Autistic regression and Landau–Kleffner syndrome: progress or confusion?

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The autistic spectrum/pervasive developmental disorders (termed autism here) are neurobehavioral conditions which are characterized by severe qualitative impairments in social reciprocity and communication, associated with stereotypical behaviors and interests[1]. Autism is frequently combined with other symptoms of neurological dysfunction, including abnormal electroencephalograms (EEGs) and clinical seizures in at least 50% of affected individuals[2,3]. A subgroup of children who develop the impairments of autism after initially normal development (termed 'autistic regression') is of particular interest[4,5]. These children have an increased incidence of abnormal EEGs similar to those found in individuals with Landau–Kleffner syndrome (LKS) (acquired epileptiform aphasia)[6,7]. Recognition of overlapping clinical and electrophysiological features in these two conditions has led to speculation that there may be a pathophysiological relationship between them. This commentary will discuss the diagnosis and treatment of autistic regression (AR) and LKS, to provide a clinical perspective on their sometimes confusing relationships.

Interictal epileptiform discharges and their neuropsychological effects

During seizures, excessively synchronized neuronal activity – ictal discharge – produces sustained epileptiform activity on EEGs and coincident clinical symptomatology. Identical epileptiform patterns, spikes and sharp waves, also occur as interictal epileptiform discharges (IEDs) which are generally less prolonged and, by definition, clinically silent. The pattern, frequency, and topography of IEDs vary considerably among individuals with different forms of clinical epilepsy, but IEDs also occur in individuals without manifest seizures. At least 3% of normally developing children, 10% of children with migraine, and 15% with autism without epilepsy have spikes on their EEGs[2,8,9]. Therefore, the occurrence of epileptiform activity is not specific for clinical seizures.

Although often asymptomatic, IEDs have also been associated with transient cognitive impairment (TCI), chronic developmental dysphasia, and developmental regression[10,11]. Simultaneous EEG and continuous performance testing have documented the following TCIs: delayed reaction time, reduced memory function, and poor performance on spatial- and verbal-response tasks with both generalized and localized epileptiform discharges despite the absence of otherwise detectable seizures[12–14]. Conversely, neuropsychological measures of short-term memory and academic achievement scores have improved after suppression of epileptiform discharges using valproic acid[14,15]. Additionally, prominent IEDs have been observed in association with delayed and aberrant language development in several studies[11,16,17]. These observations emphasize the importance of detailed analyses of individuals' cognitive functioning as well as the possibility of chronic developmental effects in the setting of severely abnormal EEGs. These data have to some extent challenged the distinctions between ictal and interictal discharges, the definitions of clinical and subclinical seizures, and the clinical axiom to avoid 'treating the EEG'.

Lastly, prominent IEDs have been associated with developmental regression in a number of childhood epilepsies. In addition to LKS, other regressive syndromes such as infantile spasms, Lennox–Gastaut syndrome, Rassmussen's encephalitis[18], continuous spike-wave syndrome of slow-wave sleep, Rolandic epilepsy with speech dyspraxia/opercular syndrome, and cognitive regression with occipital epileptiform discharges are also noteworthy[19–25]. The etiologies underlying the epileptiform activity in these conditions are quite heterogeneous, but important clinical variables contributing to their symptomatology and prognosis include the patient's age at onset and the intensity, location and duration of IEDs, particularly during sleep.

Autistic regression

Among children with autism at least 30% develop normally or nearly normally during the first year or two of life before developmental skills regress[26,27]. Importantly, their regression is not limited to language but also includes dramatic deterioration of social interaction and cognitive abilities. This process can occur acutely or insidiously and usually begins between 18 and 24 months of age. When the regression begins after the age of 2 years, the Diagnostic and Statistical Manual of Mental Disorders – 4th Edition (DSM-IV) designation of childhood

disintegrative disorder applies[1,28]. Because no separate DSM category exists for children whose onset is before the age of 24 months, the term autistic regression (AR) has been used for this group. Children with AR lose previously acquired speech and verbal understanding, withdraw from social contact, and lose their interest in toys.

Autistic regression is difficult to recognize initially and in most cases is only identified retrospectively when the child is referred for developmental evaluation. In most cases, no cause of the regression can be identified, although several rare metabolic and degenerative disorders may also occur in this age group[29]. The pathophysiology AR remains unknown, and remained relatively unstudied until the 1990s. Sleep EEGs and functional neuroimaging studies have recently identified several abnormalities in children with AR. These findings include focal and multifocal epileptiform activity on EEG and magnetoencephalography (MEG), as well as metabolic disturbances in one or both centrotemporal regions with single photon emission computerized tomography (SPECT)[30–32]. These data have suggested the possibility of an electrophysiological disruption of normal brain development analogous to that in LKS as a contributing cause of AR.

To evaluate this hypothesis, Tuchman and Rapin studied a cohort of more than 500 children with autism and correlated the incidence of prior autistic regression with the presence of clinical seizures and/or epileptiform EEGs[6]. Statistical analysis excluding the children with clinical seizures identified a significant correlation between those with AR and epileptiform EEGs. In the 335 children without epilepsy, the percentage of those with AR who had undergone epileptiform sleep EEGs was significantly higher than those without regression (19% versus 10%). Due to the retrospective nature of the study, however, the timing, duration, and recording conditions of the EEGs were inconsistent. The potential importance of these factors is indicated by a 46% incidence of epileptiform activity in children studied with an overnight EEG compared with only 14% in those with a 1-hour sleep study[2]. Additional support for a high incidence of epileptiform activity in prolonged sleep EEGs of these children also comes from a multicenter study which evaluated 50 children with AR and identified epileptiform abnormalities in 68% by EEG and 82% by MEG[7].

Landau–Kleffner syndrome

Landau–Kleffner syndrome, acquired epileptiform aphasia, is the prototype of disorders with epileptiform regression. This condition was initially described more than 40 years ago in six children attending a school for the hearing impaired[33]. Although they had unaffected hearing and previously normal language development, these children had lost their ability to understand and produce oral language in association with severely abnormal EEGs. In their original paper, Landau and Kleffner suggested that the children's language regression might be due to 'persistent convulsive discharge in brain tissue largely concerned with linguistic communication result[ing] in the functional ablation of these areas for normal linguistic behavior' (p 529). Subsequently, a follow-up study of these patients and three additional patients noted a variable prognosis and questioned whether recovery might depend on anticonvulsant treatment and/or compensatory neuropsychological processes involving non-linguistic abilities[34].

Although a rare disorder, LKS has attracted worldwide attention as a result of its unusual pathophysiology, dramatic clinical features, and variable prognosis[35–38]. The suggestion that language deficits are caused by IEDs which interfere with linguistic processing has received considerable support and prompted various pathophysiological hypotheses[36,39]. A recent and particularly intriguing hypothesis has proposed that the epileptiform discharges may produce long-term dysfunction by preventing appropriate involution of synaptic pathways at critical stages of brain development[40,41].

The usual age at onset of LKS is between 4 and 7 years, although atypical cases beginning before the age of 3 years or after 9 years have also been described. Affected children often appear as if they have become deaf due to their failure to respond to verbal language (verbal auditory agnosia) and they also frequently exhibit serious behavioral abnormalities including hyperactivity, withdrawn behavior, and temper outbursts. Nonetheless and most importantly however, these children retain their social awareness, use of gestures, and measured cognitive abilities on standardized tests of non-verbal skills. Additionally, children with LKS maintain their prior interest in toys, interactive games, and imaginative play. Therefore, their older age at onset and preserved developmental abilities in non-verbal areas usually serve to readily distinguish such children from those with autistic regression.

In association with their aphasia, children with LKS usually show considerable epileptiform activity on their EEGs. At least 70% of children have clinical seizures which are usually simple or complex partial seizures, and/or atypical absence seizures. Despite the ease of clinical seizure control in most affected children and the absence of seizures in a significant minority, their EEGs are generally resistant to the effects of anticonvulsant medications. EEG findings are most striking during sleep and include spikes and spike-wave complexes overlying both perisylvian brain regions which subserve language and auditory processing functions[42,43]. MEG studies also show bilateral epileptiform activity with consistent involvement of the left perisylvian region[7]. Despite the typically bilateral distribution of these findings, detailed electrophysiological evaluation using methohexitol and barbiturate suppression techniques have shown a unilateral epileptogenic focus in most patients in one series[40].

Interestingly, awake EEGs obtained in the early stages of LKS may also show isolated or unilateral perisylvian spike discharges. Sleep EEGs nonetheless, show extremely frequent or even constant bilateral electrocerebral seizure activity despite the absence of clinical seizures. This EEG pattern is defined as continuous spike-wave syndrome of slow-wave sleep when such electrocerebral activity occurs during 85% or more of the deep sleep recording. Continuous spike-wave syndrome of slow-wave sleep occurs in several clinical forms including one which overlaps with LKS[44].

Although the relationship of EEG findings to the cause of LKS remains under evaluation, fluctuation in the aphasia has been temporally correlated to EEG changes[45,46]. Clinical improvement has also typically followed suppression of epileptiform activity by anticonvulsants, corticosteroids, and surgical elimination of epileptogenic discharge[40,47,48]. The prognosis of LKS is variable but generally better in those with fluctuating aphasia and worse in those with onset before age 5 years[49]. A significant minority of patients recover communication abilities to a considerable degree[34,50].

In LKS, standard brain imaging with computerized axial tomography or magnetic resonance imaging is usually normal, although there have been rare associations with localized infections, demyelination, and tumors[51–53]. Case series of children with LKS using positron emission tomography and SPECT have shown abnormalities of glucose uptake and cerebral perfusion in the temporal lobes[54–57]. The pathophysiology of these abnormalities and their relationship to the EEG findings and clinical manifestations of LKS remain under investigation.

Autistic regression versus Landau–Kleffner syndrome

In most cases, children with AR and children without autism with LKS can be distinguished easily on clinical grounds based on the obvious deterioration of social, cognitive, and symbolic play skills in the former. Additionally, children with LKS have well-established language development before onset and are therefore usually older than 3 years.

As the underlying pathophysiological mechanisms are not yet defined for either of these disorders, and given the probability that the electrophysiological disturbances result from various etiologies, the continued use of the traditional clinical criteria to distinguish and separate them appears to be the best approach. There are occasional cases with overlapping features, termed 'LKS-variants', but most of these conform more to AR and, in my opinion, should be so considered. Ultimately, improved diagnostic classification will follow better understanding of the relevant pathophysiologies. In the meantime, I recommend the use of the approach suggested by Tuchman[58] in which the umbrella term, acquired epileptiform aphasias is the broad category under which acquired epileptiform aphasia (LKS), autistic epileptiform regression (AR with epileptiform EEG), and disintegrative epileptiform regression (childhood disintegrative disorder with epileptiform EEGs) are described individually. This classification acknowledges the electrophysiological similarities of these disorders, while providing for appropriate clinical distinctions, and should enhance communication among clinicians and researchers involved in the care of affected children.

Treatment of autistic regression and Landau–Kleffner syndrome

Appropriate treatment recommendations for children with AR are problematic. A cause and effect relationship between autism and EEG abnormalities has not yet been established, and no prospective controlled studies have provided evidence-based treatment recommendations. Uncontrolled case series have reported mixed results in children with AR following various therapeutic approaches including anticonvulsant medications, steroids, and most recently, multiple subpial transection (MST) surgery[59–63]. In view of the absence of data documenting therapeutic efficacy and safety, all suggested medical therapies for children with AR should be regarded as unproven at the present time.

Medical therapy for children with LKS has been studied more completely, but no specific therapeutic approach has proven to be optimal in a controlled study. Treatment success in these children is currently defined as reduction or ablation of epileptiform EEG activity and/or clinical improvement in language abilities; both of which have been reported with a variety of agents. Children with LKS are often initially treated with 'spike suppressing' anticonvul-

sants such as valproic acid, ethosuximide, and benzodiazepines which generally control seizures but have a variable effect on language recovery. In recent years, corticosteroid therapy has again re-emerged and is often used as a first or second therapeutic option[30,47,64]. Additional treatments include vigabatrin, calcium-channel blockers, and intravenous gammaglobulin[65,66]. Several of our patients have also improved after treatment with the ketogenic diet, and others have reported similar results[67]. Because patients with LKS can experience spontaneous remission and long-term recovery, any uncontrolled claims of therapeutic efficacy remain open to question.

Most recently several children with LKS (in addition to others with AR) have been treated with MST surgery. Initially introduced by Morrell and coworkers for surgical therapy of intractable epilepsy, this technique is now being used in several centers[40,61,62,69]. In uncontrolled series, MST has been reported to produce encouraging levels of gradual postoperative linguistic improvement in children with classical LKS who had been previously resistant to medical treatments[40]. The single long-term follow-up study however shows less impressive results[70].

Based on reported case series and personal experience, I continue to favor attempts to normalize the EEG in children with LKS using valproic acid, prednisone, and the ketogenic diet as my favored options. In my opinion, the role of MST surgery is unproven at present. This approach may merit consideration in severely affected, medically intractable children or in those with dramatic initial improvements after medical therapy who suffer multiple relapses or intolerable side effects, but it clearly requires further study and scientific validation.

The goal of a rigorous prospective study comparing various treatments in patients with LKS has not been realized. Clearly, the small number of patients with LKS requires collaborative investigation but despite several hopeful beginnings, no such study has yet been performed. Including children with autism, autistic regression, and 'Landau–Kleffner-variants' as well as those with classical LKS in treatment groups will likely prove to be counterproductive in establishing scientifically validated therapies.

Summary

Definitive understanding of these conditions and their optimal therapy has not yet been achieved. There is no doubt that they are important disorders, considering their severe and often permanently disabling effects. Additionally, their potential importance in enlarging our understanding of the complex interrelationships between normal and pathological influences on neuropsychological development is considerable. Additional studies to define the pathophysiology and role of epilepsy in neuropsychological regression are of continuing interest and controlled treatment trials are vitally needed. All of us can agree that the hope of identifying effective therapy for these children mandates our continued interest and investigation.

References
1. American Psychiatric Association. (1994) *Diagnostic and Statistic Manual of Mental Disorders. 4th Edn. (DSM-IV)* Washington DC: American Psychiatric Association.

2. Tuchman R, Jayakar P, Yaylali I, Villalobos R. (1998) Seizures and EEG findings in children with autism spectrum disorder. *CNS Spectrums* **3:** 61–70.

3. Tuchman R, Rapin I, Shinnar S. (1991) Autistic and dysphasic children: II. Epilepsy. *Pediatrics* **6:** 1219–25.

4. Deonna T, Ziegler AL, Moura-Serra J, Innocenti G. (1993) Autistic regression in relation to limbic pathology and epilepsy: report of two cases. *Developmental Medicine & Child Neurology* **35:** 166–76.

5. Rapin I. (1995) Autistic regression and disintegrative disorder: how important the role of epilepsy. *Seminars in Pediatric Neurology* **2:** 278–85.

6. Tuchman R, Rapin I. (1997) Regression in pervasive developmental disorders: seizures and EEG correlates. *Pediatrics* **99:** 560–6.

7. Lewine JD, Andrews R, Chez M, Patil AA, Devinsky O, Smith M, Kanner A, Davis JT, Funke M, Jones G, et al. (1999) Magnetoencephalographic patterns of epileptiform activity in children with regressive autistic spectrum disorders. *Pediatrics* **104:** 405–18.

8. Cavazutti GB, Cappella L, Nalin A. (1980) Longitudinal study of epileptiform EEG patterns in normal children. *Epilepsia* **21:** 43–55.

9. Kinast M, Lueders H, Rothner D, Erenberg G. (1982) Benign focal epileptiform discharges in childhood migraine. *Neurology* **32:** 1309–11.

10. Deonna T. (1995) Cognitive and behavioral disturbances as epileptic manifestations in children: an overview. *Seminars in Pediatric Neurology* **2:** 254–9.

11. Parry-Fielder B, Nolan TM, Collins KJ, Stojcevski Z. (1997) Developmental language disorders and epilepsy. *Journal of Pediatrics and Child Health* **33:** 277–80.

12. Aarts JHP, Binnie CD, Smit AM, Wilkins AJ. (1984) Selective cognitive impairment during focal and generalized epileptiform EEG activity. *Brain* **107:** 293–308.

13. Binnie CD. (1993) Significance and management of transitory cognitive impairment due to subclinical EEG discharges in children. *Brain and Development* **15:** 23–30.

14. Kasteleijn-Nolst Trenite DAG. (1995) Transient cognitive impairment during subclinical epileptiform EEG discharges. *Seminars in Pediatric Neurology* **2:** 246–53.

15. Plioplys AV. (1994) Autism: EEG abnormalities and clinical improvement with valproic acid. *Archives of Pediatric Adolescent Medicine* **148:** 220–2.

16. Echenne B, Cheminal R,Rivier F, Negre C, Touchon J, Billiard M. (1992) Epileptic encephalographic abnormalities and developmental dysphasias: a study of 32 patients. *Brain and Development* **14:** 216–25.

17. Picard A, Heraut FC, Bouskraoui M, Lemoine M, Lacest P, Delattee J. (1998) Sleep EEG and developmental dysphasias. *Developmental Medicine & Child Neurology* **40:** 595–9.

18. Aicardi J. (1996) Epilepsy as a non-paroxysmal disorder. *Acta Neuropediatrica* **2:** 248–57.

19. Roulet E. (1995) Syndromes of acquired epileptic aphasia and epilepsy with continuous spike-waves during sleep: models for prolonged cognitive impairment of epileptic origin. *Seminars in Pediatric Neurology* **2:** 269–77.

20. Roulet Perez E, Davidoff V, Despland P, Deonna T. (1993) Mental and behavioral deterioration of children with epilepsy and CSWS: acquired epileptic frontal syndrome. *Developmental Medicine & Child Neurology* **35:** 661–74.

21. Jayakar P, Seshia S. (1991) Electrical status epilepticus during slow-wave sleep: a review. *Clinical Neurophysiology* **8:** 299–311.

22. Weglage J, Demsky A, Pietsch M, Kurlemann G. (1997) Neuropsychological, intellectual and behavioral findings in patients with centro-temporal spikes with and without seizures. *Developmental Medicine & Child Neurology* **39:** 646–51.

23. Deonna T, Roulet F, Fantan D, Marcoz JP. (l993) Speech and oral-motor deficits of epileptic origin in BPERS. *Neuropediatrics* **24:** 83–7.

24. Shafrir Y, Prensky AL. (1995) Acquired epileptiform opercular syndrome: a second case report, review of the literature, and comparison to the Landau–Kleffner syndrome. *Epilepsia* **36:** 1050–7.

25. Nass R, Gross A, Devinsky O. (1998) Autism and autistic epileptiform regression with occipital spikes. *Developmental Medicine & Child Neurology* **40:** 453–8.

26. Gillberg C, Coleman M. (1992) *The Biology of the Autistic Syndromes. 2nd Edition*. *Clinics in Developmental Medicine No. 126.* London: Mac Keith Press.

27. Rogers SJ, DiLalla DL. (1990) Age of symptom onset in young children with pervasive developmental disorders. *Journal of the American Academy of Child and Adolescent Psychiatry* **29:** 863–72.

28. Volkmar F, Cohen D. (1989) Disintegrative disorder as "late onset" autism. *Child Psychology and Psychiatry* **30:** 717–24.

29. Lyon G, Adams RD, Kolodry EH. (1996) *Neurology of Hereditary Metabolic Diseases of Children. 2nd Edition.* New York: McGraw-Hill.

30. Chez M. (1996) Clinical spectrum of patients referred for Landau–Kleffner Syndrome previously diagnosed with PDD or autism. *Annals of Neurology* **40:** l14. (Abstract.)

31. Nass R, Gross A, Devinsky O. (1998) Patterns of EEG abnormalities in autistic spectrum disorder: correlation with clinical status and outcome. *Annals of Neurology* **44:** 578. (Abstract.)

32. O'Regan ME, Braun JK, Goodwin GM, Clarke M. (1998) Epileptic aphasia: consequence of regional hypometabolic encephalopathy. *Developmental Medicine & Child Neurology* **40:** 508–16.

33. Landau WM, Kleffner FR. (1957) Syndrome of acquired aphasia with convulsive disorder in children. *Neurology* **7:** 523–30.

34. Mantovani JF, Landau WM. (1980) Acquired aphasia with convulsive disorder: course and prognosis. *Neurology* **30:** 524–9.

35. Gordon N. (1990) Acquired aphasia in childhood: the Landau–Kleffner syndrome. *Developmental Medicine & Child Neurology* **32:** 267–74.

36. Deonna TW. (1991) Acquired epileptiform aphasia in children (Landau–Kleffner syndrome). *Clinical Neurophysiology* **8:** 288–98.

37. Paquier PP, VanDongen HR, Loonen CB. (1992) The LandauKleffner syndrome or 'acquired aphasia with convulsive disorder': long-term follow-up of six children and a review of the recent literature. *Archives of Neurology* **49:** 354–9.

38. Kaga M. (1999) Language disorders in Landau–Kleffner syndrome. *Journal of Child Neurology* **14:** 118–22.

39. Maquet P, Hirsch E, Dive D, Salmon E, Marescaux C, Franck G. (1990) Cerebral glucose utilization during sleep in Landau–Kleffner syndrome: a PET study. *Epilepsia* **31:** 778–83.

40. Morrell F, Whisler WW, Smith MC, Hoeppner TJ, deToledo-Morrell L. (1995) Landau–Kleffner syndrome: treatment with subpial intracortical transection. *Brain* **118:** 1529–46.

41. Gordon N. (1997) The Landau–Kleffner Syndrome: increased understanding. *Brain and Development* **19:** 311–16.

42. Nakano S, Okuno T, Mikawa H. (1989) Landau–Kleffner syndrome: EEG topographic studies. *Brain and Development* **11:** 43–50.

43. Stefanatos GA. (1993) Frequency modulation analysis in children with Landau–Kleffner syndrome. *Annals of the New York Academy of Sciences* **682:** 412–14.

44. Rintahaka PJ, Chugani HT, Sandar R. (1995) Landau–Kleffner syndrome with continuous spikes and waves during slow-wave sleep. *Journal of Child Neurology* **10:** 127–33.

45. Lanzi O, Veggiotti HR, Conte S, Partesana E, Resi C. (1994) A correlated fluctuation of language and EEG abnormalities in a case of Landau–Kleffner syndrome. *Brain and Development* **16:** 329–34.

46. Ming L, Xiao-yu H, Jiong I, Xi-vu W. (1996) Correlation between CSWS and aphasia in Landau–Kleffner Syndrome: a study of 3 cases. *Brain and Development* **18:** 197–200.

47. Lerman P, Lerman-Sagie T, Kivity S. (1991) Effect of early corticosteroid therapy for Landau–Kleffner syndrome. *Developmental Medicine & Child Neurology* **33:** 257–60.

48. Zardini G, Molteni B, Nardocci N, Sarti D, Avanzini G, Granata T. (1995) Linguistic development in a patient with Landau–Kleffner syndrome: nine year follow-up. *Neuropediatrics* **26:** 19–25.

49. Bishop DV. (1985) Age of onset and outcome in 'acquired aphasia with convulsive disorder' (Landau–Kleffner syndrome) *Developmental Medicine & Child Neurology* **27:** 705–12.

50. Soprano AM, Garcia EF, Caraballo R, Fejerman N. (1994) Acquired epileptic aphasia: neuropsycholgic follow-up of 12 patients. *Pediatric Neurology* 11: 230–5.
51. Perniola T, Margari L, Buttiglione M, Andreula C, Simone IL, Santostasi R. (1993) A case of Landau–Kleffner syndrome secondary to inflammatory demyelinating disease. *Epilepsia* 34: 551–6.
52. Otero E, Cordova S, Diaz F. (1989) Acquired epileptic aphasia (Landau–Kleffner syndrome) due to neurocysticercosis. *Epilepsia* 30: 569–72.
53. Nass R, Heier L, Walker R. (1993) Landau–Kleffner syndrome: temporal lobe tumor resection results in good outcome. *Pediatric Neurology* 9: 303–5.
54. Maquet P, Hirsch E, Metz-Lutz MN, Motte J, Dive D. (1995) Regional cerebral glucose metabolism in children with deterioration of one or more cognitive functions and continuous spike-wave discharges during sleep. *Brain* 118: 1497–520.
55. O'Tuama LA, Urion DK, Janicek MJ, Treves ST, Bjornson B, Moriarity JM. (1992) Regional cerebral perfusion in Landau–Kleffner syndrome and related childhood aphasias. *Journal of Nuclear Medicine* 33: 1758–65.
56. Guerreiro MM, Camargo EE, Kato M, Menezes Netto JR, Silva EA, Scotoni AE, Silveira DC, Guerreiro CA. (1996) Brain single photon emission computer tomography imaging in Landau–Kleffner syndrome. *Epilepsia* 37: 60–7.
57. DaSilva EA, Chugani D, Muzik O, Chugani H. (1997) Landau–Kleffner syndrome: metabolic abnormalities in temporal lobe are a common feature. *Journal Of Child Neurology* 12: 489–95.
58. Tuchman R. (1997) Acquired epileptiform aphasia. *Seminars in Pediatric Neurology* 4: 93–101.
59. Stefanatos GA, Grover W, Geller E. (1995) Case study: corticosteroid treatment of language regression in pervasive developmental disorder. *Journal of the American Academy of Child and Adolescent Psychiatry* 34: 1107–11.
60. Chez MG, Loeffel M, Buchanan CP. (1998) Pulse high dose steroids in combination therapy with valproic acid in epileptic aphasia patients with PDD or autism. *Annals of Neurology* 44: 539. (Abstract.)
61. Neville BG, Harkness WF, Cross JH, Cass HC, Burch VC, Lees JA, Taylor DC. (1997) Surgical treatment of severe autistic regression in childhood epilepsy. *Pediatric Neurology* 16: 137–40.
62. Nass R, Gross A, Wisoff J, Devinsky O. (1998) Autistic epileptiform regression: response to multiple subpial resections. *Annals of Neurology* 44: 554. (Abstract.)
63. Patil AA, Andrews R. (1998) Surgical treatment of autistic epileptiform regression. *Journal of Epilepsy* 11: 1–6.
64. McKinney W, McGreal DA. (1974) An aphasic syndrome in children. *Canadian Medical Assocociation Journal* 110: 637–9.
65. Appleton R, Hughes A, Beirne M, Acomb B. (1993) Vigabatrin in the Landau–Kleffner syndrome. *Developmental Medicine & Child Neurology* 35: 457–8.
66. Fayad MN, Choueiri R, Mikati M. (1997) Landau–Kleffner syndrome: consistent response to repeated intravenous gammaglobulin doses: a case report. *Epilepsia* 38: 489–94.
67. Bergqvist AGC, Brooks-Kayal AR. (1997) Ketogenic diet in the treatment of acquired epileptic aphasia. *Annals of Neurology* 42: 504. (Abstract.)
68. Morrell F, Whisler WW, Bleck TP. (1989) Multiple subpial transection: a new approach to the surgical treatment of focal epilepsy. *Journal of Neurosurgery* 70: 231–9.
69. Sawhney IM, Robertson IJ, Polkey CE, Binnie CD, Elwes RD. (1995) Multiple subpial transections: a review of 21 cases. *Journal of Neurology, Neurosurgery and Psychiatry* 58: 344–9.
70. Grete CL, VanSlyke P, Hoeppner JAB. (1999) Language outcome following multiple subpial transection for Landau–Kleffner syndrome. *Brain* 122: 561–6.

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Erratum

'Respiratory sinus arrhythmia during feeding: a measure of vagal regulation of metabolism, ingestion, and digestion in preterm infants'
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