The Report Committee for Jennifer Le Ho
Certifies that this is the approved version of the following report:

Resource Guide for Speech-Language Pathologist Practitioners: Side Effects of Seizure Medications

APPROVED BY
SUPERVISING COMMITTEE:

Supervisor:

Barbara L. Davis

Jessica H. Franco

Resource Guide for Speech-Language Practitioners: Side Effects of Seizure Medications

by

Jennifer Le Ho, B.S.C.S.D.

Report

Presented to the Faculty of the Graduate School of

The University of Texas at Austin

in Partial Fulfillment

of the Requirements

for the Degree of

Master of Arts

The University of Texas at Austin

May 2014

Dedication

To my parents, who have always been supportive of my education and career choice. To my sister, Linda, who has always encouraged me to pursue my dreams and aspirations. To Doan, thank you for your continuous support and guidance. Last but not least, to the wonderful clients that I had the pleasure of working with.

Acknowledgements

I would like to thank Dr. Barbara L. Davis and Dr. Jessica H. Franco for their guidance, support, assistance and critique during the development of this master's project. Thank you for sharing all of your wonderful knowledge and experiences.

Abstract

Resource Guide for Speech-Language Practitioners: Side Effects of Seizure Medications

Jennifer Le Ho, M.A.

The University of Texas at Austin, 2014

Supervisor: Barbara L. Davis

Side effects of seizure medications in individuals with intellectual disabilities (ID) may affect speech and language development for this population. Research information about these effects may be useful for speech-language pathologist practitioners, since they will most likely work in environments that involve assessing and treating individuals with ID. In this meta-analysis, a total of 19 articles were reviewed to examine the side effects of AEDs in individuals with ID and seizure disorders. Side effects from AEDs were found; however, research regarding how AEDs and seizure disorders affected speech and language development was not available. Based on the findings, participants on AEDs regimens experienced a variety of side effects that included behavioral side effects, adverse cognitive side effects, and non-behavioral side effects. However, information regarding AEDs side effects and speech and language development was nonexistent. Based on the findings, further research in this is much needed for practicing speech-language pathologists in this topic.

Table of Contents

List of Tables

INTRODUCTION

Side effects of seizure medications in individuals with intellectual disabilities (ID) may affect speech and language development for this population. Research information about these effects may be useful for speech-language pathologist practitioners, since they will most likely work in environments that involve assessing and treating individuals with ID. For this review, individuals with ID were selected because this population has a higher prevalence of seizure disorders (Richardson et al. 1979; Corbett 1993; Wilcox and Kerr 1996). The rationale for examining the side effects of seizure medications was due the higher prevalence of seizures in children with communication disorders in comparison to the general population (Stephenson 1999). Since speech-language pathologist practitioners may not have extensive pharmacological knowledge about seizure medications and their side effects, this review may provide resourceful information. The goals of this review were to examine what types of side effects were reported with various seizure medications and how seizure medication side effects may impact speech-language pathologist practitioners in assessing and treating individuals with ID.

As a background to considering medications effects for seizure disorders, it is important to understand the prevalence of seizure disorders in the United States, especially in individuals with ID. More than 2 million individuals in the United States are affected by seizure disorders, and individuals with intellectual disabilities (ID) are more likely to suffer from seizures disorders in contrast to the general population (Matson 2004; Wilfong 2002; Shannon 2010). Relative to the general population, individuals with ID are 26 percent more likely to have a seizure disorder (McGrother et al. 2006). According to Singh and White-Scott (2002), seizure disorders are a

concomitant neurological disorder in 40 to 50 percent of individuals with ID and developmental disabilities.

Various options for treating seizure disorders are presently available. One of the most common ways of managing seizure control is through medication regimens. These medications used to treat seizures are called anticonvulsant or antiepileptic drugs (AEDs). AEDs are frequently used to treat seizure disorders, but can yield significant side effects, especially in individuals with ID (Meador et al. 2001). Significant side effects of AEDs include behavioral or non-behavioral outcomes. Some behavioral side effects from anticonvulsants from anticonvulsants include aggression, hyperactivity, and irritability (Harbord 1999). Non-behavioral side effects from anticonvulsants have included rash, headache, gastrointestinal disturbance or drowsiness, or increase seizures (Harbord 1999). These significant side effects could affect individuals with ID relative to their ability to maintain social interactions as well as cognitive functioning. Cognitive function side effects from AEDs that have been described include difficulties with attention and memory (Motamedi & Meador 2003).

Because of the proposed effects on social interactions and cognitive function, it is important to examine effects of medications on speech and language acquisition. In this way, clinicians can better prepare for planning speech and language interventions in individuals with ID. Since seizure disorders require treatment throughout a person's lifetime, it is important to include children and adults who suffer from seizures with ID in this review. Having a better understanding of the possible side effects of AEDs will allow clinicians to better work with the client and their families most productively. Research for this topic is limited. In addition, the American Speech Language and Hearing Association (ASHA) does not yet provide specific guidelines for working with individuals who may experience medication side effects. Improving clinician understanding will ultimately

benefit both clients and their families while improving treatment for children and adults who may receive seizure medications on an ongoing basis.

Background and Terminology

For the purpose of this literature review, background and terminology will be discussed. Some of the research employs some different terminologies. In addition, much of the literature reviewed in this report employs terminologies that have changed over the years.

EPILEPSY

Epilepsy is defined as a neurological disorder that is caused by the abnormal or excessive neuronal activity within the brain (Shannon 2011). Abnormal disturbance in neuronal activity within the brain are termed seizures. Seizures can result in the loss of consciousness, involuntary movement, or convulsions (Haggerty 2002). The number of seizures an individual may experience may vary. Some individuals may experience seizures occasionally, while others may experience seizures multiple times per day (Shannon 2011). While individuals who have seizures may not have epilepsy, a person with more than two seizures is considered to have a seizure disorder called epilepsy (Shannon 2011).

Epilepsy is the second most common neurological disorder (Judd 2012). Each year, approximately 200,000 individuals are diagnosed with epilepsy; of that population, approximately 45,000 individuals are children and adolescents (Judd 2012). The highest incidence of epilepsy occurs in children under the age of 10 years and adults above the age 70 years (Judd 2012). It has been reported that African Americans and socially

disadvantaged populations have a higher prevalence of epilepsy; however, seizure disorders affect all nations and ethnicities (Judd 2012). Since there are no known cures for epilepsy to date, medication and surgical techniques are often used to manage or control seizures (Shannon 2011).

CAUSES OF EPILEPSY

There are many possible causes of epilepsy, since it may be caused by any factor that disrupts the normal pattern of neuronal activity (Shannon 2011). An abnormal imbalance of neurotransmitters may cause individuals to experience seizures (Shannon 2011). Some factors that may cause seizures that have been discussed include illnesses, abnormal brain development due to genetic factors, stroke, or trauma to the brain. It is important to understand the causes of seizures or factors that may cause seizures, since there has been reported stigma suggesting epilepsy is contagious (Shannon 2011). Although these are possible causes of seizures, it is important to keep in mind that about half of all seizure disorders have no known cause.

About 40 percent of seizures are attributed to genetic factors that result in epilepsy (Letcher 2005). Gene mutations can cause abnormal nervous system development that may cause epilepsy (Letcher 2005). The majority of generalized epilepsy disorders and some partial epilepsy disorders have genetic components associated with the cause of epilepsy (Letcher 2005).

Next, it is important understand some of the most common types of seizures that affect individuals with epilepsy disorders. If the cause of the seizures is known, a better understanding of what deficits may arise if the seizures occur in a specific location in the brain is possible.

TYPES OF SEIZURES

Many different types of seizures have been described by physicians (Shannon 2011). Seizures can be divided into two major categories: focal seizures and generalized seizures. Focal seizures are also known as partial seizures, which mean these seizures presents itself in a specific location in the brain (Shannon 2011).

Focal seizures are divided into two categories called complex partial seizures and simple focal seizures (Shannon 2011). In complex partial seizures, individuals typically experience change or loss of consciousness, where an individual may experience a dream-like state (Shannon 2011). An individual with a complex partial seizure may be characterized by having repetitive behavior that may occur involuntarily (Shannon 2011). Repetitive behaviors may include blinks, mouth movements, twitches, or continue activities before seizures occur (Shannon 2011). Complex partial seizures are characterized by loss of consciousness. In contrast, individuals with simple complex seizures will remain conscious but the seizure is accompanied with atypical sensations (Shannon 2011). Individuals with simple partial complex seizures may experience changes in moods, such as happiness, anger, or nausea (Shannon 2011). The majority of people with epilepsy usually have focal seizures, such as temporal lobe seizures that may cause the hippocampus to shrink overtime (Shannon 2011). Shrinking of the hippocampus over time that may cause impairments in learning and memory (Shannon 2011).

Individuals with generalized seizures usually experience abnormal neuronal activity on both hemispheres of the brain (Shannon 2011). Generalized seizures may cause individuals to experience loss of consciousness, falls, or severe muscle spasms (Shannon 2011). Since there are many different types of generalized seizures, some

examples of generalized seizures include tonic seizures, clonic seizures, and clonic-tonic seizures (Shannon 2011).

For this review, only a few major categories have been discussed since some seizure disorders do not have a specific pattern to categorize them. It is important to keep in mind that these types of seizures are not the only types.

TREATMENT OF EPILEPSY

Treatment of epilepsy typically consists of medical and surgical techniques for approximately 70 percent of individuals (Shannon 2011). Although the majority of individuals with epilepsy may be treated with medication or surgical techniques, not all individuals benefit from such treatments (Shannon 2011). Use of antiepileptic drugs (AEDs) is the most common treatment for controlling epilepsy (Shannon 2011).

There are many different AEDs drugs available to treat epilepsy that yield different benefits and side effects. In order to find the right prescription medication for individuals with epilepsy, factors such as type of seizures, personal lifestyle, age, and frequency of seizures play a critical role (Shannon 2011).

AEDs are categorized as new AEDs and old AEDs. Newer AEDs consist of carbamazepine, valproate, lamotrigine, oxcarbazepine, or phenytoin (Shannon 2011). AEDs, such as ethosuximide are mostly used for individuals with absence seizures. Other medications that are also commonly prescribed include clonazepam, phenobarbital, and primidone. Newer AEDs include tiagabine, gabapentin, topiramate, levetiracetam, and felbamate. For intractable seizures, these drugs may be used in combination with other drugs if seizures are not responsive to the medication. For the majority of individuals with epilepsy, seizures can be managed with one AED, but for those who use multiple drugs have an increased incidence of side effects (Shannon 2011). Types of medications

are available for seizure control and more information about AEDs will be provided later in the report.

When an individual with epilepsy does not respond to treatment with medication, these individuals are further evaluated in order to see if they are candidates for surgery. Before these individuals are considered for surgery, many factors are taken into consideration. Factors include the location of the seizure and how this location affects an individual's daily living activities. Although surgery may significantly reduce the frequency of seizures, surgery used to treat epilepsy may not work at all (Shannon 2011).

This general information about surgical techniques for epilepsy may be important for clinicians in terms of thinking about which functions of the brain may be impaired after surgery. Thinking about impairments relative to the parts of the brain removed may help clinicians be more knowledgeable when working with their clients and their families by providing appropriate support and treatment plans relative to the area of neural differences.

INTELLECTUAL DISABILITY

Since this review focused on individuals with ID, it is important to define ID and how it relates to seizure disorders. Side effects of medication may be more pronounced in this population. Many articles refer to individuals with ID as 'mentally retarded', or 'cognitively impaired'. For this review, the term intellectual disabilities or individuals with ID are used.

A few types of epilepsy are treated with surgery when medications are ineffective. Removal of a seizure focus is one of the most common surgical procedures. A small part of an area of the brain is removed (Shannon 2001). Physicians may refer to this type of procedure as a lobectomy or lesionectomy (Shannon 2011). When doctors cannot remove

a section of the brain where seizures originate, they may use a procedure called multiple subpial transection (Shannon 2011). In order to prevent seizures from spreading into other parts of the brain, surgeons make a series of cuts around sections of the brain (Shannon 2011).

Corpus callosotomy is a surgical procedure performed by surgeons by severing the neural connections between the hemispheres of the brain (Shannon 2011). This procedure is usually performed on children who have severe seizures that spread from one side of the brain to the other (Shannon 2011). When seizures that occur on one side of the brain and does not respond to medication treatment, children with seizures may have a hemispherectomy and hemispherotomy (Shannon 2011). Surgeons consider these procedures as very extreme since the procedures involve removing half of the cortex of the brain (Shannon 2011).

According to Ferrara (2010), individuals with ID are characterized as having impairments or delays in cognitive, social, practical, and abstract learning skills, which may cause difficulties with communication, health and safety, and school performance. Intellectual disabilities are usually categorized through cognitive assessments. These cognitive assessments can classify individuals with ID in four categories: mild, moderate, severe, and profound levels of disability.

Individuals with mild disability have an intelligence quotient (IQ) range of 52 to 69 (Ferrara 2010). These individuals make up about 75 to 90 percent of all cases of ID (Ferrara 2010). Children with mild disabilities have delays in learning to walk, talk, and to feed themselves than other typically developing children (Ferro 2010). Many children with mild disabilities may go undiagnosed until later in their school years (Ferrara 2010). As children with mild disabilities mature, they may acquire practical, social, and job skills (Ferro 2010).

Individuals with moderate disabilities have an IQ range of 36 to 51 (Ferro 2010). This population makes up about 10 to 25 percent of all cases of ID (Ferro 2010). Children with moderate disability have apparent delays in speech development and motor (Ferro 2010). These individuals will most likely not acquire academic skills, but may learn some basic communication skills (Ferro 2010). Adults with moderate disability may acquire skills for completing simple tasks and potentially travel independently in familiar places (Ferro 2010). These individuals usually require supervision and may not live independently (Ferro 2010).

Individuals with severe disability have an IQ range of 20 to 35 (Ferro 2010). These individuals make up 10 to 25 percent of all cases of ID (Ferro 2010). Children with severe disability have difficulties in speech, language, and motor development (Ferro 2010). However, these individuals may acquire some self-help skills and basic communication skills, and learn to walk with assistance (Ferro 2010). Adults with severe disability may learn to follow daily routines in a safe environment, but require supervision (Ferro 2010).

Individuals with profound disability have an IQ range of less than 20 are usually diagnosed shortly after birth (Ferro 2010). Children with profound disability typically have other medical issues that need additional monitoring and nursing care (Ferro 2010). These individuals have developmental delays in all areas of development (Ferro 2010). With intensive therapy, children with profound disability may learn how to use their legs, hands, and jaws (Ferro 2010). In adulthood, these individuals may acquire some speech and may learn to walk (Ferro 2010). These individuals require full support and supervision in their daily living (Ferro 2010).

Causes of Intellectual Disabilities

Intellectual disabilities may be caused by genetic factors, such as chromosomal abnormalities (Ferrara 2010). Although genetic factors may play a role in ID, other factors that may cause ID may occur from complications during pregnancy or childbirth (Ferro 2010). Complications from pregnancy or childbirth may result in damage to the fetal brain and central nervous system (Ferrara 2010). ID may also result from lack of proper nutrition or poor nutrition and medical care during pregnancy (Ferrara 2010).

Relationship Between ID And Seizure Medication

In the introduction, it was noted that individuals with ID were more likely to have seizure disorders compared to the general population in the United States. Many individuals with ID use AEDs to manage and control seizures. However, various AEDs may yield undesirable side effects. According Harbord (2002), these findings revealed that children with ID have a three times greater chance to experience a behavioral side effect from AEDs in comparison to children without ID. Researchers are not sure why children with ID are more likely to experience behavioral side effects from AEDs, but it is important for clinicians to be aware of when medications are changed.

Services for Individuals with Seizures

Since many speech-language pathologist practitioners work in school settings, information about qualifying services for children in school may be a useful guide for when assessing children to see if they are eligible for services.

Individuals with epilepsy may experience cognitive side effects that may influence their level of functions in their learning or work environment (Judd 2012). Cognitive side effects from seizures are not an uncommon occurrence for individuals with epilepsy. Since epilepsy may affect a child's learning ability and subsequent

development, it may cause children to miss important instruction in the classroom (Judd 2012). Therefore, it is important for parents, caregivers, and clinicians to be aware of what resources are available for their children (Judd 2012).

Many of the resources available for children with epilepsy are mandated under the nation's special education law known as the Individuals with Disabilities Education Act (IDEA) (Judd 2012). IDEA is broken down into two types of services: *early intervention* and *special education and related services*. *Early intervention* is a system that is designed to provide services for infants, below the age of three, and their families. For older children, the *special education and related services* provide assistance through public schools for preschoolers and school-aged children. This service is for children from the age of 3 to 21 (Judd 2012). In order for children to become eligible for these services, each child must complete a comprehensive and individual evaluation to determine whether a child has a disability, to have more information on how the disability affects the child's abilities in developmentally and academically, and to provide documentation of how the child's disability relates to providing special accommodations (Judd 2012).

For children with epilepsy, services are usually provided under a sub-section of the IDEA called Other Health Impairment (OHI). Under the OHI, these impairments mean that the child has a limitation on strength, vitality, or alertness, relative to his educational environment (Judd 2012) To provide services for these impairments, individuals must have an acute or chronic illness such as asthma, attention deficit hyperactivity disorder or attention deficit disorder, and epilepsy. Many other illnesses may be included are not limited to the ones above (Judd 2012). As long as the child's illness negatively affects their educational performance, they may be eligible to receive services (Judd 2012).

If a child is eligible for services within the classroom, accommodations may be offered to the individual (Judd 2012). The Individualized Education Plan team typically plans special accommodations for individuals who are eligible for services (Judd 2012). Special accommodations are usually provided in the classroom that include providing instruction in different formats such as pictures, or by addressing health concerns through flexibility in regards to school absence in case of adjusting to new medications or treatments (Judd 2012). For those individuals who have seizures, a private area may be provided for seizure recovery or rest (Judd 2012).

Anticonvulsants/Antiepileptic Medication

AEDS FOR VARIED TYPES OF SEIZURES

Anticonvulsants or antiepileptic medications are designed to control seizures. They represent one of the most common treatments for individuals with seizure disorders. It is important to know that anticonvulsant medications are not limited in treating seizures, but are also used to treat mood disorders as well (Andrews 2010). To have a better understanding of AEDs and seizures, types of AEDs used for diverse types of seizures will be reviewed. Table 1 below lists older generation AEDs and their uses. Older generation AEDs include: phenobarbital, phenytoin, valproic acid, ethosuximide, clonazepam, and carbamazepine. These medications are referred as older generation AEDs because there were no new AEDs approved from 1978 to 1993 (Hung & Shih 2011). Carbamazepine is used to treat partial and generalized tonic-clonic seizures (Hung & Shih 2011). It has a similar chemical structure to tricyclic antidepressants and has a similar mechanism of action as Phenytoin (Hung & Shih 2011). Side effects from carbamazepine include diplopia, headache, dizziness, and nausea (Hung & Shih 2011).

Clonazepam is used to treat absence seizures, myoclonic jerks, and tonic-clonic seizures. Since Clonazepam causes excessive sedation and possible tolerance of the drug, this drug has limited use (Hung & Shih 2011).

Ethosuximide is typically used as a first-line AED for patients with generalized absence seizures (Hung and Shih 2011). Side effects from ethosuximide include: headache, vomiting, nausea, abdominal pain, sedation, and headache. Phenobartbital is used to treat partial and generalized tonic-clonic seizures (Hung & Shih 2011). Phenobarbital is as effective in preventing seizures as carbamazepine and phenytoin, but is usually prescribed as second-line AED because of the significant cognitive side effects (Hung and Shih 2011). Reported side effects of phenobarbital include hyperactivity and aggression in children, and excessive fatigue in adults (Hung & Shih 2011). It is also important to note that phenobarbital interacts with other medications by causing a significant increase of metabolism rate in other AEDs (Hung & Shih 2011).

Phenytoin is also used to treat partial and tonic-clonic seizures. Common side effects of phenytoin are gingival hyperplasia, hirsutism, acne, and facial coarsening (Hung & Shih 2011). If the concentration of phenytoin is greater than 20 milligrams, other cognitive symptoms may include: ataxia, dysarthria, and lethargy (Hung & Shih 2011). Phenytoin is usually uses as a first-line AED in emergencies (Hung & Shih 2011). Valproic acid is one of the older AEDs that may be used for treating all types of seizure disorders (Hung & Shih 2011). This AED may be prescribed for absence, partial, and generalized tonic-clonic seizures (Hung & Shih 2011). Common side effects of valproic acid are gastrointestinal tract disturbances that include: anorexia, vomiting, tremor, and weight gain (Hung & Shih 2011).

Since older generation AEDs have been around longer, there is more information on side effects of these medications.

Name of Drugs	Treatment for which types of seizures
Carbamazepine	Partial and generalized seizures
Clonazepam	Myoclonic seizure
Ethosuximide	Absence seizure
Phenobarbital	Partial and generalized seizures
Phenytoin	Partial and generalized seizures
Valproic acid	Absence, partial, and generalized seizures
Gabapentin	Partial seizure

Table 1: Antiepileptic Drugs- Older AEDs

Table 2 contains names and treatment goals for Newer AEDs. Hung and Shih (2011) reported that newer generation AEDs seem to have less severe side effects and are better tolerated among patients, except for felbamate and lamotrigine. These newer generation AEDs are typically used as an adjunctive treatment for seizure disorders due to the lack of research of their efficacy as a single treatment for seizure disorders (Hung & Shih 2011). Newer generation AEDs such as gabapentin, lamotrigine, levetiracetam, oxcarbazepine, tiagabine, topiramate, and zonisamide are used to treat partial seizures.

Felbamate is one of the newer AED that is used for treatment for partial seizures and Lennox-Gastaut syndrome in children (Hung & Shih 2011). Felbamate have been reported to cause an increase of concentrations of phenytoin, phenobarbital, and valproic acid (Hung & Shih 2011). It also causes the decrease concentration of carbamazepine (Hung & Shih 2011). Since Felbamate interacts with many of the other AEDs, it has largely been replaced by other AEDs alternatives (Hung & Shih 2011). Gabapentin is

used to treat partial seizures, other neuropathies, and is approved for treating postherpetic neuralgia (Hung & Shih 2011). Adverse effects are generally mild for gabapentin (Hung & Shih 2011). Specific adverse effects were not mentioned for gabapentin. Topiramate is used for refractory partial seizures and may reduce the effectiveness of oral contraceptives, increase phenytoin concentrations, and decrease valproic acid concentrations (Hung & Shih 2011). Levetiracetam is used for partial seizures with our without secondary generalization (Hung & Shih 2011). This drug has no known significant drug interaction with other AEDS and has mild side effects (depression) (UCB Pharma 2011). Tiagabine is another AED used for the treating of partial seizures. This AED has generally mild adverse reactions (Hung & Shih 2011). However, patients who use tiagabine had a recurrence of status epilepticus while receiving treatment with this drug (Aspen Pharma 2011) Additionally, tiagabine has no know drug interaction to other AEDs (Hung & Shih 2011). Zonisamide is used as an adjunctive treatment for adults with partial seizures (Hung & Shih 2011). Side effects from zonisamide include decreased sweating, hyperthermia, and renal calculi (Hung & Shih 2011). Children have a more likelihood of experiencing hyperthermia relative to adults (Hung & Shih 2011). Other drugs such as phenytoin and carbamazepine may affect the metabolism of zonisamide, but this drug has no know effects on other AEDs (Hung & Shih 2011).

Lamotrigine is used as an adjunctive treatment for refractory partial seizures and Lennox-Gastaut syndrome (Hung & Shih 2011). One of the major side effects for this AED is the risk of life-threatening rash, such as Steven-Johnson syndrome or toxic epidermal necrolysis (Guberman et al. 1999). These risks of life-threatening rashes increase when valproic acid is administered simultaneously (Hung & Shih 2011). Other AEDs such as carbamazepine, phenobarbital, and phenytoin have been reported to

increase the metabolic rate of lamotrigine, while valproic acid has been reported to reduce (Hung & Shih 2011).

Name of Drugs	Treatment for which types of seizures
Felbamate	Partial seizure and Lennox-Gastaut syndrome in children
Lamotrigine	Partial seizure
Levetiracetam	Partial seizure
Oxcarbazepine	Partial seizure
Tiagabine	Partial seizure
Topiramate	Partial seizure
Zonisamide	Partial seizure

Table 2: Antiepileptic Drugs- Newer AEDs

Family and Cultural Impact on Development

DAILY LIVING WITH EPILEPSY

Many individuals with epilepsy live relatively normal lives. About 80 percent are helped through medication and modern therapies (Shannon 2010). For those individuals with epilepsy who are resistant to therapies, seizures may significantly affect daily life, for their families, and peers. Individuals with seizures from childhood that are resistant to treatment tend to have a shorter life expectancy in comparison to those with epilepsy that respond to treatment (Shannon 2010). However, shorter life expectancy may be the cause of an illness that causes epilepsy, and not from the complication of having seizures in

itself (Shannon 2010). Shannon (2010) does not address daily living of individuals with epilepsy and ID, but only addresses daily living of individuals with epilepsy.

Some people with epilepsy, particularly children, may experience more behavior and emotional side effects (Shannon 2010). For children to experience emotional and behavioral changes is not uncommon for this group (Shannon 2010). Counseling services are available for families and caretakers to help them cope with epilepsy, as well as epilepsy support groups (Shannon 2010). Although Shannon (2010) does not specifically address individuals with ID and seizure disorders, these services may be valuable to these individuals' family as well.

For many individuals with epilepsy, having seizures may restrict their overall independence, but they are able to participate in some recreational activities (Shannon 2010). Many individuals with seizure disorders are more likely able to participate in recreational activities, but for individuals with ID and seizure disorders this may be impossible due to the delays of critical developmental areas, such as motor skills.

Sports are considered relatively safe for individuals with epilepsy. However these individuals must follow proper safety precautions and have supervision (Shannon 2010). Sports that are considered relatively safe for individuals with epilepsy such as jogging or football may reduce seizures because of the physical exercise (Shannon 2010). It is important for individuals with seizures to practice cautious and supervision recreational activities in order to avoid injury (Shannon 2010). From this information, individuals with epilepsy may live a relatively normal life and most likely would have a higher quality of life than individuals with ID and seizures disorders due to limitations.

IMPACT FOR CAREGIVERS/FAMILY AND INDIVIDUAL WITH EPILEPSY

Caregivers and family members play an extremely important role for individuals with epilepsy. Caregivers and family members give insight in about to how epilepsy affects their family dynamics, consequences of the illness, and quality of life for caregivers and their loved ones (Asato et al. 2009). According to Asato et al. (2009), caregivers for an individual with epilepsy are more likely to experience elevated levels of stress in comparison to caregivers for other chronic illnesses. One of the issues that may contribute in higher stress levels is that caregivers are more involved in the child's life. Caregivers are involved in making sure their loved ones are physically and mentally healthy and adhering to treatment. Other factors that may contribute to elevated stress levels for caregivers may involve parental/caregiver concern for their child's learning and future development progress (Asato et al. 2009). Children who struggle in school subjects, such as math and reading, may not succeed in their overall academic achievement as the demands for higher-level tasks increases from transitioning from primary to secondary school. Asato et al. (2009) does not address quality of life of individuals with ID and seizure disorders and their families.

In adolescents with epilepsy, caregivers and adolescents have relatively the same ratings on quality of life measures in domains such as quality of life consequences of seizures, adherence to therapies, and productivity (Asato et al. 2009). Epilepsy in adolescents may hinder psychosocial and natural maturation processes that may lead to cognitive and behavioral challenges (Asato et al. 2009). As a result, adolescents with epilepsy experience a higher risk of having depression, anxiety, embarrassment, and cognitive and behavioral challenges (Asato et al. 2009).

In Gallagher (2010), one of the major concerns reported for adolescents with epilepsy was experiencing peer stigma. Peer stigma may significantly affect the overall

mental health of an adolescent with epilepsy (Gallagher 2010). Since peers may often lack the knowledge about the nature of epilepsy, such as believing that seizures are contagious, it may lead to them excluding their peers with epilepsy (Gallagher 2010). Bishop and Boag (2006) revealed that teachers surveyed in the United States have stigmatizing notions regarding epilepsy and persons with seizure disorders. Interestingly, Bishop and Boag (2006) reported that 90 percent of teachers surveyed would like to know more about seizures and seizure management, although the investigators reported that there were resources readily available through *The Epilepsy Foundation* website.

Adolescents rely heavily on their caregivers, since caregivers try their best to make sure their loved ones stick to daily routines. It can be challenging for caregivers if they try to keep their loved one safe, but at the same time, it hinders the child in developing independence. This can result into increase in depression, behavioral problems, and anger (Asato et al. 2009). This may also apply for individuals with ID and seizure disorders since the majority of the levels of intellectual disabilities are unable to live independently and require supervision from caregivers.

In addition to emotional and psychological effects on family members caring for individuals with epilepsy, financial burdens are important issues. According to Odell et al. (2007), the average financial cost of emergency outpatient services averaged about $3,255 and in-patient emergency services averaged about $12,555. These emergency services accounts for the direct cost of seizure disorders that include emergency medical services, diagnostic testing, treatment procedures, medical treatment, follow-up costs, and treatment of other comorbidities (Odell at al. 2007). There are also indirect costs, which include the cost of time spent away from work, absence from school, or parents or caregivers losing their jobs (Odell et al. 2007). It is also important to acknowledge that individuals with epilepsy have incomes that are less than the general population average

(Odell et al. 2007). This may lead to a more financial burden since each year the rise in health care costs and may make it difficult for individuals with epilepsy and their family members (Odell et al. 2007). Since Odell et al. (2007) did not mention financial burdens specifically for individuals with ID and seizure disorders, it may be challenging to estimate the financial burdens for them and their families. As mentioned earlier, individuals with ID and seizure disorders may have other comorbidities that may require treatment, which potentially may lead to a greater financial burden than individuals with only seizure disorders.

Overall, many factors play a role in how epilepsy affects the quality of life (QOL) for the individual with epilepsy and their family. Because these studies did not mention QOL for individuals with ID and seizure disorders, it may be challenging to evaluate the QOL impact for these people and their families. However, Hoare (1993) reported that individuals with early onset intractable epilepsy, in addition to other disabilities, have an extremely negative effect on their QOL. Factors that may influence QOL for individuals with seizures and their families are dependent on severity of the seizure, management of seizures, adverse side effects of AEDs, adjustment to the child's overall development, and limitations on family life (Hoare 1993).

EFFECTS OF SEIZURES ON EDUCATION

Researchers have concluded that epilepsy disorders may affect academic performance in individuals with seizures (Gallagher 2011). Since the impact of seizure disorders varies in each individual due to the type, severity, and frequency of seizures, it is difficult to generalize the process of learning of each individual. Gallagher (2011) did not mention information regarding the education status of individuals with ID and seizure

disorders, which makes it challenging to determine specifically the effects of seizures on education for this group.

The learning process of each individual is comprised of a series of abilities, such as an individual's cognitive ability, attention skills, concentration skills, communication, listening, memory, and critical thinking skills (Gallagher 2011). It is also important to note that each individual may have difference experiences and beliefs that would influence his overall academic performance. The effects of seizures may result in the impairment of emotional and cognitive abilities, which may hinder productivity in the work place or school environment. Gallagher (2011) did not mention socio-economic status or parental education, but these factors may play a major role in the level of experience each individual may acquire.

Austin et al. (1999) have reported that children may have normal IQs before their first seizure. They also found that children with epilepsy had more difficulty with math, reading, and language in school relative to their peers. Children with severe epilepsy were more likely to be behind than their typically developing peers. Since epilepsy affects different aspect of cognition due to the nature of the disorder, these effects may have a negative impact for academic success (Austin et al. 1999). In order to keep students moving towards academic success, it's important for students with epilepsy to be surrounded by supportive teachers, mentors, and parents.

Many of these reports exclude information about individuals with ID and seizure disorders. Since there is a lack of information about the QOL and effects of seizures on education, it is difficult to determine or generalize the overall QOL and education status for these individuals and their families.

EFFECTS OF SEIZURES ON SPEECH AND LANGUAGE DEVELOPMENT

Speech and language development play a critical role in the academic success of children, so it is important to understand how epilepsy affects this critical aspect of development in order to plan appropriate accommodations with teachers, families, and other practitioners. If there is a delay in speech and language development as a result of epilepsy, it may negatively impact a child's academic success, which may also affect overall psychosocial and emotional health. Since one of the goals in this report is to address how seizure disorders affect speech and language development, it is important to discuss the relationship between epilepsy and speech and language. In this meta-analysis, research regarding the effects of seizure disorders in individuals with ID on speech and language development was not found. All of the research found in this topic excluded individuals with other neurological comorbidities. Caplan (2002), Caplan et al. (2008; 2009), Sellasie et al. (2008), Strekas et al. (2013) did not mention the reason for excluding this population, but it may be because individuals with ID may have limited communication skills based on their level of disability.

In a study that examined language development in children with pediatric epilepsy, Caplan et al. (2009), found that children with epilepsy scored one standard deviation lower than their age-match control group in language assessments. Children were 6 to 15.5 years in age with history of seizures, but did not include children with ID and seizures. As the age of the children increased, children with epilepsy had more language impairments compared to their peers (Caplan et al. 2009). As children transition from primary schools to secondary schools, there is a higher demand on their language-based learning skills, so that may be one of the reasons for the difference (Caplan et al. 2009). Based on Caplan and colleagues' findings, children may not have the same

linguistic deficits because these deficits may be dependent on other factors, such as age, socioeconomic status, and duration of illness.

Selassie et al. (2008) examined the expressive and receptive language, oral motor ability, memory, and intelligence of children 20 six-year-old children with epilepsy. They excluded all children with neuro-impairments or learning disabilities. The authors found statistically significant differences between expressive and receptive grammar, and receptive vocabulary. However, Selassie et al. (2008) found that children with epilepsy scored a lower performance IQ, oral motor ability, articulation, and short-term memory compared to children without epilepsy. Since this study only included participants who were six-years-old, it may explain why there was not a significant difference between expressive and receptive grammar. As mentioned earlier, language-based skills may not be as demanding in children in this particular age range compared to older children and adolescents.

Another important aspect of language development is the narrative ability of children. Strekas et al. (2013) evaluated the narrative abilities of 25 children with epilepsy (CWE). The CWE were assessed through narrative assessments and then compared to children without epilepsy. The children ages ranged from 50 to 155 months and did not have other neurological conditions or syndromes. Strekas et al. (2013) found CWE scored poorly on structural analysis of storytelling and listener judgment compared to their peers. Listeners' perceptions of CWE's narratives production were judged to be less coherent in terms of syntax and lexically complexity (Strekas et al. 2013). CWE who had a more recent onset of seizures did not have the same functional deficits in language production compared to CWE who had chronic seizures. As for speech perception, CWE did not show differences in prosody and fluency from listeners' perception (Strekas et al. 2013). It was noted that older children's narratives were longer and more complex in

which requires higher-ordered tasks such as planning and organization (Strekas et al. 2013).

In addition to how epilepsy may affect speech and language, research findings have shown that children with epilepsy may have difficulties with formulating and organizing thoughts that may affect their overall social communication skills. Caplan (2002) examined the social communication skills of 92 children with complex partial seizure disorder, 51 children with primary generalized epilepsy, and 117 children developing typically. All the participants were 5 to 16.9 years in age. The found that children with complex partial seizures were found to have cohesion deficits and formal thought disorders. For example, children were unable to tie together continuous clauses, and sentences (Caplan et al. 2002). Meanwhile, children with partial generalized epilepsy had mild cohesion deficits. Having lack of cohesion and thought process may severely impact academic success because language-based skills demands increases as children transition from primary school to secondary school as mentioned earlier. Caplan et al. (2002) concluded that children with CPS and PGE may have deficits in communication skills.

Given the lack of research for speech and language development in individuals with ID and seizure disorders, this meta-analysis will investigate the side effects of AEDs on speech and language development in individuals with ID and seizure disorders. Specifically, the aim of this meta-analysis is to provide a resource for clinicians about the possible side effects of AEDs that used for treating individuals with ID and seizure disorders. It is important for clinicians to understand what types of side effects were reported with various seizure medications and how seizure medication side effects may impact speech-language pathologist practitioners in assessing and treating individuals with ID.

METHODS

For this meta-analysis of the effects of seizure disorders and medication on speech and language development in children with ID, a literature search was conducted by accessing databases through the University of Texas at Austin library. Databases that were used to access articles include Medline, CINAHL, PubMed, and ERIC. Google Scholar was also used to find research articles for this literature review. Although articles on Google Scholar required payment, the title of articles that were searched through Google Scholar, were input into the search engine of the University of Texas at Austin's library. The inclusion criteria of the review had to include individuals with ID who are taking AEDs and have epilepsy. Since the articles found were limited, all the articles were included if the participant was taking at least one AED.

Search terms that were used for the meta-analysis included, *intellectual disabilities, epilepsy, seizure disorders, mental retardation, anticonvulsants side effects, behavioral side effects,* and *developmental disabilities,* and *speech and language*. Other search terms were used to find more articles because with those search terms above, a limited number of article were located. From there, other search terms included *oxacarbazepine, carbamazepine, valproic acid, phenytoin, levetiracetam, topiramate, phenobarbital*, and *lamotrigine*. Articles were also found through the reference lists from other articles and seizure medication reviews.

A total of 60 articles that included children with intellectual disabilities and also included information about medication side effects were identified in the search. Of the 60 articles found, 42 of those were excluded in the review for the following reasons: some of the medications used to treat individuals with ID with epilepsy were not AEDs;

the literature included individuals with ID, but did not provide specific results pertaining to them, and some literature did not include individuals with ID.

RESULTS

OVERVIEW

This section will discuss the overview of the findings of 19 identified articles. Nineteen articles met the inclusion criteria. The 19 articles reviewed involved the use of AEDs in treating seizure disorders in individuals with ID and seizure disorder and side effects. Seventeen articles were identified as experimental studies and two articles were identified as case reports. The number of participants in case studies was two, and the number of participants in the studies was 1,754. Eighteen of 19 articles measured behavioral side effects and non-behavioral side effects from AEDs. Seven of 19 articles were based on observation from investigators or from either medical, staff, or caregiver reports. Two of the 19 studies reviewed, investigated the effects of AEDs on social skills and psychopathological adverse events in individuals with ID with seizure disorders. Thirteen studies only included individuals with ID and seizure disorders. Meanwhile, six studies included individuals with ID and seizure disorders and individuals with seizure disorders in their study. Five of 19 articles reviewed did not analyze their data with any measure of statistical analysis. However, 14 of 19 articles used statistical analysis in evaluating their data.

PARTICIPANT SELECTION

Based on the findings of the 19 articles reviewed, inclusion and exclusion criteria were not used in participant selection in many of the articles. Participants included in the studies included either only adults or children and adolescents. A few studies included individuals with seizure disorders along with participants with ID and seizure disorders. Harbord (2002), Khurana et al. (1996), and McKee et al. (2004) included only children,

adolescents or both within their participant selection. However, Gidal et al. (2000) included children and adults in their evaluation of LTG therapy.

DATA COLLECTION AND ANALYSIS

Data collection and analysis in these articles used a variety of different methods that were not consistent across studies. Data – based studies reviewed used a variety of scales and checklists. Ettinger et al. (2008), McKee et al. (2004), and Martin et al. (2009) used *the Aberrant Behavior Checklist* as one of their data collection methods. Helmstaedter et al. (2008) was the only study that used *the Barratt Impulsiveness Scale-11and Fragebogens zur Personlichkeit be zerebralen Erkrankungen* in their data collection. Coppola et al. (2008) used *Holmfrid Quality of Life Inventory*. Matson, Luke, and Mayville (2004) and Martin et al. (2009) and Matson et al. (2001) used *Matson Evaluation of Drug Side Effects,* Hurtado et al. (2006) used *Challenging Behavior Scale* and *Ritualistic Behavior Rating Scale*. McKee et al. (2004) *Habilitative Improvement Scale* in the evaluation of side effects in AEDs. Based on the review of the data collection and analysis, data-based studies did not have a uniform or consistent method of collection data and analysis.

REPORTED AEDS SIDE EFFECTS

Reported side effects from AEDs in the 19 articles reviewed included: aggression, hyperactivity, agitation, irritability, self-injurious behaviors, increased energy, disruptive vocalizations, psychotic-like behavior, drowsiness, fatigue, decrease in alertness, concentration, and appetite, lethargy, paranoia, stereotypy, increase in seizures, disorientation, abnormal movement, rash, hirsutism, tremor, headaches, mood swings, gastrointestinal symptoms (i.e., vomiting, abdominal pain), slurred speech, abnormal

white blood cell count, sleep disorders, memory problems, infections (ear, nose and throat), and mental state disorders (i.e., depression, paranoia).

Older and Newer Generation AEDs

Fourteen articles reviewed used newer AEDs (Levetiracetam, Topiramate, Gabapentin, Lamotrigine) as a treatment for seizure disorders or as an adjunctive to seizure treatment. This may be the result of increased research in newer generation AEDs in relatively recent years. Only three articles reviewed involved in the treatment of seizure disorders using older generation AEDs (phenytoin, carbamazepine, valproic acid, clonazepam). Two articles reviewed incorporated both newer and older generation AEDs in their treatment evaluation. All participants had exposure to more than one AED during the time of treatment. All participants included in the articles were taken at least one AED in their treatment regimen.

Goals of the Studies

The main goals of the 19 articles reviewed involved investigating or observing the behavioral side effects, the efficacy, tolerability, and safety of AEDs. Other goals of the studies reviewed included: examining effects of AEDs on social skills, the relationship in AEDs and antipsychotic medication, and cognitive or non-behavioral side effects of AEDs. A summary of each article is located in the appendix. The summary and critique of the literature will be discussed in the next section.

A brief summary and critique of the literature will be discussed in this section. Summary of the 19 articles and references are available in the appendix section. The critique will evaluate: criteria of participant recruitment, cultural component, language status of the participants, additional services the participants may have received (i.e. physical therapy, speech therapy), data collection, and data analysis.

CASE STUDIES

Table 3 displays the summary and critique of the two case studies reviewed. Coffey (2013) described the use of Phenytoin in an individual with Autism, seizures, and ID to resolve self-injuries. An extensive case history of the participant was provided that included: behavior problems, behavioral interventions, hospital visits, additional services and medications. However, the following information was excluded: inclusion and exclusion criteria, cultural information, and where was the language information. Before treatment, it was reported that the participant received behavior therapy that was ineffective. Coffey (2013) reported when Phenytoin was added to the participant's medication regimen, the self-injurious behaviors resolved, but data analyses were not conducted. Since the data collect was observational, baselines measures were also not included.

Kalachnik et al. (2003) provided descriptions of an individual with ID and seizure disorders have exacerbated behaviors when using Clonazepam. Similarly to Coffey (2013), the following information was missing: inclusion or exclusion criteria, cultural information, where the authors obtained language information, and additional services. Although Kalachnik et al. (2003) and Coffey (2013) reported information about their participants receiving additional services, the frequency and who implemented these additional services was not described. Both studies reported the language status of their participants. Kalachnik et al. (2003) reported "very good" receptive language skills, but did not provide information regarding expressive-language skills, while the participant in Coffey (2013) was described as nonverbal. Coffey (2013) and Kalachnik et al. (2003) both used observational data and treatment history. In contrast, Kalachnik et al. (2003) used a specific criterion in order to record tantrum behaviors, while Coffey (2013) did not establish specific criteria to record data.

Article	Participant(s)	Side Effects	Critique
Coffey (2013)	21-year-old nonverbal male with Autism, ID, and seizure disorder. Received behavioral interventions, but ineffective	Resolved self-injurious behaviors: heading banging, biting	Missing information: participant selection criteria, patient characteristics, cultural information, data analysis, and outcome measures, additional services
Kalachnik et al. (2003)	49-year-old male with ID and tonic-clonic seizures. History of challenging behaviors. Receptive language was described as "good"	Exacerbated self-injurious behaviors Aggression towards other people: hitting, biting, head-butting Aggression towards property	Limited demographic information Missing information: cultural component, language assessment, procedural, baseline measures, seizure frequency, definition of significance

Table 3: Summary of Case Studies

SOCIAL SKILLS AND PSYCHOLOGICAL STUDIES

Table 4 provides a brief summary and critique of one article that examined the social skills and one study examined psychopathological adverse events (PAEs) of participants with ID and seizure disorders. Matson, Luke, & Mayville (2004) and Mula, Trimble, & Sander (2004) did not include: participant selection criteria, cultural information, language status, and additional services. Mula, Trimble, & Sander (2004) used the *International League Against Epilepsy* (ILAE) classification for seizure and seizure types; however, Matson, Luke, & Mayville (2004) did not provide information about seizure classification. Both studies included demographic information such as sex, age, and ethnicity. Matson, Luke, & Mayville (2004) and Mula, Trimble, & Sander (2004) both conducted data analyses. Matson, Luke, & Mayville (2004) used an *Analysis of Variance (ANOVA)*, but baseline, outcome measures, and significance were not

defined. In contrast, Mula, Trimble, & Sander (2004) reported baseline and outcome measures using the *Fisher's exact test, Pearson coefficient,* and *ANOVA*, but did not define significance. Matson, Luke, & Mayville (2004) used The *Matson Evaluation of Social Skills for Individuals with Severe Retardation (MESSIER)*. Mula, Trimble, & Sander (2004) used the *DSM-IV* to classify the psychopathological adverse events (PAEs) in 118 patients with ID and with LEV treatment. Matson, Luke, and Mayville (2004) reported a significantly lower score in the positive nonverbal subscale in the Phenytoin group, but did not include additional information about the language abilities of the group.

Article	Participant(s)	Side Effects	Critique
Matson, Luke, and Mayville (2004)	130 participants (60 male, 70 female) with ID and seizure disorders. Participant characteristics were provided.	No side effects reported.	Missing information: participant selection criteria, cultural information, outcome measures, definition of significance, how seizure types were classified, language status, and additional services
Mula, Trimble, and Sander (2004)	118 participants (64 males, 54 females) with ID. Demographic and patient variables provided. DSM-IV criteria used for PAEs.	PAEs Agitation Anger Hostile Behavior	Missing information: Patient selection criteria, cultural information, who conducted IQ testing, language assessment, data collection, additional services, and caregiver role

Table 4: Summary of Social Skill and Psychological Effects Studies

OBSERVATIONAL STUDIES

Table 5 provides a summary of articles that were observational in nature, formal or informal assessments, or collected data from medical reports. Coffey (2013),

Kalachnik et al. (2003), and Mula, Trimble, and Sander (2004) were described in the previous section.

Singh & White-Scott (2002) examined the usefulness of Topiramate (TPM) in 20 patients with ID and seizure disorders. Unlike Coffey (2013) and Kalachnik et al. (2003), Singh & White-Scott (2002) included participant selection criteria, detailed demographical information that included seizure frequency and type. However, cultural information, language abilities, data analyses, and additional services were not mentioned. Additionally, level of ID of each participant was determined by a combination of IQ scores and psychological evaluation. Since reports were rated by the investigators, caregiver ratings may have provided a more accurate representation of participants' overall improvement.

Harbord (2002) reviewed the AEDs histories of 216 children and adolescents with epilepsy to determine the incidence of behavioral and non-behavioral significant side effects (SSE). Similarly to Coffey (2013) and Kalachnik et al. (2003), Harbord (2002) did not include: participant selection criteria, data analyses, cultural information, and patient characteristics. Harbord (2002) also did not describe language abilities or if the participants received additional services during the study that was similar to Singh & Scott-White (2002) findings. Data was collected through parent reports that included: which AEDs were used and which AEDs were discontinued due to SSE. Harbord (2002) did not describe behavioral SSEs, but did not describe non-behavioral SSEs.

Dinkelacker et al. (2003) described the emergent of adverse effects of LEV in 33 patients with refractory epilepsy. Demographic and patient characteristics were provided. The following information was not included: cultural information or language abilities of participants, level of ID of participants, additional services, baseline measures, and data analyses. Dinkelacker et al. (2003) reported success with LEV therapy and side effects,

but results were not corroborated with baseline measures. Dinkelacker et al. (2003) and Singh & Scott-white (2002) were the few studies in this section that used participant selection criteria.

Bootsma et al. (2004) examined the use of TPM in 470 participants in a real-life setting. Similar to the studies discussed previously, Bootsma et al. (2004) did not include: cultural information, language status, participant selection criteria, additional services, and where was the ID information obtained. Bootsma et al. (2004) classified seizure types according to the *ILAE* guidelines that were also used in Singh & Scott-White (2002). Bootsma et al. (2004) reported significant findings based on patient records, but did not define what was considered significant. Although the investigators did not assess language abilities of the participants, dysphasia was reported in the results and the investigators did not provide further details in regards to where the language measure was obtained.

Article	Participant(s)	Side Effects	Critique
Coffey (2013)	21-year-old nonverbal male with Autism, ID, and seizure disorder. Received behavioral interventions, but ineffective	Resolved self-injurious behaviors: heading banging, biting	Missing information: participant selection criteria, patient characteristics, cultural information, data analysis, and outcome measures
Kalachnik et al. (2003)	49-year-old male with ID and tonic-clonic seizures. History of challenging behaviors. Receptive language was described as "good"	Exacerbated self-injurious behaviors Aggression towards other people: hitting, biting, head-butting Aggression towards property	Limited demographic information Missing information: cultural component, language assessment, procedural, baseline measures, seizure frequency, definition of significance
Singh and White-Scott (2002)	20 participants (12 males, 8 females) with ID or DD. Participant selection criteria provided.	Behavior problems, decreased alertness, drowsiness, increase in seizures, abnormal movement, disorientation, unsteadiness, pneumonia, low platelets, and low white blood cell count	Missing information: what assessments were used to classify IQ; additional services; who classified seizure type; how data was analyzed, baseline for global improvement, language abilities, cultural information, data analysis, and definition of significance
Harbord (2002)	216 children and adolescents (107 girls, 109 boys) All had seizure disorders. IQ testing used to determine participants with ID.	Behavioral side effects (not described) Non-behavioral side effects: rash, drowsiness, Hirsutism, tremor, increase seizures, headaches, lethargy, and excess weight	Limited demographic information. Missing information: patient characteristics, cultural component, IQ tests and administration, participant selection criteria, data collection, behavioral side effects, additional services, and seizure type
Dinkelacker et al. (2003)	33 patients with history of refractory epilepsy. Patient characteristics and demographic information were provided	Increased aggression, increased irritability, fatigue, sleep disorders, memory problems, gastrointestinal adverse effects, and depression	Missing information: cultural component, level of ID, baseline and outcome measures, language status, data analysis, additional services, how were adverse effects defined/recorded

Table 5: Summary of Observational Studies

Table 5: Summary of Observational Studies (Continued)

Bootsma et al. (2004)	470 participants were identified (160 patients with ID) through medical information system. Demographic and patient characteristics provided.	Weight loss Mood problems Gastrointestinal problems Dysphasia Cognitive slowing	Missing information: cultural component, Level of ID, language abilities, definition of significance, additional services, participant selection criteria
Mula, Trimble, and Sander (2004)	118 participants (64 males, 54 females) with ID. Demographic and patient variables provided. DSM-IV criteria used for PAEs.	PAEs Agitation Anger Hostile Behavior	Missing information: Patient selection criteria, cultural information, who conducted IQ testing, language assessment, data collection, additional services, and caregiver role

EXPERIMENTAL STUDIES

Hanzel et al. (2000) explored the relationship between barbiturate AEDs and antipsychotic medications in seven individual with ID and seizure disorders. Participants were diagnosed with ID according to the *DSM-IV* criteria (Hanzel et al. 2000). The following information that was not included: assessment of language abilities, additional services, baseline measures, participant selection criteria, and cultural information. Data collection was obtained by index behaviors measured by residential staff or unit psychologist; however, index behaviors were not defined. Data analyses were conducted using an *a priori* analysis; *Wilcoxon matched-pairs signed-ranks* test, and *t*-test (Hanzel et al. 2000). Hanzel et al. (2002) reported decrease in behavioral problems, but baseline measures were not conducted to verify the findings.

Helmstaedter et al. (2008) examined the behavioral changes in patients receiving Levetiracetam (LEV) and evaluated the effects of LEV on impulse control and aggression

in 288 outpatients with epilepsy. As described previously in Hanzel et al. (2000), Helmstaedter et al. (2008) also did not include the following information: participant selection criteria, baseline measures, cultural information, language abilities, and additional services. Helmstaedter et al. (2008) was one of the few studies that had a control and experimental group; however, data analyses were only provided for the control group, since the experimental group did not match. Helmstaedter et al. (2008) obtained data by using the *Barratt Impulsiveness Scale-11* and *Fragebogens zur Personlichkeit be zerebralen Erkrankungen (FPZ)* questionnaire (Helmstaedter et al. 2008). Similarly to Hanzel et al. (2000), Helmstaedter et al. (2008) did not report baseline measures and outcomes to validate their findings.

Coppola et al. (2008) assessed the behavioral and cognitive effects in 34 participants with ID and seizure disorders following treatment with Topiramate (TPM). Contrast to Hanzel et al. (2000) and Helmstaedter et al. (2008), Coppola et al. (2008) used inclusion and exclusion criteria in participant selection. Additionally, ID diagnoses were evaluated according to *DSM-IV* criteria, as well as severity of ID of the participants. Similarly to Hanzel et al. (2000) and Helmstaedter et al. (2008), Coppola et al. (2008) did not include cultural information, baseline measures, additional services information, and language status of the participants. Data was measured and collected from caregivers by using the *Holmfrid Quality of Life Inventory*. Data analysis was evaluated by *SSPS 10.0* software for Windows (Coppola et al. 2008). As identified in previous studies described, Coppola et al. (2008) reported results that lacked baseline and outcome measures.

Beran and Gibson (1998) examined the emergence of provoked aggressive behavior in treatment with Lamotrigine (LTG) in 19 participants with ID and seizure disorders. The following information was missing: participant selection criteria, cultural information, additional services information, language abilities, and level of ID. The

following missing information was similar to the findings in Helmstaedter et al. (2008), and Hanzel et al. (2000). Results were provided through description of behavior observed in each participant. Beran and Gibson (1998) reported results that were strictly observational from parent reports, but did not report how patients' behavior was prior to LTG therapy.

Ettinger et al. (1998) described the significant positive or negative psychotropic effects of LTG in 7 individuals with ID and seizure disorders. Similarly to Beran and Gibson (1998), Ettinger et al. (1998) did not include the following information: participant selection specification, baseline measures, cultural information, additional services information, and data analyses. Data was collected and recorded by supervising staff or caregivers and then reported to investigator; however, Ettinger et al. (1998) did not conduct data analyses. Ettinger et al. (1998) provided detailed narratives case reports for 3 of 7 participants were reported in the results, but did not provide reports for the remaining participants and did not specify the reason for this. Information from the case report indicated that two participants had some vocalization and one participant was nonverbal, but the language abilities of the rest of the participants were not reported.

Khurana et al. (1996) examined the efficacy, tolerability, and safety of adjunctive Gabapentin in 32 children with refractory partial epilepsy. Similarly to Coppola et al. (2008), Khurana et al. (1996) identified participants according to inclusion and exclusion criteria through patient records at a children's hospital. The following information was not included: cultural information, additional services information, level of ID, and seizure type. Although information regarding diagnoses of ID and seizure disorders was provided, investigators did not provide information as to who diagnosed these participants. Investigators used a scale to rate adverse events; however, the rating scale did not appear to be representative in terms of the level of impact from the AED's side

effects. As mentioned earlier in Singh & Scott-White (2002), it may be more of an accurate representation if the caregiver coded the adverse event ratings rather than the investigators. Khurana et al. (1996) reported outcome measures, but did not establish baseline measures.

Gidal et al. (2000) evaluated the efficacy of LTG in 44 participants with ID and seizure disorders. Gidal et al. (2002) only used inclusion criteria in participant selection. Similarly to articles discussed previously, Gidal et al. (2003) did not provide the following information: exclusion criteria, additional services information, cultural information, and language abilities. Adverse drug effects data were obtained from nurses and medical reports and *Student t*-test was used to analyze the data collected (Gidal et al. 2000). In contrast to previous studies mentioned, Gidal et al. (2000), reported results that were corroborated with pre- and post measures.

Matson et al. (2001) provided descriptive characteristics of 248 participants with ID and seizure disorders and examined the side effects of AEDs. Matson et al. (2001) did not provide the following information: participant selection criteria, cultural information, additional services, language abilities, seizure type, or who diagnosed ID. Although information regarding who diagnosed the participants with ID was not mentioned, ID diagnoses were evaluated according to the *DSM-IV* criteria (Matson et al. 2001). Matson et al. (2001) reported limited information regarding language abilities. Authors reported that most of the participants were nonverbal, but did not mention what was used to assess language. Matson et al. (2001) reported that all of the participants had other comorbidities, but they did not mention further information about treatment. Clinical psychologists administered the *Matson Evaluation of Drug Side Effects (MEDS)* (Matson et al. 2001). Matson et al. (2001) analyzed data through descriptive analyses and also

used the *ANOVA* to analyze data (Matson et al. 2001). Similar to Khurana et al. (1996), Matson et al. (2001) reported significant findings, but did not include baseline measures.

Hurtado et al. (2006) evaluated the behavioral changes in 35 participants with ID or acquired brain damage with refractory epilepsy on LEV therapy. Hurtado et al. (2006) did not include the following information: participant selection criteria, cultural information, language assessments, seizure type and level of ID. Although the investigators did mention that the language status was derived from neurological reports, there was no additional information regarding which type of assessment was used. Hurtado et al. (2006) conducted data analyses through the *Wilcoxon signed rank test, Mann-Whitney U Test, Spearman P, and Pearson r*. As mentioned in Khurana et al. (1996) and Matson et al. (2001), Hurtado et al. (2006) reported improvement in patient ratings; however, baseline measures were missing.

Martin et al. (2009) examined the efficacy and behavioral effects of TPM in 29 participants with ID and seizure disorders. Martin et al. (2009) used inclusion criteria, but did not use exclusion criteria in the selection of participants. Similar to Hurtado et al. (2006), Martin et al. (2009) did not include the following information: cultural information, additional services, or who diagnosed ID. Classification of ID diagnoses was evaluated according to *ICD-10* criteria, but the authors did not mention who evaluated these participants (Martin et al. 2009). Similar to Matson, Luke, and Mayville (2004), Martin et al. (2009) used the *MESSIER* for evaluating social skills and behavioral disturbance was measured through *ABC* (Martin et al. 2009). Adverse events were coded according to the *WHO Adverse Reaction Terminology*, and responder rates were based on caregivers' diaries (Martin et al. 2009). Similar to Gidal et al. (2000), Martin et al. (2009) reported results that included baseline measures.

McKee et al. (2004) examined the effects of add-on Lamotrigine (LTG) treatment on seizure reduction, safety, tolerability, and behaviors in 22 participants with ID and seizure disorders. As mentioned in Coppola et al. (1998) and Khurana et al. (1996), McKee et al. (2004) used inclusion and exclusion criteria in the selection of participants. Similar to Martin et al. (2009), McKee et al. (2004) did not include: cultural information, additional services information, and language status. Epilepsy was diagnosed according to the *ILAE* guidelines and severity of ID was diagnosed according to the *DSM-IV Revised* criteria (McKee et al. 2004). Caregivers also completed the *Habilitative Improvement Scale (HIS)* (McKee et al. 2004). Investigators coded the adverse events, but they did include more information regarding reported adverse events. Investigators used appropriate measures in evaluating these participants. Since the investigators completed the *ABC* ratings, the results may reflect a more accurate representation if the caregivers completed the *ABC* ratings. Similar to Gidal et al. (2000), McKee et al. (2004) included baseline measure to support their findings.

Article	Participant(s)	Side Effects	Critique
Hanzel et al. (2000)	7 individuals with ID and seizure disorders	Self-injurious behavior, property destruction, disruptive vocalizations, verbal threats and reported decrease in aggression	Missing information: language abilities, participant selection criteria, cultural information, additional services

Table 6: Summary of Experimental Studies

Table 6: Summary of Experimental Studies (Continued)

Helmstaedter et al. (2008)	288 participants were divided in a control and experimental group Demographic and patient characteristics were provided	Aggression Better concentration Increased energy	Missing information: participant selection criteria, limited demographic information, cultural information, who gave participants ID diagnoses or level of ID, baseline and outcome measures not included, language abilities, and additional services
Coppola et al. (2008)	34 participants (16 males, 13 females) with ID and seizure disorder	Aggressiveness Psychotic-like behavior, decreased in appetite, tiredness, drowsiness, decrease in concentration and alertness	Missing information: additional information, cultural information, language abilities, baseline and outcome measures
Beran and Gibson (1998)	19 participants (16 male, 3 women) with ID and seizure disorder	Aggressive behavior, paranoia, withdrawn, lethargy, depression	Limited demographic information. Missing information: cultural component, measurement of adverse behavior, language abilities, level of ID, seizure type, additional services, participant selection criteria, data analysis
Ettinger et al. (1998)	7 participants with ID (5 of 7 had Lennox-Gastaut syndrome)	Increased in irritability, hyperactivity, and stereotypy	Limited demographic information. Missing information: patient selection criteria, case reports for rest of participants, cultural information, level of ID, additional services, baseline and outcome measures, data analysis, language abilities of rest of participants
Khurana et al. (1996)	32 children with refractory partial epilepsy	Rash, hyperactivity, increased aggression, violent outbursts, mood swings, increased impulsivity and irritability	Limited participant demographics. Missing information: cultural information, level of ID, language abilities, baseline and outcome measures, additional services, Vague coding scale

Table 6: Summary of Experimental Studies (Continued)

Gidal et al. (2000)	54 participants (25 men, 19 women) with profound ID and seizure disorder.	Self-injurious behavior, gastrointestinal symptoms	Limited demographic data Missing information: cultural component, language status, additional services
Matson et al. (2001)	248 participants with ID and seizure disorders were divided into one control and experimental group	Abnormal white blood cell count, disturbed gait, balance disorders, self-injurious behaviors	Missing information: participant selection criteria, cultural information, additional services, seizure type, treatment of other comorbidities
Hurtado et al. (2006)	35 participants with refractory seizures. Demographic and patient characteristics were provided.	Problem behaviors, verbal aggression, reduction in seizures	Limited demographic information. Missing information: patient selection criteria, language assessment, level of ID, additional services, challenging behavior data, baseline and outcome measures
Martin et al. (2009)	29 participants with Cerebral Palsy. Participant characteristics provided.	Gastrointestinal disorder, nervousness, tiredness, injuries, mental state disorders	Limited demographic information. Missing information: language abilities, cultural information, patient selection exclusion criteria, where IQ information obtained, additional services
McKee et al. (2004)	22 participants with ID and seizure disorder	Vomiting Somnolence Abdominal pain Dizziness	Missing information: cultural information, language status, additional services

DISCUSSION

Based on the findings of the 19 article reviewed, AEDs may cause a variety of adverse side effects in individuals with ID and seizure disorders. The most common side effects from AEDs in individuals with ID and seizure disorders included: aggression, irritability, lethargy, and gastrointestinal problems. These side effects were not limited to a specific age group, but were also found in across all participants of different ages. Over a half of the articles reviewed were experimental studies, while the rest of the articles reviewed were observational studies. Almost half of the articles obtained data through caregiver reports, medical staff reports, and patient records. Although findings reported side effects of AEDs, information regarding how seizure disorders and AEDs affect speech and language development in individuals with ID was not available. Majority of the articles reviewed focused solely on behavioral side effects and did not address speech and language development of these participants.

SIDE EFFECTS OF AEDS

Self-injurious behaviors and aggression were a few of the most frequent side effects that were reported in the review of 19 articles. Kalachnik et al. (2003), Matson et al. (2006), Hanzel et al. (2000), and Gidal et al. (2000) reported self-injurious behaviors during AEDs treatment. It appeared that self-injurious behaviors were reported regardless of which type of AEDs were used and that individuals with ID had more adverse reactions relative to participants without ID. Kalachnik et al. (2003), Dinkelacker et al. (2003), Helmstaedter et al. (2008), Coppola et al. (2008), Beran and Gibson (1998), Khurana et al. (1996), and Hurtado et al. (2006) reported aggression in participants regardless of type of AED treatment.

Other non-behavioral side effects that were frequently reported included gastrointestinal problems. Dinkelacker et al. (2003), Bootsma et al. (2004), Gidal et al. (2000), Martin et al. (2009), and McKee et al. (2004) reported gastrointestinal problems in participants on AED treatment. Bootsma et al. (2004), Mula, Trimble, and Sander (2004), Coppola et al. (2008), Beran and Gibson (2008), and Dinkelacker et al. (2003) reported psychiatric problems in some participants exposed to AED treatment. Singh and White-Scott (2002), Coppola et al. (1998), and Bootsma et al. (2004) reported adverse cognitive side effects in participants during AED treatment. These adverse cognitive side effects included decrease in concentration and alertness, drowsiness, and cognitive slowing. Dinkelacker et al. (2003) also reported memory problems in participants on Levetiracetam. Harbord (2002) reported an increase in seizures, rash, headaches, and excess weight in participants exposed to AEDs. Positive side effects of AEDs were also reported in addition to the adverse side effects of AEDs. Coffey (2013) reported improvement and resolution of self-injuries in an individual with ID and Autism with treatment with Phenytoin. Helmstaedter et al. (2008) reported increase in energy and better concentration in participants on Levetiracetam. Hurtado et al. (2006) reported a decrease in seizure in participants on Levetiracetam.

Based on the findings, side effects from AEDs appear to be present in many individuals with seizures and ID. However, more research needs to be conducted in order to establish more reliable data in distinguishing which symptoms were already present before AEDs therapy treatment began. With this information, it may help clinicians distinguish which behaviors were already present before therapy in order to be more aware in formulating new goals and treatment options. It is also important for practicing clinicians to be aware of potential side effects of AEDs so that they can modify appropriately in the therapy environment in order to keep clinician and client safe. In

addition to modifying the therapy environment to ensure safety for both client and clinician, knowing these side effects may help clinicians counsel caregivers on how to keep their loved ones safe as well.

NEWER GENERATION AEDS

Based on the findings, almost all of the articles, reviewed reported side effects from AED therapy such as behavioral or non-behavioral side effect, regardless of the brand of medication. It was important to note that multiple studies included participants who were taking concomitant medications due to various comorbidities. Since the authors did not address effects of concomitant medications, the information regarding these side effects was unknown. This information is important for clinicians to be aware of, since they are more likely to work with medically fragile populations. Since this review did not cover all of the various newer generation AEDs described in a previous sections, clinicians do not have the information for possible side effects for other newer generation AEDs.

Based on the results of studies that involved topiramate (TPM) therapy, TPM appear to have a variety of side effects. Since the studies reported adverse behaviors, such as aggression, this may be important for clinicians to take into consideration during therapy treatment. For example, the clinician may incorporate breaks or escapes for the client to reduce negative behaviors. Helmstaedter et al. (2008), Dinkelacker et al. (2003), Hurtado et al. (2006) reported aggression in participants on Levetiracetam therapy. All of the articles that involved Levetiracetam therapy reported aggression as one of the side effects in participants. Coppola et al. (2008) and Singh and White-Scott (2002) reported behavioral problems and aggression in participants on Topiramate therapy, but also reported other non-behavioral side effects such as decreased in alertness and

concentration. Martin et al. (2009), Coppola et al. (2008), and Bootsma et al. (2004) reported similar side effects in participants on Topiramate therapy, such as mood, mental state disorders, and psychotic-like behaviors. Bootsma et al. (2004) and Martin et al. (2009) reported gastrointestinal problems in participants on Topiramate therapy. Almost all of the studies that involved Topiramate therapy reported adverse cognitive side effects, such as cognitive slowing and decrease in alertness and concentration.

Side effects reported from studies that used Lamotrigine (LTG) therapy were variable across studies reviewed. This may negatively impact practicing clinicians in preparation for modifying the therapy environment or be prepared incase something unexpected occurs, since clinicians may not be aware of all the side effects. Side effects from LTG therapy reported aggression, stereotypy, self-injurious behaviors and gastrointestinal problems. Beran and Gibson (1998) and Gidal et al. (2000) reported aggressive and self-injurious behaviors in participants on Lamotrigine therapy. Ettinger et al. (1998) reported increase in irritability, hyperactivity, and stereotypy in participants on Lamotrigine therapy. Gidal et al. (2000) and McKee et al. (2004) reported gastrointestinal problems in participants on Lamotrigine therapy. Beran and Gibson (1998) was the only study reviewed that reported depression and paranoia in participants on Lamotrigine therapy.

OLDER GENERATION AEDS

Based on the findings of this review, older generation AEDs were just as likely to cause side effects compared to newer generation AEDs. Certain older generation AEDs may exacerbate pre-existing problem behaviors that were reported in Kalachnik et al. (2003) and Khurana et al. (1996). Khurana et al. (1996) reported increased aggression, violence, and irritability in participants on Gabapentin therapy. Kalachnik et al. (2003)

reported increased aggressive and self-injurious behaviors in a participant on Clonazepam therapy. This is important for clinicians to be aware that both older and newer generation AEDs may potentially cause many adverse effects, which may require clinicians to be prepared in working with clients and their family.

Coffey (2013) was the only study that had resolution with behavioral problems on Phenytoin therapy. Matson, Luke, and Mayville (2004) did not report behavioral side effects, but did report impaired social skills in participants on Phenytoin therapy. Hanzel et al. (2000) reported self-injurious behaviors, aggressive behaviors, and disruptive vocalizations in participants on multiple older generation AEDs (phenobarbital, phenytoin, Valproic acid, and Carbamazepine). Matson et al. (2001) also reported self-injurious behaviors along with disturbed gait, slurred speech, and aggression in participants on a variety of older generation AEDs.

OLDER AND NEWER GENERATION AEDS

As mentioned in previous sections, it is important for clinicians to be aware of different medication interactions; however, more research needs to be conducted to further understand AEDs side effects. It clinicians were able to identify specific side effects in AEDs, it may help them devise therapy goals, as well as providing appropriate counseling for caregivers. Older and newer generation AEDs were evaluated together in one of 19 articles reviewed. Harbord (2000) reported significant behavioral side effects in participants on a variety of AEDs. In particular, Harbord (2000) reported an increase of side effects in individuals with ID while on AEDs regimen. It appeared that participants on older or newer AEDs would most likely experience side effects, especially if they are taking concomitant AEDs. Harbord (2000) reported similar adverse cognitive side effects, such as drowsiness and lethargy as previously mentioned articles that were

reported in Singh and White-Scott (2002), Coppola et al. (1998), and Bootsma et al. (2004).

SPEECH AND LANGUAGE DEVELOPMENT

Based on the findings in the review of 19 articles, a limited number of articles addressed speech and language status of participants with ID and seizure disorders. Although there was information regarding the behavioral component in this population, some studies reported that many participants were non-verbal; a few had some words, and relative strength in receptive language. However, based on these findings, there was no information provided that included how AEDs side effects affect speech and language in individuals with ID and seizure disorders. These participants' language status was lacking additional information. This lack of direct information on speech and language would make it difficult for clinicians to incorporate this information into therapy straightforwardly. Knowing the side effects of AEDs on speech and language development may help clinician distinguish whether if certain treatment goals should be continued or discontinued. It may also help clinicians decide if these medication side effects interfere in the success of the clients' speech and language goals.

One of 19 articles reviewed evaluated the social skills of individuals with ID and seizure disorders. Matson, Luke, and Mayville (2004) examined social skills in their participants, but did not include the language status or abilities of each participant. Although Matson and colleagues measured language and social skills in patients with seizures and ID, the results provided were insufficient for practicing clinicians to use in their treatment plans. They reported significantly lower scores in the positive non-verbal subscale in the *MESSIER* in participants taking phenytoin, but did not provide further information to what this score outcome might mean in terms of speech and language

development. Additional research involving speech and language component and side effects of AEDs is critical in developing appropriate treatment goals for this population that accommodate the effects of medications for seizures.

Kalachnik et al. (2003), Ettinger et al. (1998), Coffey (2003), and Hurtado et al. (2006) were the few authors who reported language status of participants. Studies that reported language status of participant were missing additional information in regards to how the language was assessed and where investigators obtained language information. The findings show that there was essentially no information regarding how seizure medication side effects affect speech and language development in individuals with ID and seizures. The lack of speech and language information in regards to seizure medication side effects may negatively impact practicing clinicians, since working with individuals with ID and seizure disorders is not uncommon in the field of speech therapy.

CULTURAL AND FAMILY COMPONENT

Based on the findings, none of the 19 articles included cultural information or family dynamics pertaining to the participants. The lack of cultural and family information may negatively impact practicing clinician, since clinicians often counsel families and caregivers during treatment therapy. As mentioned earlier in previous sections, individuals with ID rely heavily on their caregivers in their daily living. Caring for individuals with ID or any other medical issues may be considerably stressful for families, such as financial burdens. If clinicians have access to resources that involve stress levels of caregivers in culturally diverse populations, it may help facilitate appropriate counseling support for clients and their families. This would help families avoid spending money on therapy that does not accommodate their needs. Since caregivers play a major role in the lives of individuals with ID, it is important to consider

cultural and family dynamics when working with these individuals and their families. Having knowledge about cultural information is imperative for clinicians, since communication disorders are not limited to certain ethnicities. Research is needed in this area of interest in order for clinicians to provide support and counseling for clients and their families.

FUTURE RESEARCH

Future research should examine how AEDs and seizure disorders affect speech and language development as well as the ongoing intervention process in individuals with ID. Many of the articles reviewed reported side effects of AEDs without information on how these effects impact speech and language development. This information is important for clinicians to be aware of in order to plan appropriate interventions, since many work settings will include individuals with ID and seizure disorders. Other research avenues should assess how cultural and family dynamics may affect side effects of AEDs in individuals with ID, especially since clinicians work with culturally diverse clients and their families. It is also important to examine stress levels of caregivers and how treatment affects their family dynamic. Knowing this information may help clinicians provide appropriate counseling and support for the clients and their family. Lastly, it is important to examine the side effects of AEDs interactions with other medications, since many individuals with ID and seizure disorders were on more than one drug.

CONCLUSION

In this meta-analysis, a total of 19 articles were reviewed to examine the side effects of AEDs in individuals with ID and seizure disorders. Behavioral side effects from AEDs were found; however, research regarding how AEDs and seizure disorders affected speech and language development or therapeutic outcomes was not available. Many of the articles reviewed lacked necessary information and data collection and analysis varied. Based on the findings, participants on AEDs regimens experienced a variety of side effects that included behavioral side effects, adverse cognitive side effects, and non-behavioral side effects. Further research is needed in examining AEDs side effects on speech and language development, as this may be useful information for practicing clinicians who work with these clients.

Appendix

Goals of Article	Participants	Data Collection	Data Analysis	Medication Use/Target	Results	Side Effects	Critique
To explore the relationship between barbiturate AEDs and antipsychotic medication dose. (Hanzel et al. 2000)	A total of 7 individuals with ID were included in this study, 2 dropped due to sudden death and stroke. All participants were diagnosed with ID according to the DSM-IV criteria. Demographic information included: age, sex, degree of ID, other diagnoses, and seizure type. All participants used different AEDs and antipsychotic medication with different dosage.	Index behaviors measured by residential living area staffed by unit psychologists. Data was collected from each participant over three time intervals (A, B, C) for the analysis of challenging behaviors. Index behavior rate measures were calculated by dividing the intervals during which the index behavior occurred by the total number of intervals. Only physical aggression was analyzed because this was the only index behavior displayed by all five individuals. Other behaviors were included, but some of the data included are represented in percentages and non-percentages.	A mean relative change score was computed for each index behavior. Period A to C was analyzed using dependent-groups one-tailed t-test. An a priori analysis was used for period A versus period B. The Wilcoxon matched-pairs signed-ranks test was used to compare period B versus period C.	These medications were used for physical aggression and self-injurious behaviors and for tonic-clonic and complex partial seizures. Reduction of medication to reduce behavior rates. Phenobarbital, Phenytoin, Valproic acid, Carbamazepine, Chlordiazepoxide Thioridazine Chlorprothixene	All five participants' seizures were stable across the three measurement periods. Physical aggression decreased by 82.3% from period A to B. 93.8% from periods A to C and by 19.2 % from periods B to C. A significant reduction in the psychotic medication dose from 146 mg to 98 mg/day to 106 to 88 mg/day occurred after barbiturate AEDs were discontinued. Period A to B: no additional improvement of behavior rates after antipsychotic medication reduction with the reduction of antipsychotic medication. Period A to B: behavioral rates were not significant. Period A to C: decrease in physical aggression after the lowest antipsychotic medication dose was reached compared to baseline. Combined index behaviors decreased by 81.5% from periods A to B, 96.3% from periods A to C and 44.8% periods B to C.	Decrease physical aggression. Other reported injuries include: self-injurious behavior, property destruction, disruptive vocalizations, and verbal threats were reported, but were not analyzed.	No information regarding language abilities of the participants. No inclusion and exclusion criteria provided. No cultural information about the participants provided. No baseline measures were mentioned. Authors did not say what values are considered significant for these parameters. No mention if the participants were receiving additional services.
The goals of the study were to observe behavioral changes in patients receiving Levetiracetam (LEV) and to answer the question of whether LEV exerts a specific effect on impulse control and aggression. (Helmstaedter et al. 2008)	288 outpatients with epilepsy Demographic data was provided: male gender, age, ID, psychiatric history, idiopathic, age of onset of epilepsy, number of AEDs, time of introduction of last AED, and good responders. Control group and LEV group	The Barratt Impulsiveness Scale-11 Fragebogens zur Personlichkeit be zerebralen Erkrankungen	Validity of patient reports were evaluated through cross-tabulations of patients with proxy reports Statistics were calculated by using SSPS 14.0 Step wise regression analysis	LEV used for seizure control	41% of patients reported good seizure control. 40% reported good improvement. ID patients responded less well that those for whom there was no such information. 37% of patients reported negative side effects (12% severe, 25% moderate) 22% of patients noticed positive change (7% very positive, 15% moderate) 41% of patients reported no change. 9% of control group reported any change after introduction of the last AED. Patients with ID reported negative side effects more often than patients with normal development. Side effects were not related to gender, type of epilepsy, dose, time on LEV, number of AEDs There were no significant relationship between psychiatric history and reporting of behavioral side effects of LEV. 39% of patients reported an increase in aggression. 31% reported increase in energy. 25% reported increase in concentration/attention. Of all 288 patients, 59% reported a behavior change.	Aggression Better concentration Increased energy	No inclusion and exclusion criteria for each participant. No information on ethnicity or cultural component. Patients with ID were included in the study, but information was taken from records, no formal assessment. No language measures. Reported increase/decrease in negative and positive behaviors, but baseline measures were not included. Control group did not match experiment group. No mention of language for the participants with ID or the severity of their disability. No mention if the participants were receiving additional services.
To assess behavioral and cognitive effects following treatment with Topiramate in children and adolescents with epilepsy with mild to profound ID.	34 participants (16 males and 13 females) enrolled in the study 5 participants dropped out within the first 2-weeks of TPM therapy	Holmfrid Quality of Life Inventory Inventory was read by two neuropsychologist to caregivers	Statistical Analysis was performed with the SPSS 10.0 program for Windows.	TPM used to control both partial and generalized epileptic seizures in pediatric patients.	Results at 3 months: Worsening of total score 20 of 29 patients (69%). Results at 6 months: 9 of the 29 children dropped out of the study. 7 participants dropped because of persistence of seizures and 2 because of adverse side effects (aggressiveness and psychotic-like behavior, decreased appetite). For the remaining patients, 9 patients' score worsened, and 11 remained unchanged. Results at 12 months: 2 more patients dropped out because of poor efficacy of seizure frequency. Remaining 18 patients: 6 reported worsening scores (6%) and 12 patients' scores were unchanged. Worsening of behavior occurred in 19 patients (66%) at 3 months. (Activation	Aggressiveness Psychotic-like behavior Decreased in appetite Tiredness and drowsiness Decrease in concentration and alertness	No cultural information regarding the participants was included. No information if these participants were receiving additional services. No information about language development was provided. Reported worsening of behaviors or symptoms but did not provide baseline measures.

(Coppola et al. 2008)					and tiredness and drowsiness seemed to be most affected) 6-12 months follow-up: behaviors scores remained worsened in 65 and 45% of cases 38% decrease in concentration 24% reported decrease in alertness		
To examine the relationship between social skills of individuals with ID and AEDs. (Matson, Luke, and Mayville 2004)	130 participants (Male 60, female 70) from Pinecrest developmental center Ethnicity of the participants were provided (Caucasian and African American) Some of the participants had other diagnosis such as one or more psychological conditions Participants were divided into two groups and were matched on variables of age, gender and level of ID.	The Matson Evaluation of Social Skills for individuals with severe retardation (MESSIER) used to measure social skills. Data was collected from direct-care workers who worked with the participant for a minimum of 6 months prior to the study. Data was reported on a Likert scale.	ANOVA statistical analysis	Phenytoin Carbamazepine Valproic Acid AEDs used for seizure control	No significant differences were found between carbamazepine group and the carbamazepine control group on any of MESSIER subscales. No significant differences were found between Valproic acid group and the Valproic acid control group on any of MESSIER subscales. Significant differences were found between the phenytoin group and the phenytoin-control group. Phenytoin group had a significantly lower score on the positive non-verbal subscale on the MESSIER. Phenytoin group had a significantly lower score on the General Positive subscale than the phenytoin-control group	No side effects reported.	No inclusion or exclusion criteria. No cultural information provided. No language assessment was conducted. No baseline measures reported. Missing information regarding language status and level of ID
To report the emergence of a syndrome of aggressive behavior provoked by Lamotrigine (LTG) in patients with epilepsy and intellectual challenge. (Beran and Gibson 1998)	19 participants (16 male and 3 women; age 17-54 years). Referred from centers that specialized in intellectual disability and who had LTG added to their AED regimen Demographic data: age, sex, and use of LTG, other AEDs, assessment of patients' behavior, subsequent to any behavior changes. Patients had poorly controlled seizures.	Information regarding how data was collected for each participant was not provided, However, there is a table that provided information: patients, dosages, and behavioral changes during LTG treatment. Data for patients who were taking more than 3 AEDs were not included.	No data analysis	LTG used as an add-on AED regimen for patients with poorly controlled epilepsy.	5 of 19 patients discontinued LTG due to aggressive behavior (shouting, slamming doors, or damaging furniture, demonstrated violent behaviors) 1 of 19 patients had signs of aggressive behaviors when LTG was discontinued and patient was exposed to vigabatrin and later when a trial of tiagabine was initiated (unrelated to LTG). In these 5 patients, 2 of 19 patients had LTG discontinued due to unacceptable aggressive behavior, but LTG was reintroduced consequent of inability to control seizures (and continued to have aggressive behaviors) Aggressive behaviors in all 5 patients stopped when LTG was discontinued. For the 12 patients who continued LTG therapy without interruption: 4 of 12 had behavior problems other than aggression (paranoia, lethargy, depression, withdrawn); 4 patients had no change in behavior; 3 patients showed aggression; 1 patients showed behavioral improvement with LTG treatment.	Aggressive behavior Paranoia Seemed withdrawn Lethargy Depression	No inclusion or exclusion criteria reported. No cultural information included. No language status of participants. No information about the level of ID for these patients was. Missing information
To describe significant positive of negative psychotrophic effects of LTG observed in epilepsy patients with ID. (Ettinger et al. 1998)	7 patients who had ID were selected from 20 patients who had LTG. 5 of 7 patients had Lennox-Gastaut syndrome (LGS) Demographic information was provided: age, sex	Aberrant Behavioral Checklist (ABC): questions are classified under categories by "irritability, lethargy, stereotypy-abnormal repetitive behaviors, hyperactivity, and inappropriate speech" 1 residential staff member who was familiar with the patient and the parents of the 2 patients living at home to answer each question comparing behaviors before the introduction of LTG,	No data analysis	LTG used in addition to other AEDs for seizure control.	Case Reports: Patient 4 had behavioral improvement. Patient 4 became less hyperactive, less irritable, demonstrated more compliance with simple instructions. Behavioral improvements remain intact during the 6-month follow-up. Patient 5 had behavioral deterioration with the increase dosage of LTG. Patient 5 became more irritable, displaying temper tantrums, and becoming less cooperative, became hyperactive and difficulty with standing or sitting in one spot. Developed a new behavior of smearing feces. These behaviors were present during the 6-month follow-up. Patient 6 had behavioral deterioration. Within 1-month of LTG treatment, increase of LTG dosage, behavioral deterioration worsened (irritability, crying, screaming, temper tantrums, hyperactive, restlessness and inability to sit still, and stereotypy increased). Behavioral problems continued for 9 months with LTG treatment. Behavioral problems resolved when LTG was stopped, but with the same VPA	Increased irritability Increased hyperactivity Increased stereotypy	Limited demographic information. Missing information: patient selection criteria, case reports for rest of participants, cultural information, level of ID, additional services, baseline and outcome measures, data analysis, language abilities of rest of participants

		with a time point after maintenance LTG dose had been achieved. Summary of patient data was provided in addition to 3 of 7 brief case reports of some of the participants.			dose. Improvement in behavior continued (up to 3-months follow-up). Data for the rest of the participants from table: Patient 1: decreased irritability, lethargy, hyperactivity, and perseveration. Patient 2: decreased in irritability, hyperactivity, and increased cooperation. Patient 3: decreased in lethargy, and increased in cooperation and social engagement. Patient 7: increased in irritability.		
To resolve self-injury with phenytoin in a man with autism and ID (Coffey 2013)	Extensive patient history provided 21-year-old man Diagnosed with ID and Autism Self-injurious behaviors Non-verbal; required full-time home care Behavioral intervention was reported ineffective for this individual	The data provided was anecdotal from a physician The information provided was based on observation	No data analysis	Medications used for self-injurious behaviors due to Frontal Lobe seizures Phenytoin for injurious behaviors Lorazepam for injurious behaviors	Self-injurious behaviors resolved with phenytoin Physician reported that patient returned to the hospital on two occasions, each associated with subtherapeutic serum phenytoin levels.	Self-injurious behaviors: biting, hitting, head banging were resolved with phenytoin	Missing information: participant selection criteria, patient characteristics, cultural information, data analysis, and outcome measures
To determine the usefulness of Topiramate in individuals with intractable mixed seizures with ID and developmental disabilities (DD) (Singh and White-Scott 2002)	Participants selected from 368 epilepsy patients who were older than 21 and had ID and DD. Study included 20 patients (8 females; 12 males). Inclusion criteria: mixed seizures that were uncontrolled by treatment with standard or newer AEDs, or intolerable adverse effects with current AED therapy. Exclusion criteria: patients with history of renal stones Demographic information included	Information collected through caregiver reports and physician evaluation. The investigator rated improvement as worse, none, minimal, moderate or marked. Patients assessed their own improvements, but authors did not mention any information about the patients' language abilities.	No information regarding how the data was analyzed. Percentages of those who had seizure reduction were provided. No method of how the data was analyzed.	Topiramate was used as an add-on AED to target seizure control Other AEDs that the patients used were combinations of phenytoin, carbamazepine, phenobarbital, primidone, lamotrigine, or divalproate sodium.	4 patients discontinued the study Seizure frequency was reduced in 11 of 16 patients (69%) Two patients were seizure free (13%) No change in seizure frequency in three patients Seizure duration reduced in 7 patients (44%) Global improvement based on investigator, showed improvement was moderate in 15 patients, and none to minimal in 3 patients. Overall improvement was rated as excellent by 13 patients, fair to good by one patient and poor to fair or fair by 4 patients. Reductions in baseline AED dosages were achieved in 13 patients Improved alertness was evidenced in 11 of 16 patients (69%) Emergency room visits for seizures did not increase or increase (Reported, but no data to support)	Behavior problem Decreased alertness Drowsiness Increase in seizures Abnormal movement (due to valproate) Disorientation, unsteadiness, and pneumonia Low platelets Low White blood cell count	Missing information: what assessments were used to classify IQ; additional services; who classified seizure type; how data was analyzed, baseline for global improvement, language abilities, cultural information, data analysis, and definition of significance
To review the AED histories of a cohort of children with epilepsy to determine the incidence of SSE (significant side effects) and other factors that may have influenced the incidence of SSE. (Harbord 2000)	216 children and adolescents (107 girls and 109 boys, age ranged 3 months to 18 years). All participants were seen by the author over a two-year period. Consultations occurred in 3 settings: hospital outpatient clinics, hospital in-patients, and private practices.	Parent reports Author did not mention how data from parent reports were recorded.	No data analysis	AEDs: Carbamazepine, Clobazam, Clonazepam, Ethosuximide, Lamotrigine, Phenobarbitone, Phenytoin, Sodium Valproate, and Vigabatrin were used to control seizures.	SSE occurred in 15% of drug exposures (7% due to behavioral changes: irritability, aggression or hyperactivity; 8% were due other factors: rash, headache, gastrointestinal disturbance or drowsiness). Behavioral SSEs were found most often with Clobazam, Clonazepam, and Phenobarbital (13-17%). Behavioral SSEs were found least often with controlled released Carbamazepine, Ethosuximide, and Lamotrigine (2-4%). Non-behavioral SSEs were most common with regular Carbamazepine, Phenytoin, and Phenobarbitone (16-21%) and least often with sodium valproate and Clobazam (2-3%). 57 children (26%) experienced at least on SSE (19 children had SSEs to more than one AED; 12 children experienced SSEs with 2 AEDs; 6 children experienced SSEs with 3 AEDs; 1 child experienced SSEs with 4 AEDs). 27 of 67 children (40%) had SSEs compared with 30 (20%) of those with normal cognition and development. This was due to difference in behavioral SSE in	Behavioral SSEs were not described. Non-behavioral SSE include: rash Drowsiness Hirsutism Tremor More seizures Headaches Lethargy Excess weight	Limited demographic information. Missing information: patient characteristics, cultural component, IQ tests and administration, participant selection criteria, data collection, behavioral side effects, additional services, and seizure type

					children with ID (28%) and only 6% of those with normal cognition. Children with ID were exposed to an average of 3 AEDs compared to an average of 1.9 for typically developing children. (Implied that children with ID had more refractory seizures). Comparing incidence: children with ID had one SSE for every 5.3 AEDs, compared with 1: 8.6 AEDs for the typically developing group. Behavioral SSE occurred in 1 : 9.6 AEDs for children with ID and 1 : 31.8 in the typically developing group. Non-behavioral SSE incidence were similar: 1 : 11.9 AEDs in children with ID and 1 : 11.7 AEDs in typically developing.		
To present the authors' experience with the efficacy, safety, and tolerability of gabapentin in children with intractable epilepsy. (Khurana et al. 1996)	32 children with refractory partial epilepsy who received Gabapentin as an add-on medication to their AED regimen. Inclusion and exclusion criteria included	Data was collected through monthly evaluations and phone-interviews with main-caregiver of each participant. Response to therapy was divided into categories. Adverse experiences was coded on a severity score from 0 (nonexistent) to 3 (severe enough to warrant discontinuation, additional therapy, or both)	The Wilcoxon Rank Sum Test was used to determine differences between baseline and gabapentin therapy in response scores, response rate, and in the adverse effects score. Student t test The Mann-Whitney rank sum test The Fisher Exact Test The Pearson product-moment correlations were used in data analysis.	Gabapentin used as an add-on AED for refractory partial seizures.	Efficacy: 11 patients had a greater 50% reduction in seizures frequency. 4 had improvement of 25 to 50% seizure frequency. 16 patients had no significant responses to the change in seizure frequencies. 2 patients became seizure free and 4 patients were almost seizure free. 4 of 11 patients 10 years of age or older had more than 50% reduction in frequency of seizures. 7 of 21 children younger than 10 years had a more than 50% improvement. Mean age of the group that responded with a better than 50% improvements were 7.4 years and the mean age for the group that did not respond was 9.3 years. 7 patients discontinued Gabapentin due to lack of efficacy and 1 because of skin rash. 2 patients discontinued Gabapentin despite of seizure improvements due to behavioral problems. 3rd patient discontinued Gabapentin due to lack of efficacy and behavioral problems. There were no effects of age or of the presence or absence of ID on the number of AEDs before or during gabapentin therapy. 17 patients had adverse experience and 15 of 17 had behavioral problems. Behavioral problems for 4 patients required physician intervention. Of the 4 patients that required physician intervention, 3 reverted back to baseline after stopping Gabapentin therapy. 11 children had increased impulsiveness, irritability, and hyperactivity. 1 child had a rash, and 1 child had facial edema from apparent exacerbation of pre-existing choreoathetosis. 14 of 15 patients who had experienced behavioral side effects were 10 years or younger and 1 patient who had experienced behavioral side effects was over 10 years of age. Of the 15 patients who had experienced behavioral side effects, all of the patients had ID with baseline attention deficit disorder, behavioral problems, or both. 7 of 21 patients (10 years old or younger than 10 years of age) with ID did not have adverse effects. None of 6 typically developing patients and 1 participant with ID (older than 10 years of age) had behavioral adverse effects.	Rash Hyperactivity Displayed more aggressive and violent outbursts and mood swings Increased impulsiveness Increased irritability Facial edema Exacerbation of pre-existing choreoathetosis	Limited participant demographics. Missing information: cultural information, level of ID, language abilities, baseline and outcome measures, additional services, Vague coding scale
To evaluate the efficacy of LTG in developmentally disabled persons with epilepsy. (Gidal et al. 2000)	25 men and 19 women with the age range of 8 to 59 years. Medical and pharmacy records were review to identify all patients who had or were receiving LTG.	Phase 1: baseline period of 2-months before initiation of LTG. Phase 2: designated as the drug-escalated period (3 months). Phase 3: treatment observation period). Adverse effect data was collected from nursing and medical progress notes.	Percentage of change in frequency were calculated: (treatment period average-baseline average)/ baseline average X 100 Student t test was used to compare phase 1 and phase 3 for paired data. Statistical significance was	LTG used for intractable seizure disorders in patients with ID and epilepsy. Patients were taking other AEDs: carbamazepine, phenytoin, phenobarbital, primidone, valproic acid, gabapentin, and felbamate	Seizure frequency reduction greater than 75% was seen in 32% (n=14) of patients 23% of patients (n=10) had a 50-74% reduction in seizure frequency. 11% of patients (n=5) experienced 25-49% reduction in seizure frequency. 14% of patients (n=6) had between 0 and 24% reduction in seizure frequency. 21% of patients had an increase of seizure frequencies. Significant reductions of 48% were noted in the frequency of generalized tonic-clonic seizures. No significance in partial seizure reductions, or in mixed-typed seizures. 6 patients were seizure free during treatment evaluation period. No episode of status epilepticus occurred. Reported adverse drug effects: gastrointestinal symptoms (vomiting) noted in two patients; 5 of 44 patients displayed self-injurious behaviors at baseline and after treatment these behaviors increased.	Self-injurious behaviors Gastrointestinal symptoms	Limited demographic data Missing information: cultural component, language status, additional services

			assigned P<0.05		Treatment was discontinued for 11% of patients due to adverse effects.		
To provide descriptive characteristics of individuals with ID and seizure disorders. (Matson, Mayville, Bamburg, and Eckholdt 2001)	248 participants diagnosed with ID based on DSM-IV criteria. Level of ID included. Demographic data provided. Participants were divided into one control group and one experimental group	Collected data through the Matson Evaluation of Drug Side effects (MEDS) Clinical psychologists were trained to administer the MEDS. Likert scale Measures that required for physiological and lab findings were obtained their patient records.	ANOVA-significant level is P<0.01 Descriptive analysis	AEDs for seizure control Phenobarbital Divalproex Carbamazepine Phenytoin Gabapentin Primidone	No significant main interactions were found between the different AEDs. When type of AED was used for the independent variable and MEDS score was used as the dependent variable, no significance was found. Descriptive analysis: most endorsed items were abnormal white blood cell count, disturbed gait, balance disorders, self-injurious behaviors, and aggression or destructiveness Other measures using ANOVA were not significant. However significant differences were found in the severity of subscales for endocrine/genitourinary and CNS–general. Type of medication taken by participants for items in which a between-group significance was found.	Abnormal white blood cell count Disturbed gait Balance disorders Self-injurious behaviors Aggression or destructiveness Slurred speech Toothache Menstrual changes	Missing information: participant selection criteria, cultural information, additional services, seizure type, treatment of other comorbidities
Share authors' clinical experience with treatment-emergent adverse effects of Levetiracetam (LEV) (Dinkelacker et al. 2003)	33 patients with a long history of refractory epilepsy were included. Computer-based library of medical records were used. Inclusion and exclusion criteria provided. Demographic information provided Patient characteristics included	Efficacy and aggressive symptoms were derived from patients' record, including MRI scans 1-3 prior to aggressive episodes.	No data analysis	LEV used as an add-on therapy for refractory epilepsy	Group 1: 14 patients experienced irritability that did not require change in AEDs. These symptoms were rated as mild. 5 of 14 patients had learning disabilities. Group 2: 10 patients had moderate irritability that required change in medication. 1 patient had pronounced and 2 patients had moderate learning disabilities. Group 3: 9 patients showed overt physical aggression. Patients in -group 3 had some history of aggression. 7 of 9 individuals threaten others or exerted physical aggression. 2 of 9 patients required psychiatric emergency services. Highest percentage of learning disabilities was found in the group with severe aggressive symptoms.	Increased aggression Increased irritability Fatigue Sleep disorders Memory problems Gastrointestinal adverse effects Depression	Missing information: cultural component, level of ID, baseline and outcome measures, language status, data analysis, additional services, how were adverse effects defined/recorded
Performed a systematic audit of Topiramate (TPM) use in "real-life" setting of our center, analyzing all patients who had received or who is still using TPM. (Bootsma et al. 2004)	470 patients were identified through a medical information system (166 patients had ID) Demographic information and patient characteristics were provided. Epilepsy and seizure were classified under the ILAE. Gender was equally distributed Mean age of study was 34.9	Data collected through patient records. Treating neurologists were asked additional information incase of any uncertainty.	Kaplan-Meier analysis for retention rates SPSS 10.0 analysis Mann-Whitney U test and Pearson coefficient for ordinal data	TPM used for refractory epilepsy	TPM titration schedules were provided. Most frequent applied strategy was not a fixed scheduled, but varies due to patient response and seizure frequency. Most frequent side effects were mental slowing, and language problems at 6, 12, and 18 months. Weight loss was reported in early stages of treatment. Mood problems (agitation) reported at 18 months and urogenital problems at 24 months of follow-up. At 6 months, 49% reported side effects. At 12 months 47% reported side effects. At 18 months, 48.4% reported side effects. At 34 months, 38.2% reported side effects. 269 of 470 patients discontinued at some point TPM: 27% quit due to adverse effects; 17.2% quit due to lack of efficacy; 14% quit due to a combination of reasons. The most common reason for discontinuing TPM was due to cognitive slowing (27%), dysphasia (16%), and mood disorders (hyperirritability, agitation, aggression) (11.9%). Gastrointestinal complaints occurred in 10.1% of patients.	Weight loss Mood problems Gastrointestinal problems Dysphasia Cognitive slowing	Missing information: cultural component, Level of ID, language abilities, definition of significance, additional services, participant selection criteria
To investigate the prevalence and psychopathological features of psychiatric adverse events (PAEs) in patients with learning disabilities (LD) with LEV therapy.	118 (64 males and 54 females) of 517 patients with epilepsy were identified with LD. Demographic data and distribution of variables associated with PAEs was provided. Epilepsy and seizure diagnoses were based on ILAE classification.	Data was obtained through evaluating patients at each visit.	Fisher's exact test and Pearson coefficient ANOVA	LEV used to treat epilepsy in patients with LD.	15 patients experience PAEs during LEV therapy. 2 developed an affective disorder; 2 developed emotional liability; 9 developed aggressive behavior; and 2 had personality changes such as agitation, anger and hostile behavior. 10 discontinued LEV due to PAEs; 3 received dose reduction and 2 remained on the same dose. Psychotropic drug prescription was required in three patients while 1 patient was admitted to the hospital because of PAEs. Did not find specific seizure pattern associated to PAEs onset. 3 patients were seizure free during PAEs, one was seizure free but behavior deteriorated after a cluster of seizures, five experienced no change in seizure	PAEs Agitation Anger Hostile behavior	Missing information: Patient selection criteria, cultural information, who conducted IQ testing, language assessment, data collection, additional services, and caregiver role

(Mula, Trimble, and Sander 2004)					frequency, five had seizure reduction, and only one patient experienced seizure worsening. Significant association between patients with and without PAEs with psychiatric history and a previous history of status epilepticus.		
To evaluate whether treatment with LEV adversely impacts behavior in people with ID and/or acquired brain damage. (Hurtado et al. 2006)	35 individual with refractory epilepsy were observed over 3 years. Demographic and patient characteristics were provided (Cognitive status; LEV status; No. of seizure types; seizure change on LEV, convulsive seizures on LEV, RBS, challenging frequency, behavior difficulty, scale challenge, no. of other AEDs, and taking neuroleptics). Language competence was derived from neurological reports.	Ritualistic behavior rating scale (RBS) Challenging Behavior scale (CBS) Details relating to history of challenging behavior, side effects from previous AEDs, etc. were obtained from medical files Behavior measures were recorded in two separate 8-week intervals: once when on LEV and once off LEV. Seizure diaries were kept my care staff	Wilcoxon analysis Mann-Whitney U test Spearman P Pearson r P>0.05 was considered significant	LEV used as an add-on AED for refractory epilepsy.	Frequency and severity of ritualistic behaviors were rated higher on RBS scale. Only 5 patients obtained better ratings while on LEV. CBS scale: patients taking LEV were more likely to have problem behaviors. Frequency of challenging behavior and level of severity were significantly higher in patients on LEV. Challenge scores were significantly higher in patients on LE. 20 patients received higher rating on the computed challenged measure when on LEV; 14 obtained a score at least 50% higher. Only 6 patients obtained a lower rating (behavior improved). Verbal aggression was rated as significantly more challenging and shouting as more frequent and challenging when patients were on LEV. Patients had significantly fewer seizures on LEV. 17 of 28 patients with seizures experienced reduction in seizures. No significant differences were found between seizure type and seizure frequency. Did not find significant correlation between seizure reduction and behavioral worsening for patients.	Report did not include specific behaviors	Limited demographic information. Missing information: patient selection criteria, language assessment, level of ID, additional services, challenging behavior data, baseline and outcome measures
To examine the effectiveness and behavioral outcomes of patients with ID treated with TPM for epilepsy. (Martin et al. 2009)	29 patients with Cerebral Palsy were identified from Epilepsy Centre Kork (Seguin Clinic for Persons with Severe ID). Inclusion: patients with epilepsy (less that 4 years old) with any type of seizures and ID that had unsatisfactory results with previous AEDs and TPM were considered.	Social skills behavior data was collected through MESSIER and behavioral disturbance through ABC WHO Adverse Reaction Terminology was used to code adverse events Monthly seizure rates were calculated Responder rates were based on caregivers' diaries. Baseline measures were provided to see changes over the course of the study.	No formal data analysis because data was observational in nature. Wilcoxon's asymptotic test and modified ITT (m-ITT) were used as an exploratory measure	TPM used to treat epilepsy in patients with ID.	Slight improvement in all subscales of the ABC except for hyperactivity. Evaluation from the MESSIER revealed some improvement in all subscales for both groups with an exception of minimal deterioration on scale M6. Seizure frequencies decreased from m-ITT group during TPM treatment (V2-V5). 8 patients (38.1%) experience increase in seizure frequency and 13 patients (61.9%) experienced a seizure reduction. 7 patients had at least 50% reduction in seizures; 3 patients had a reduction of at least 75% of seizures, and 1 patient experienced complete seizure freedom. 57 treatment-emergent adverse events (TEAEs) were reported in 21 of 29 patients (72.4%). 23 of these (40.4%) were at least possibly related to TPM treatment. 5 serious TEAEs occurred in 4 patients (fracture tibia head, abscess in left popliteal fossa with recurrent edema, and rheumatic fever.) Two deaths occurred; Sudden unexpected death in epilepsy was assumed, but no autopsy was performed. Serious TEAEs were judged to not be causal due to TPM treatment. Physicians rated tolerability as "very good" or "good" in 82.8% of 24 patients. Cognitive tolerability was rated as "very good" or "good" in 79.3% of 24 patients.	Gastrointestinal disorders Nervousness/restlessness Tiredness/sedation Ear/nose/throat infections, injuries Mental state disorders	Limited demographic information. Missing information: language abilities, cultural information, patient selection exclusion criteria, where IQ information obtained, additional services
To examine the effects of adjunctive LTG therapy on seizure reduction, safety and tolerability, and behaviors in adolescents with ID through a sub-analysis.	22 patients (age range 14 to 20 years) were included. Inclusion criteria: patients (12 to 20 years old) who had a diagnosis of epilepsy classified by the ILAE; diagnosis of ID based on the DSM-IV Revised criteria; body	Seizure counts were obtained through caregiver reports (investigator coded and reviewed at predetermined intervals) Investigator assessment of clinical status (rated as mild, moderate, or marked deterioration or change, or mild, moderate, or marked	Focused on percentage reduction of patients' seizure frequency. All data summarized by using descriptive statistics. t-tests were used to	LTG therapy for refractory epilepsy in adolescents with ID.	During maintenance interval: 25% of patients were seizure free; 45% of patients had 75% reduction in seizure, and 60% of patients had 50% in reduction of seizures. During optimization phase, 15% of patients were seizure free, 45% of patients had a 50% reduction in seizures, and 40% of patients had a 75% reduction in seizures. HIS mean score was significantly improved. Group mean scores showed better adaptive functioning compared with baseline. ABC scores revealed the participants had significant improvement. Statistically significant improvements were noted in the areas of lethargy, hyperactivity, and stereotypy. Investigator concluded that overall clinical status for completers was improved. 80% of patients had no change in adverse events	Vomiting Dizziness Somnolence Abdominal pain	Missing information: cultural information, language status, additional services

(McKee et al. 2004)	weight of 25kg or more; receiving 3 AEDs at enrollment; and experienced at least two seizures per month during the 3 months prior to enrollment and during each of two baseline periods of 4 weeks in duration. Exclusion criteria: if patients had used of any investigational drug within 4 weeks of initiation of the study, had a vagal nerve stimulator place, or had been previously exposed to LTG. Demographics (age, sex, race) and patient characteristics (severity of ID; seizure etiology; most common AEDs used, etc.) were provided.	improvement) ABC scores obtained during assessments conducted during screening phase and at the baseline, escalation, maintenance, and optimization phases. Habilitative Improvement Scale (HIS) scores completed by caregivers. Adverse events were defined and were recorded by caregivers. Investigator at the clinic reviewed and compiled the data.	examine changes from baseline on the ABC scores and HIS scores during the maintenance and optimization phases. All efficacy data reporting was based on data summaries for completers only (n = 20). All demographic and safety reporting was based on data summaries for patients entering the escalation period and taking at least one dose of LTG (n = 22).		at the end of the study. 15% of patients had some improvement in adverse events from baseline to the end of the maintenance phase (with addition of LTG dosage). Social function improved in 50% of patients.14% of patients experienced vomiting during the optimization phase. No other drug-related was reported in more than 10% of patients in the group. Dizziness, somnolence, and abdominal pain were infrequently reported (n =2; 9%)		
To describe an individual with ID who displayed behavioral exacerbation associated with the use of clonazepam, which was prescribed to treat problem behaviors. (Kalachnik, Hanzel, Sevenich, and Harder 2003)	49-year-old male with severe ID and had tonic-clonic seizures resulting from asphyxia during birth. Single-case study: all information and data were collected through patient's medical records and behavioral records. Receptive language skills were reported as good. Participant continued to receive non-psychopharmacological interventions	Tantrum behavior was measured in the residential setting in 15-minute partial interval recording. Rate of tantrum behavior for each drug and dose condition was computed by dividing the number of intervals in which tantrum behavior occurred by the total number of intervals during the drug and dose condition. If more than one type of tantrum behavior was recorded for an interval, the interval was counted only once. Observational data included.	Error bars were based on 95% confidence bands derived from z-approximation to the normal distribution for proportional data.	Clonazepam therapy used to treat challenging behavior in an individual with ID and seizure disorder.	Condition 1 and 2: Clonazepam was prescribed at 2 mg/day, 8.6 and 9.3 tantrums occurred per week. Conditions 3 to 5: Clonazepam was reduced and 5.6, 6.3, and 6.1 tantrums occurred per week, respectively. Condition 6 to 8: Clonazepam was discontinued, tantrums decreased to 1.5, 0.2, and 0.2 per week, respectively. Statistically significant percentage changes of total intervals containing tantrums were detected at 0.05 level of significance.	Exacerbated tantrum behaviors: Aggression to other people (hitting, kicking, head butting) Aggression towards property Self-injurious behaviors	Limited demographic information Missing information: cultural component, language assessment, procedural, baseline measures, seizure frequency, definition of significance

References

Andrews, L.W. (Ed). Anticonvulsants. (2010). Encyclopedia of Depression (Vol. 1, pp. 28-30). Santa Barbara, CA: Greenwood Press.

Asato, M. R., Manjunath, R., Sheth, R. D., Phelps, S. J., Wheless, J. W., Hovinga, C. A., . . . Zingaro, W. M. (2009). Adolescent and caregiver experiences with epilepsy. J Child Neurol, 24(5), 562-571.

Austin J.K., Huberty TJ, Huster G.A., Dunn D.W. (1999) Does academic achievement in children with epilepsy change over time? Dev Med Child Neurol 41, 473–479.

Beran, R. G., & Gibson, R. J. (1998). Aggressive behaviour in intellectually challenged patients with epilepsy treated with lamotrigine. Epilepsia, 39(3), 280-282.

Bishop, M., & Boag, E. M. (2006). Teachers' knowledge about epilepsy and attitudes toward students with epilepsy: Results of a national survey. Epilepsy & Behavior, 8(2), 397-405.

Bootsma, H. P., Coolen, F., Aldenkamp, A. P., Arends, J., Diepman, L., Hulsman, J., Lambrecht, L., Leenen, M., Majoie, M., Schellekens, A., & de Krom, M. (2004). Topiramate in clinical practice: Long-term experience in patients with refractory epilepsy referred to a tertiary epilepsy center. Epilepsy Behavior, 5(3), 380-387.

Coffey, M. J. (2013). Resolution of self-injury with phenytoin in a man with autism and intellectual disability: The role of frontal lobe seizures and catatonia. J ECT, 29(1), 12-13.

Coppola, G., Verrotti, A., Resicato, G., Ferrarelli, S., Auricchio, G., Operto, F. F., & Pascotto, A. (2008). Topiramate in children and adolescents with epilepsy and mental retardation: A prospective study on behavior and cognitive effects. Epilepsy Behavior, 12(2), 253-256.

Corbett J. (1993) Epilepsy and mental handicap. In: A Textbook of Epilepsy, 3rd edn (eds J. Laidlaw, A. Richens & J. Oxley), pp. 631–.6 Churchill Livingstone, Edinburgh.

Dinkelacker, V., Dietl, T., Widman, G., Lengler, U., & Elger, C. E. (2003). Aggressive behavior of epilepsy patients in the course of levetiracetam add-on therapy: Report of 33 mild to severe cases. Epilepsy & Behavior, 4(5), 537-547.

Epilepsy. (2012). In S. J. Judd (Ed.), Health Reference Series. Learning Disabilities Sourcebook (4th ed., pp. 225-232). Detroit: Omnigraphics

Ettinger, A. B., Weisbrot, D. M., Saracco, J., Dhoon, A., Kanner, A., & Devinsky, Y. (1998). Positive and negative psychotropic effects of lamotrigine in patients with epilepsy and mental retardation. Epilepsia, 39(8), 874-877.

Ferro, M. A., Landgraf, J. M., & Speechley, K. N. (2013). Factor structure of the child health questionnaire parent form-50 and predictors of health-related quality of life in children with epilepsy. Qual Life Res, 22(8), 2201-2211.

Gabitril, tiagabine [product information]; 2010. Aspenpharma

Gidal, B. E., Walker, J. K., Lott, R. S., Shaw, R., Speth, J., Marty, K. J., & Rutecki, P. (2000). Efficacy of lamotrigine in institutionalized developmentally disabled patients with epilepsy: A retrospective evaluation. Seizure, 9(2), 131-136.

Guberman A.H., Besag F.M., Brodie M.J., et al. (1999). Lamotrigine-associated rash: risk/ benefit considerations in adults and children. Epilepsia, 40(7), 985–91.

Haggerty, M. (2002). Seizure Disorder. In D. S. Blanchfield & J. L. Longe (Eds.), The Gale Encyclopedia of Medicine (2nd ed., Vol. 4, pp. 2984-2990). Detroit: Gale.

Hanzel, T. E., Bauernfeind, J. D., Kalachnik, J. E., & Harder, S. R. (2000). Results of barbiturate antiepileptic drug discontinuation on antipsychotic medication dose in individuals with intellectual disability. Journal of Intellectual Disability Research, 44(2), 155-163.

Harbord, M. G. (2000). Significant anticonvulsant side effects in children and adolescents. Journal of Clinical Neuroscience, 7(3), 213-216.

Helmstaedter, C., Fritz, N. E., Kockelmann, E., Kosanetzky, N., & Elger, C. E. (2008). Positive and negative psychotropic effects of levetiracetam. Epilepsy Behavior, 13(3), 535-541.

Hoare, P. (1993). The quality of life of children with chronic epilepsy and their families. Seizure, 2(4), 269-275.

Hung, O. L., & Shih, R. D. (2011). Antiepileptic drugs: the old and the new. Emerg Med Clin North Am, 29(1), 141-150.

Hurtado, B., Koepp, M. J., Sander, J. W., & Thompson, P. J. (2006). The impact of levetiracetam on challenging behavior. Epilepsy Behavior, 8(3), 588-592.

Kalachnik, J.E., Hanzel, T.E., Sevenich, R., & Harder, S.R. (2003). Brief report: clonazepam behavioral side effects with an individual with mental retardation. Journal of Autism and Developmental Disorders, 33(3), 349-354.

Keppra, levetiracetam [product information]. Keppra UCB Pharma, Smyrna (GA), 2010.

Kerr M. (1996) Epilepsy in people with learning disability. Aspects of Epilepsy, 3,1 –6.

Khurana, D.S., Riviello, J., Helmers, S., Holmes, G., Anderson, J., & Mikati, M. (1996). Efficacy of gabapentin therapy in children with refractory partial seizures. Journal of pediatrics, 128(6), 829-833.

Letcher, M. G. (2005). Epilepsy. In B. Narins (Ed.), The Gale Encyclopedia of Genetic Disorders (2nd ed., Vol. 1, pp. 422-425). Detroit: Gale.

Living with Epilepsy. (2010). In J. B. Shannon (Ed.), Health Reference Series. Brain Disorders Sourcebook (3rd ed., pp. 541-546). Detroit: Omnigraphics.

Martin, P., Schreiner, A., Rettig, K., & Schauble, B. (2009). Topiramate in patients with epilepsy and intellectual disability. Epilepsy Behavior, 14(3), 496-502.

Matson, J. L., Luke, M. A., & Mayville, S. B. (2004). The effects of antiepileptic medications on the social skills of individuals with mental retardation. Res Dev Disabil, 25(2), 219-228.

Matson, J.L, Mayville, E.A, & Bamburg, J.W. (2001). An analysis of side effect profiles of anti-seizure medications in persons with intellectual disability using the matson evaluation of drugs side effects. Journal of intellectual and developmental disability, 26(4), 283-295.

McGrother, C. W., Bhaumik, S., Thorp, C. F., Hauck, A., Branford, D., & Watson, J. M. (2006). Epilepsy in adults with intellectual disabilities: Prevalence, associations and service implications. Seizure, 15(6), 376-386.

McKee, J.R., Sunder, T.R, Vuong, A., & Hammer, A.E. (2004). Adjunctive lamotrigine for refractory epilepsy in adolescents with mental retardation. Journal of child neurology, 21(5), 372-379.

Motamedi, G., & Meador, K. (2003). Epilepsy and cognition. Epilepsy & Behavior, 4, 25-38.

Mula, M., Trimble, M. R., & Sander, J. W. A. S. (2004). Psychiatric adverse events in patients with epilepsy and learning disabilities taking levetiracetam. Seizure, 13(1), 55-57.

O'Dell, C., Wheless, J. W., & Cloyd, J. (2007). The personal and financial impact of repetitive or prolonged seizures on the patient and family. J Child Neurol, 22(5 Suppl), 61S-70S.

Pedley, T. A., & Engel, J. (1998). Epilepsy: a comprehensive textbook. Philadelphia: Lippincott-Raven.

Richarson, S.A., et al. (1979). Some characteristics of a population of mentally retarded young adults in a british city: A basis for estimating some service needs. Journal of Intellectual Disability Research, 23(4), 275-285.

Singh, B. K., & White-Scott, S. (2002). Role of topiramate in adults with intractable epilepsy, mental retardation, and developmental disabilities. Seizure, 11(1), 47-50.

Treating Epilepsy. (2010). In J. B. Shannon (Ed.), Health Reference Series. Brain Disorders Sourcebook (3rd ed., pp. 527-540). Detroit: Omnigraphics.

Webster, N. J. (2008). Epilepsy. In Y. Zhang (Ed.), Encyclopedia of Global Health (Vol. 2, pp. 617-618). Thousand Oaks, CA: SAGE Publications.

What Is Epilepsy? (2010). In J. B. Shannon (Ed.), Health Reference Series. Brain Disorders Sourcebook (3rd ed., pp. 519-525). Detroit: Omnigraphics.

Wilfong, A. A. (2002). Treatment considerations: role of vagus nerve stimulator. Epilepsy & Behavior, 3(6, Supplement 1), 41-44.