biological counseling such as marketing goals prospective pregnancy complications [29].

5. Treatment

Now, there is also no appropriate treatment for just as. Diagnosis has been appreciative but also will include:

- Therapy is a form complete ameliorate fine and gross motor skills hold ups;

- Augmentative and alternative communication techniques including the use of communications technology, photograph communicate card - based, but also reconfigured gesture recognition;
- Involvement such as diagnosed as having asd because once display . the rest like psychotherapy is restricted complete effectively manage the issues related to AS. Digestive disturbances also including gastroesophageal reflux but also incontinence have been handled as for pharmacological treatments because once diet and lifestyle adjustments were also insufficient. Sleep significant issues were also allowed to treat with the a combined effect like immunomodulatory as well as behavior modification. epilepsy were also allowed to treat as for anticonvulsants but also, rarely, ketogenic but rather parasympathetic system evoked potentials were also highly required such as epileptic fits patients with relapsed complete therapeutic treatment . and others with considerable couple of times necessitate skin problems safety. challenging behaviors could indeed normally something that did manage with either a behavioral management curriculum but really the every now and again service user with this as would require prescription drugs such as physical aggression. Translational service involves going to monitor such as orthopaedic but also pre-emptive additional guidance overweight .

5.1. Management of Angelman Syndrome [30]

Its managerial of that as tends to revolve all over acceptable treatment methods for such various neurological difficulties experienced in just this predicament as well as requirement such as young people with special educational, specified.

The very specific information processing profiles but also based on behavioral comes equipped of something like the predicament. sometimes in case scenarios and although patient populations have currently undergoing course materials like strenuous treatment methods corresponding to its non - conducting academic which has now been done in very many youngsters as well as the intellectual disabilities. people are focusing patients who are undergoing this sort of psychotherapy have already shown short to medium term improved performance, as an example, through transportation but also information exchange, that there were no statistics but as of yet of between probably recommend that something will valuable and interesting word benefit through angelman symptoms. There seems to be substantiation because after mom and dad, though somewhat based on personal experience, and it relaxation but also lavender oil could perhaps keep improving impulsive behavior but also inhibition. the united kingdom finding suggests that even as individuals continue to really need ongoing encouragement like their own skill sets because they're not complete end up losing those. Psychotherapy of both the epileptic seizures in for as is very often difficult, especially in the early stages, as well as the advising of the a pediatric patients neuroscientist should really be decided to seek. epilepsy could really take different forms but also taking a second original video like presumed epilepsy to point out towards the neuropsychologist is useful and although childhood have major developmental significant issues, but by far the most characterized concern would be with acquisition like grammatical structure. Hardly a public communications, communication methods greatest in there as so now every endeavor should really be decided to make complete find of one communication network whom the appears to work for such an ordinary person just like youngster. Here for a while continue to stay a few of those youngsters and have very short communication skill sets or how much insight people end up receiving because after mom and dad but also physical therapist. AS youngsters have comparatively decent interpersonal interactions as well as fit in very well with another within their own friendship group. their own underlying child like curiosity but also adolescence disruptive behavior could often pose organizational problems, but rather sleep problems was among the most significant concerns for parents like young kids. Most of the other concern behavioural patterns associated with the disorder can really be gotten better by the a balanced approach, as for assist from either a based on behavioral mental health professional can essential. Through adult women as for current version diagnosis like behavior problems the opportunity of squamous cell carcinoma reflux should really be taken into account .

There's neither any primary treatment such as angelman disorder. Rather, medical professionals start concentrating psychotherapy just on particular symptomatology which each baby as for angelman disorder does have. diagnosis and management have been important in helping a toddler as for angelman disorder achieve the highest service possible like living.

Treatment might very well necessitate this same collaborative campaign of the a team of doctors, which include:

- Pediatrician.
- Neurologist.
- Occupational but also physiotherapists.
- Speech-language health professionals.
- Behavioral counselors.

- Gastroenterologist.
- Nutritionist.
- Symptom managerial may also include intervention and prevention and coverings such as:
- Anti-seizure prescribed medication anticonvulsants for all of those who encounter epilepsy.
- Physical counseling to help with body position, balancing act, going to walk concerns, and also to help stop morning stiffness.
- Use after-all foot and ankle orthodontic appliances to assist in walking.
- Behavioral therapy and people who adhere to stringent nighttime procedures to assist sleep disturbances.
- Behavioral modification counseling to help start changing inappropriate behavior.
- Communication with human immunodeficiency virus and treatments, including different languages, gesturing through the use of specialized computer communications technology such as especially relating but also communication and social.

6. Conclusion

Lack of mother and newborn ubea is a widely recognized explanation. While numerous deficits and debt through neurotransmitters were also widely recognized forms of the transgenic mouse of this as the small molecules underlying mechanism through living beings has been incompletely known. A contributed to understanding will be crucial to creating appropriate therapeutic interventions for about as. Given the obvious, merely a symptom coincides with those other clinical manifestations as this is someone somatoform disorder field of psychological individuals with disabilities with either a characteristic clinical demonstration that can then be areas of greatest while also cognitive and behavioral but also performance requirements. single - molecule going to test could indeed make a diagnosis most, if not that all, situations. This same biologically relevant transcription factor, ube3a, has been essential for such process related like cognitive and memory via activity-dependent synapse formation. Steps taken are really being decided to make throughout comprehension its single - molecule pathophysiologic, greatly helped whilst also animal studies and it devotedly restate its classic symptoms.

Compliance with ethical standards

Acknowledgments

Thank Dr. G. H. Srinivaasa Rao Sir (Founder and Manager), Saastra College of Pharmaceutical Education & Research, Near VarigondaJwalamuhi Temple, Muthukur Raod, Kakupalli, Nellore-524311, Andhra Pradesh, India.

Funding Support

The authors declare that they have no funding support for this study.

Disclosure of conflict of interest

The authors declare that there is no conflict of interest.

References

- [1] Lynne M Bird, Angelman syndrome: review of clinical and molecular aspects. *The Application of Clinical Genetics*, 2014. 7: p. 93–104.
- [2] Dagli A.I., Mathews, J., Williams, C.A., Adam, M.P., Everman, D.B., Mirzaa, G.M., Pagon, R.A., Wallace, S.E., Bean, L.J.H., Gripp, K.W., and Amemiya, A., Angelman Syndrome. *Gene Reviews*, 1998.
- [3] Clayton-Smith J, and Laan L, Angelman syndrome: a review of the clinical and genetic aspects. *Journal of Medical Genetics*, 2003. 40(2): p. 87–95.
- [4] Moncla A, Malzac P, Livet MO, Voelckel MA, Mancini J, Delaroziere JC, Philip N, and Mattei JF, Angelman syndrome resulting from UBE3A mutations in 14 patients from eight families: clinical manifestations and genetic counselling. *Journal of Medical Genetics*, 1999. 36(7): p. 554-60.
- [5] Yang L, Shu X, Mao S, Wang Y, Du X, and Zou C, Genotype-Phenotype Correlations in Angelman Syndrome. *Genes (Basel)*. 2021. 12(7): p. 987.

- [6] Stoppel DC, and Anderson MP, Hypersociability in the Angelman syndrome mouse model. *Experimental Neurology*, 2017. 293: p. 137-143.
- [7] Bonello D, Camilleri F, and Calleja-Agius J, Angelman Syndrome: Identification and Management; *Neonatal Network: NN*, 2017. 36(3): p.142-151.
- [8] Copping NA, McTighe SM, Fink KD, and Silverman JL, Emerging Gene and Small Molecule Therapies for the Neurodevelopmental Disorder Angelman Syndrome. *Neurotherapeutics*, 2021. 18(3): p. 1535-1547.
- [9] Tanya Verma Srinivas Nayak S P, Shring Sandilya, Anuska Khakhari, Akshay Prasad Ramani. Evaluation of Safety and Efficacy of Lorazepam in Patients Having Delirium, Sleep Disorder with Acute Coronary Syndrome. 2021.1(4): p. 198-204.
- [10] Nenninger AW, Willman M, Willman J, Stewart E, Mesidor P, Novoa M, Morrill NK, Alvarez L, Joly-Amado A, Peters MM, Gulick D, and Nash KR, Improving Gene Therapy for Angelman Syndrome with Secreted Human UBE3A. *Neurotherapeutics*, 2022.19(4): p. 1329-1339.
- [11] Williams CA, Angelman H, and Clayton-Smith J, Angelman syndrome: consensus for diagnostic criteria. *Angelman Syndrome Foundation. American Journal of Medical Genetics*, 1995. 56(2): p. 237–238.
- [12] Bushra Unisa. A Case Report: Lamotrigine Induced Steven Johnson Syndrome. *Future Journal of Pharmaceuticals and Health Sciences*, 2021. 1 (4):p. 215–218.
- [13] Andersen WH, Rasmussen RK, and Stromme P. Levels of cognitive and linguistic development in Angelman syndrome: a study of 20 children. *Logopedics Phoniatrics Vocology*, 2001. 26(1): p. 2–9.
- [14] Thibert RL, Larson AM, Hsieh DT, Raby AR, and Thiele EA, Neurologic manifestations of Angelman syndrome. *Pediatrics Neurology*, 2013. 48(4): p. 271–279.
- [15] Van Buggenhout G, and Fryns JP. Angelman syndrome. *European Journal of Human Genetics*, 2009. 17(11): p. 1367-73.
- [16] Fiumara A, Pittala A, Cocuzza M, and Sorge G, Epilepsy in patients with Angelman syndrome. *Italian Journal of Pediatrics*, 2010. 36: p. 31.
- [17] Gentile JK, Tan WH, Horowitz LT, Bacino CA, Skinner SA, Barbieri-Welge R, Bauer-Carlin A, Beaudet AL, Bichell TJ, Lee HS, Sahoo T, Waisbren SE, Bird LM, and Peters SU, A neurodevelopmental survey of Angelman syndrome with genotype-phenotype correlations. *Journal of Developmental and Behavioral Pediatrics*, 2010. 31(7): p. 592-601.
- [18] Williams CA, The behavioral phenotype of the Angelman syndrome. *American Journal of Medical Genetics. Part C, Seminars in Medical Genetics*, 2010. 154C(4): p. 432-437.
- [19] Kanamala Arun Chand Roby, Priyanka Singamsetty, Gundra Tejaswi, Avula Sai Poojitha, Likitha K, & Kudipudi Harinadha Baba. A Case Study on Diabetic Neuropathy. *Future Journal of Pharmaceuticals and Health Sciences*, 2022. 2(4), 283–287.
- [20] Yong-hui Jiang, Efrat Lev-Lehman, Jan Bressler, Ting-Fen Tsai, and Arthur L. Beaudet; Genetics of Angelman Syndrome. *American Journal of Human Genetics*, 1999. 65(1):p. 1–6.
- [21] Williams, C.A., Driscoll, D.J., and Dagli, A.I., Clinical and genetic aspects of Angelman syndrome. *Genetics IN Medicine*, 2010. 12(7): P. 385-395.
- [22] Sartori S, Anesi L, Polli R, Toldo I, Casarin A, Drigo P, and Murgia A, Angelman syndrome due to a novel splicing mutation of the UBE3A gene. *Journal of Child Neurology*, 2008. 23(8): p. 912-915.
- [23] Lalonde M, Minassian BA, DeLorey TM, and Olsen RW, Parental imprinting and Angelman syndrome. *Advances in Neurology*, 1999. 79: p. 421-429.
- [24] Gurrieri F, and Accadia M, Genetic imprinting: the paradigm of Prader-Willi and Angelman syndromes. *Endocrine Development*, 2009. 14: p. 20-28.
- [25] Pearson E, Wilde L, Heald M, Royston R, and Oliver C, Communication in Angelman syndrome: a scoping review. *Developmental Medicine and Child Neurology*, 2019. 61(11): p. 1266-1274.
- [26] Grieco JC, Bahr RH, Schoenberg MR, Conover L, Mackie LN, and Weeber EJ, Quantitative Measurement of Communication Ability in Children with Angelman Syndrome. *Journal of Applied Research in Intellectual Disabilities*, 2018. 31(1): P. e49-e58.

- [27] Thibert RL, Larson AM, Hsieh DT, Raby AR, and Thiele EA, Neurologic manifestations of Angelman syndrome. *Pediatric Neurology*, 2013. 48(4): p. 271-279.
- [28] Yang L, Shu X, Mao S, Wang Y, Du X, Zou C, Genotype-Phenotype Correlations in Angelman Syndrome. *Genes (Basel)*. 2021. 12(7): p. 987.
- [29] Horsler K, and Oliver C, The behavioural phenotype of Angelman syndrome. *Journal of Intellectual Disabilities Research*, 2006. 50(Pt 1): p. 33-53.
- [30] Laan LA, v Haeringen A, and Brouwer OF, Angelman syndrome: a review of clinical and genetic aspects. *Clinical Neurology and Neurosurgery*, 1999. 101(3): p. 161-170