2003

Psychosocial subtyping and brain metabolism in children with epilepsy.

David W. Collins
University of Windsor

PSYCHOSOCIAL SUBTYPING AND BRAIN METABOLISM IN CHILDREN WITH EPILEPSY

by

David W. Collins

A Dissertation
Submitted to the Faculty of Graduate Studies and Research
through the Department of Psychology
in Partial Fulfillment of the Requirements for
the Degree of Doctor of Philosophy at the
University of Windsor

Windsor, Ontario, Canada

2003

Your file Votre référence
ISBN: 0-612-96368-3
Our file Notre référence
ISBN: 0-612-96368-3

Abstract

Past research has indicated that psychosocial dysfunction in children with epilepsy is a significant area of concern. Psychosocial functioning in children with epilepsy has typically been broadly defined in relation to various control groups. The present investigation provided a more multidimensional classification to examine psychosocial functioning in these children. In Study 1, behavioural ratings from the Personality Inventory for Children–Revised (PIC-R) were subjected to cluster analyses, yielding a psychosocial typology. Based on clinical scale elevations of the mean PIC-R profiles, the participants were classified into six subtypes of psychosocial functioning: Cognitive-Somatic, Cognitive-Internalized, Cognitive-Externalized, Cognitive-Social Isolation, Internalized Psychopathology, and Somatic Concern. A second study was conducted to examine the relation between PET indices of brain metabolism and the psychosocial subtypes derived in Study 1. The finding indicated that four of the psychosocial subtypes were differentiated from controls by decreased glucose metabolism in specific brain areas. The heterogeneity of psychosocial deficits in children with epilepsy and the possible neural substrate contributing to such pattern of deficits were discussed.

Acknowledgments

First, I would like to thank my advisor Byron Rourke for his encouragement, guidance, and humour throughout my doctoral studies. He has greatly influenced my views of both child neuropsychology, and developmental psychology in general. Byron has always tried to instill in his students the notion that the questions we ask, and not the answers, are of most importance. He has also taught me everything one has to know about Canadian jazz (the answer is always "Oscar Peterson").

I would like to thank Robert Rothermel, at the Children's Hospital of Michigan, for allowing me to use data collected in his lab, and for his general support and enthusiasm about this project. I would also like to thank Harry and Diane Chugani for providing me with PET data, and Michael Behen for helping me analyze these complex data.

I would like to thank members of my committee, Joe Casey, Darren Fuerst, Noel Hurley, Noel Williams, and Keith Yeates for their valued contributions to this dissertation.

I would also like to thank my family and friends, for their patience, support and encouragement throughout the years. In particular, I would like to express my deepest gratitude to my wife Julie, whom I consider my *sine qua non*. She has provided support, inspiration, and invaluable assistance through this endeavour. Thank you.

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Introduction

Epilepsy is considered one of the most common neurological disorders worldwide, and has been identified as an important problem for world mental health (Andermann, 2000). Overall prevalence rates vary, but are generally between 0.3 and 3% of the population. It most often manifests in childhood or adolescence (Williams & Sharp, 2000). In the United States, epilepsy occurs in 4 of 1000 children, with a lifetime prevalence of 4-9 per 1000 in 10-year-old children (Hauser & Hesdorffer, 1990). The negative impact of epilepsy in children includes problems in cognition, behaviour, adaptive functioning, and social competence. Given the high incidence of epilepsy in children and the potential sequelae of this disorder, continued study of pediatric epilepsy is warranted.

Because of interest in the cognitive and psychosocial consequences of childhood epilepsy, neuropsychologists have figured prominently in the study, assessment, and treatment of individuals with seizure disorders (Haynes & Bennett, 1992). Psychosocial functioning in particular has become an important area of study for neuropsychologists, who have increasingly focused on social development and adaptation to informal learning situations as key areas of functioning (Davis, Parr, & Lan, 1997; DeLuca, Rourke, & Del Dotto, 1991; Rourke, 1995; 1999).

There is now much evidence to suggest that psychosocial difficulties may be the most significant sequelae of epilepsy. Although there has been much research addressing psychosocial functioning in children with epilepsy, the approach to measuring such functioning has been quite variable across studies. Often, investigators have used open-ended questionnaires or brief rating scales and have studied children with epilepsy using a contrasting-groups approach. As a result, psychosocial functioning in children with epilepsy has typically been broadly defined relative to various control groups.

There is an increasing trend in research towards a multietiological approach to studying the impact of epilepsy on a variety of outcome measures (Hermann, Whitman, & Anton, 1992). While more attention is now being directed toward the potential risk factors of behavioural difficulties in children with epilepsy, little is understood regarding how neurological factors contribute to psychosocial difficulties in these children. Direct

measures of brain function are seldom included as potential risk factors for neuropsychological dysfunction, either cognitive or psychosocial.

The prevailing approach to studying the neurological contribution to psychological functioning has been to examine seizure variables as predictors of psychosocial outcome. However, this view may be overly simplistic. Although seizures may contribute to brain dysfunction, there is evidence that neurological dysfunction in individuals with epilepsy is not limited to seizure activity. Thus the nature of seizure activity may be only a crude marker of the underlying brain dysfunction. A potentially important risk factor for psychological and social problems in epilepsy is alterations in the efficiency of cerebral metabolism (Hermann, Whitman, & Anton, 1992).

This paper begins with an overview of psychosocial functioning and brain metabolism in children with epilepsy. This consists of a summary of the general features of epilepsy, followed by a review of brain metabolism and psychosocial difficulties in children with this disorder. The purpose of this review is to demonstrate the theoretical and empirical basis for advancing a more comprehensive brain-behaviour investigation of psychosocial functioning in this population. Following this general review, findings from two novel studies addressing psychosocial functioning and brain metabolism in children with epilepsy are presented.

General Features of Epilepsy

The term epilepsy refers to any condition of recurrent high voltage cerebral discharges of sudden onset and cessation (Caplan, 1998). Such discharges are referred to as seizures. Burst of synchronous neuronal firing become progressively more active, and may recruit other neurons. Seizures may spread throughout the brain through cortical projections, or to the contralateral hemisphere via the corpus callosum, and the anterior and posterior commissures.

The neurophysiological mechanisms underlying seizures are not fully understood. Seizure activity may arise from some specific cerebral abnormalities, including congenital anomalies related to dysfunctional neuronal development, ischemic and hypoxic cellular injury, hemorrhage, metabolic disturbances, toxicity, trauma, and CNS infections (Barron, Fennell, & Voeller, 1995). There are numerous abnormalities at the cellular level that may contribute to epileptogenic activity. Defects in ion channels (e.g.,

sodium, potassium, calcium) may result in excessive depolarization and a tendency for epileptiform activity (Williams & Sharp, 2000). Excessive excitatory neurotransmitter (glutamate and aspartate) and/or deficient inhibitory neurotransmitter (γ-aminobutyric acid (GABA) and glycine) activity may also result in seizure activity (McIntosh, 1992). Indeed, the effectiveness of many anti-convulsant drugs may be related to enhancement of GABA systems. Activity in subcortical structures such as the thalamus and basal ganglia has also been linked to the initiation, propagation and suppression of seizure activity (Baron et al., 1995). Although epilepsy has often been viewed as an imbalance between excitatory and inhibitory neurophysiological systems, this may be an oversimplification. It is likely that different mechanisms underlie epileptogenesis in different seizure disorders.

Controversy exists as to whether seizures *per se* damage the developing brain. There is evidence that continued seizures may be associated with progressive neuronal loss in the hippocampal formation in individuals with temporal lobe epilepsy (Gaillard, 2000). Findings from studies of brain volume using magnetic resonance imaging (MRI) suggest that recurrent seizures in adults, particularly generalized and in males, can damage the brain (Meldrum, 2001). There is also evidence from animal studies that seizures during early development have long-term detrimental effects on brain development (Holmes, Gairsa, Chevassus-Au-Louis, & Ben-Ari, 1998). However, it is difficult to separate the primary disease process in epilepsy from the consequences of seizure activity. That is, it is uncertain to what extent brain damage in epilepsy may be related to the cause versus the consequence of seizure activity.

Age appears to have a significant impact on the interaction between neuronal and seizure activity. The incidence of seizures is highest in the first decade of life and status epilepticus is more common in children than in adults (Holmes, 1997). Developmentally, ongoing seizure activity may significantly alter the structure and physiology of neural systems, and such alterations may modulate further seizure activity. Potential modulation mechanisms may include increased axonal branching, neuronal loss, astrocytic proliferation, and synaptic reorganization (Williams & Sharp, 2000). Animal studies have shown that the immature brain is more susceptible to seizures than the adult one, and that early seizures lower the threshold for seizures later in life (Holmes et al., 1998;

Moshé, Albala, Ackermann, & Engel, 1983). However, the immature animal brain appears considerably more resistant to injury from prolonged seizure than the adult brain (Camfield, 1997). There is a particular problem of generalizing findings to humans in this research area. In animal studies, seizures have been induced in young animals with otherwise healthy brains. In humans, most neonatal seizures are a result of underlying brain pathology.

An individual is typically diagnosed with epilepsy after two or more unprovoked seizures. The estimated risk of recurrence after a single seizure varies between 27% and 81% (MacDonald, 2001). The initial approach to diagnosis involves confirmation of abnormal electrical brain activity with EEG methods. Although scalp electrode EEG findings are used as the definitive marker for epileptogenesis, EEG results may be normal in a significant proportion of individuals with epilepsy (Williams & Sharp, 2000). Nonetheless, current nosological systems of epilepsy rely a great deal on EEG findings. Adjunctive neuroimaging studies may be used to address possible secondary etiologies, such as infections, vascular disorders, and metabolic abnormalities. Magnetic resonance imaging (MRI) has been used to rule out epileptogenic brain lesions such as tumors, infarcts, and cortical dysplaisias. Positron emission tomography (PET) and single-photon emission tomography (SPECT) have frequently been used in seizure foci detection.

The cornerstone of the clinical management of epilepsy is therapy with antiepileptic drugs (AEDs). Effective treatment of seizures with AEDs occurs in approximately 70-80% of the pediatric population (MacDonald, 2001; Williams & Sharp, 2000). However, AEDs can interfere with neurological and neuropsychological functioning. From a research point of view, this has made it difficult to disentangle the effects of epilepsy from the effects of AEDs on cognitive and motor functioning. Nonetheless, the deleterious effects of traditional AEDs have been studied, and are generally similar in both adults and in children. In general, phenobarbital has been consistently associated with detrimental cognitive effects, whereas valproate, carbamazepine, and phenytoin have fewer and less pronounced adverse effects (Baron et al., 1995; Bennett, 1992). Less is known concerning the sequelae of newer AEDs, such as gabapentin, and lamotrigine, although initial findings tend to show less adverse

cognitive and behavioural events compared to the traditional AEDs (Meador, Gilliam, Kanner, & Pellock, 2001).

Approximately 20-30% of children with epilepsy have medically resistant, or intractable seizures (Williams & Sharp, 2000). Surgery is a common alternative treatment, usually in the form of removal of brain tissue believed to be generating the seizures. Temporal lobe epilepsy accounts for the largest group of patients with medically intractable epilepsy who are successfully treated with neurosurgery. There is growing evidence that surgical intervention during childhood is relatively safe and that it is effective at reducing seizure frequency (Willie, 1998).

The Commission on Classification and Terminology of the International League Against Epilepsy (ILAE; 1989) has developed classification schemes for epilepsy both by seizure type and by etiology. When possible, epileptic disorders are classified by both schemes. With regard to etiology, the cause of recurrent seizures is considered either symptomatic or idiopathic. In symptomatic epilepsy, the cause is identified and may include structural brain anomalies, metabolic dysfunction, cerebral infarcts, CNS infections, or brain trauma. Only 30% of epilepsy cases are attributable to known causes, and children with symptomatic epilepsy tend to have seizures that are more treatment resistant (Williams & Sharp, 2000). The majority of children with epilepsy have seizures of unknown origin, referred to as idiopathic seizures.

Some forms of epilepsy appear to have an important genetic cause. There is evidence of a strong genetic component to idiopathic generalized epileptic disorders of childhood (Duchowny & Harvey, 1996). Further, some seizure types have been linked to specific chromosomes (Delgado-Escueta et al., 1994; Ronen, Rosales, Connolly, Anderson, & Leppert, 1993). Twin studies indicate that age of seizure onset may be genetically determined (Segal, Chapman, & Barlow, 1991).

The ILAE seizure-type classification scheme for epilepsy is based on the spread of the electrical discharge, either focal or widespread. Partial seizures are those that originate and remain localized to a specific area of the brain. Often such seizures are preceded by a specific symptom such as sudden anxiety, fear, dizziness, or some form of sensory experience. These preceding symptoms are referred to as "auras". The clinical manifestations of partial seizures, as well as the auras, often reflect the affected brain

areas. Partial seizures are further delineated into simple versus complex. With simple partial seizures, there is no loss of consciousness or amnesia for events during the seizure period. Complex partial seizures involve an alteration of consciousness, and often a temporary postictal (i.e., post-seizure) state of confusion and fatigue. Further, complex partial seizures are often accompanied or followed by automatic and repetitive behaviors, referred to as automatisms.

The other seizure type is more widespread, or generalized. Primary generalized epilepsy is characterized by synchronous bilateral electrical discharges in the brain. Seizure onset is sudden, without aura, and may involve loss of consciousness. If partial seizures subsequently spread to other brain areas, they are classified as secondarily generalized. Primary generalized seizures are further classified as absence, convulsive, atonic, or myoclonic type. Absence seizures (formerly "petit mal") are brief staring episodes involving sudden termination of activity. A common generalized convulsive type is the tonic-clonic seizure (formerly "grand mal"), a sudden tonic stiffening of the trunk and limbs followed by clonic rhythmic jerking. Atonic (or akinetic) seizures involve an abrupt loss of muscle tone that produces a fall. Myoclonic seizures are brief, single, symmetrical jerks involving the neck and upper extremities that occur after awakening.

Seizure type may be related to general prognosis, as there is some evidence linking worse outcomes with multiple seizure types, atonic seizures, infantile spasms, generalized atonic-clonic seizures, and status epilepticus (Macdonald, 2001). There are also specific epileptic syndromes that begin in childhood and follow a developmental course. The etiology of the various syndromes may be symptomatic or idiopathic. They are differentiated by seizure type, EEG correlates, age of seizure onset, clinical course, and neuropsychological functioning. Examples of epileptic syndromes are West syndrome (infantile spasms), Lennox-Gastaut syndrome, benign focal epilepsy of childhood, juvenile myoclonic epilepsy, and Landau-Kleffner syndrome.

Brain Metabolism in Children with Epilepsy

The last two decades have witnessed significant developments in medical brain imaging, particularly with the advent of noninvasive functional imaging techniques. These techniques have progressively transferred from research setting to clinical practice,

and from use exclusively in adults to use in children. Consequently, imaging studies now play an increasingly important role in the evaluation of children with epilepsy. One neuroimaging method frequently used in the study of epilepsy is positron emission tomography (PET).

PET is a neuroimaging technique that uses positron emittor tracers in order to map brain activity. PET techniques can be used to study a variety of brain processes, such as glucose and oxygen metabolism, protein synthesis, neurotransmitter uptake, and specific ligand binding (Richardson, 2001). Novel tracers continue to be developed to study epileptogenic cortex (Chugani & Chugani, 2000). Such agents include FMZ (^{11}C-flumazenil) for the study of GABA-benzodiazepine receptors, and AMT (α-[^{11}C]methyl-L-tryptophan) for the study of serotonin synthesis. One disadvantage to PET procedure is the need for radioactive agents, which prohibits normal control studies. Another problem with PET research is that this technique remains limited to a small number of centres.

PET techniques have been used in children to help identify the etiology of seizures in variable forms of epilepsy and epilepsy syndromes (Chugani, 1994). Most PET studies of epilepsy have traced glucose metabolism during interictal periods. Interictal PET studies of fluoro-deoxyglucose (FDG) indicate a 60-90% incidence of dysfunctional glucose utilization (hypometabolism) in the temporal lobes of individuals with temporal lobe epilepsy (Richardson, 2001). Although this has been reported in both adults and children, children with recent-onset epilepsy appear to have less frequent and less pronounced metabolic abnormalities compared to adults with chronic epilepsy (Gaillard, 2000).

Hypometabolic PET zones correspond to the locations of the epileptogenic foci, and typically extend beyond the ictal onset area. These findings of super-ictal hypometabolism have precluded the use of PET to define epileptogenic boundaries for surgical resection. It is presently unclear to what extent cortical areas of hypometabolism may be of clinical prognostic value in terms of surgical outcome in epilepsy patients (Chugani, 1994; Richardson, 2001).

There have been few reports on the neuropsychological correlates of brain metabolism in epilepsy. Kikuchi, Kubota, Hattori, Oya, and Mikuni (2001) found that abnormal temporal lobe metabolism ipsilateral to the seizure focus was related to lower

performance on neuropsychological measures of intelligence and memory in adults with temporal lobe epilepsy. Salanova et al (1992) reported that lateralized memory impairments, determined through intracarotid sodium amytal procedures, were associated with ipsilateral temporal lobe PET hypometabolism, but were not found contralateral to the hypometabolic zone. Rausch, Henry, Ary, Engel, and Mazziotta (1994) found that relative PET hypometabolism of the left hemisphere correlated with lower cognitive performance in 13 adults with unilateral temporal lobe epilepsy. Moreover, hypometabolism of the left lateral temporal lobe and thalamus were independently associated with verbal memory difficulties.

Lee et al. (2001) reported an association between cognitive performances, epilepsy, and brain metabolism in children with Sturge-Weber syndrome. Specifically, they found that higher overall IQ was associated with a shorter duration of epilepsy, and larger brain areas of significantly asymmetric metabolism. This suggested that chronicity of epilepsy may contribute to cognitive decline, and that severely hypometabolic cortex may facilitate effective functional brain reorganization processes in young children. However, children with Sturge-Weber syndrome have associated neurological problems not typically seen in idiopathic epilepsy (e.g., angiomas), and tend to have overall impaired intellectual functioning.

Overall, PET studies have established that cerebral metabolic dysfunction is commonly found in patients with epilepsy. Moreover, these metabolic anomalies usually extend beyond the seizure foci. The clinical and neuropsychological significance of these hypometabolic zones are currently under investigation. There is some indication that lateralization of these metabolic anomalies may be related to cognitive functioning.

Overview of Cognitive Sequelae of Epilepsy

Children with epilepsy are at high risk for academic difficulties (Bennett, 1992; Dodson, 1993; Williams & Sharp, 2000). Children with epilepsy have been found to be at greater academic risk than children with other chronic diseases, such as asthma (Austin, Huberty, Huster, & Dunn, 1998). A number of possibilities have been suggested, including a variety of clinical seizure variables as well as non-seizure variables.

In terms of clinical seizure variables, age of seizure onset appears to be an important determinant of neuropsychological impairment across a variety of seizure types (O'Leary et al., 1983; Strauss, Hunter, & Wada, 1995). However, seizure type and location are not generally related to either general IQ performance or academic achievement. Studies showing a relation between age of seizure onset and IQ may be confounded by the inclusion of children with neurodevelopmental disorders (Williams & Sharp, 2000).

With regard to non-seizure variables, studies have examined both cognitive and psychosocial functioning. Patients with well-controlled epilepsy rarely demonstrate significant impairment in general intellectual functioning (Bourgeois, Prensky, Palkes, Talent, & Busch, 1983; Camfield et al., 1984; Smith, Craft, Collins, Mattson, & Cramer, 1986). The evidence appears to converge on the presences of circumscribed deficits in memory, attention, and language function (Aldenkamp, Alpherts, Dekker, & Overweg, 1990; Jambaque, Dellatolas, Dulac, Ponsot, & Signoret, 1993; Milberg, Grieffenstein, Lewis, & Rourke, 1980; Quadfasel & Pruyer, 1955; Schoenfeld et al., 1999; Semrud-Clikeman & Wical, 1999).

In addition to cognitive factors, there is evidence that psychosocial factors may be important determinants of academic performance. Sturniolo and Galletti (1994) found that children with epilepsy who were performing poorly at school had difficulty with emotional adjustment, in addition to deficits in attention and visual motor functioning. Seizure-related variables were not associated with academic performance in these children. Mitchell, Chavez, Lee, and Guzman (1991) also reported that psychosocial variables, and not seizure variables, were major determinants of academic achievement. It is noteworthy that while most children with epilepsy have normal intelligence and stable intellectual ability, a large number of them appear to be at high risk of psychosocial difficulties (Rugland, 1990).

Psychosocial Functioning in Children with Epilepsy

General findings

Throughout much of the 20th century it had been held that epilepsy was associated with a specific behavioral profile, the so-called "epileptic personality". This notion then became limited to individuals with temporal lobe epilepsy (i.e., temporal lobe epilepsy

personality). However, the existence of a characteristic behavioural syndrome that is associated with a particular form of epilepsy remains controversial, and largely unsupported (Devinsky & Najjar, 1999; Mungas, 1992). Nonetheless, there is much converging evidence in the literature that individuals with epilepsy show difficulties in specific areas of psychosocial functioning. Psychopathology, usually in the form of depression, and psychosocial problems are relatively frequent among adults with epilepsy (Kanner, 2001). Like adults, children with epilepsy appear particularly prone to psychosocial difficulties (Carleton-Ford, Miller, Brown, Nealeigh, & Jennings, 1995).

Children with a history of epilepsy have elevated rates of depression and anxiety (Ettinger, et al., 1998). Caregiver reports in these children typically involve significantly more internalizing than externalizing behaviour problems (Huberty, Austin, Risinger, & McNelis, 1992; McDermott, Mani, & Krishnaswami, 1995). Carleton-Ford et al. (1995) found that children with epilepsy have significantly more home behaviour problems, have more problems with impulsiveness, and are three times more likely to become depressed compared to healthy controls. Children with epilepsy also tend to have greater overall dissatisfaction with themselves compared to healthy controls (Margalit & Heiman, 1983). Dorenbaum, Cappelli, Keene, and McGrath (1985) reported that the highest risk for maladjustment in children with epilepsy is in social functioning. In comparison to the normative sample, children with epilepsy were more socially withdrawn, had fewer friends, and in general had less contact with other children. Similarly, Huberty, Austin, Harezlak, Dunn, and Ambrosius (2000) found that parents and teachers tend to rate social problems as the highest in children with epilepsy.

Parents of children with epilepsy often believe that epilepsy affects their children adversely, and tend to have lower expectations for these children compared to siblings (Hoare & Kerley, 1991). Children with epilepsy are rated by their parents as having less social competence and more behavioural problems than siblings (Schoenfeld et al., 1999). Careleton-Ford et al. (1995) have argued that to some extent, poor social and psychological adjustment result from self-fulfilling prophecies stemming from parental reactions to epilepsy. Parents and caregivers may unintentionally create or aggravate poor social and psychological adjustment because of low expectations and a tendency to overprotect these children.

It does not appear that the psychosocial difficulties associated with epilepsy are limited to the demands of having a chronic illness. Compared to children with other chronic illnesses such as asthma, children with epilepsy have lower self-esteem, higher levels of depression, and more school behaviour problems (Austin, 1989). Like epilepsy, asthma involves unpredictable episodes, regular medications, frequent medical attention, and frightening attacks. It thus appears that unique neurobiological and psychosocial factors contribute to behaviour problems in children with epilepsy (Austin, Risinger, & Beckett, 1992; Hermann & Whitman, 1984).

Social difficulties associated with epilepsy may first appear in childhood, but often progress into adulthood. Camfield, Camfield, Smith, Gordon, and Dooley (1993) studied social outcome in early adulthood of children with epilepsy and normal intelligence. They reported a high percentage of unfavourable outcomes in this group such as school failure, financial dependency, and social isolation. With the exception of a history of high seizure frequency, social outcomes were not related to biological factors. Rather, a history of learning disability was associated with poor social outcomes. Kokkonen, Kokkonen, Saukkonen, and Pennanen (1997) reported similar findings. They found that compared to controls, young adults with a history of childhood epilepsy were at risk for social adjustment problems, including school failure, dependent lifestyles, and low socio-economic status. Having epilepsy did not predispose individuals for poor social development; these risks were largely related to the presence of learning disabilities and low intellectual functioning. These findings suggested that neurological and cognitive impairments that may accompany epilepsy are important determinants of social development.

In sum, children with epilepsy show higher rates of psychosocial and behaviour problems than healthy children. Because there is little research on psychosocial subtyping in epilepsy, these psychosocial difficulties and problematic behaviours tend to be broadly defined. Behavioural problems and psychosocial functioning in children with epilepsy may best be viewed within a multifactorial model, involving neurobiological, medical, and psychosocial variables (Hermann et al., 1992).

Neurological correlates of psychosocial functioning

The relation between neurological status and psychosocial functioning is unclear. Most studies have only examined the impact of seizure-related variables on psychosocial functioning, and rarely has this been the primary focus of the study. Kokkonen et al. (1997) reported that individuals with localized types of epilepsy fared better in terms of social development than those with other forms. Similarly, Huberty et al. (1992) reported that teacher ratings of adaptive skills were significantly lower in children with secondary generalized epilepsy than in other forms of epilepsy.

Many studies have found seizure frequency to be a significant determinant of psychosocial functioning (Austin et al., 1992; Camfield et al., 1993; Schoenfeld et al., 1999). Schoenfeld et al. (1999) found that frequency of seizures during the preceding year emerged as the strongest predictor of behavioral difficulties, while age of seizure onset was the strongest predictor of cognitive impairment. In contrast, Hermann, Schwartz, Karnes, and Vahdat (1980) reported that later age of seizure onset was associated with behavioural problems more often than cognitive difficulties. It thus appears that there is a complex relation between cognitive functioning, psychosocial functioning, age of seizure onset, and seizure frequency.

Two studies have directly examined parental ratings of behaviour and brain glucose metabolism in children with epilepsy. Juhász, Behen, Muzik, Chugani, and Chugani (2001) used PET to investigate abnormal brain function in children with epilepsy and aggressive behaviours. Aggression was measured using a parental rating form, the Child Behaviour Checklist (CBCL; Achenback, 1991). They reported that children with epilepsy, aggressive behaviours, and pervasive developmental delays showed specific patterns of bilateral medial prefrontal and temporal glucose hypometabolism compared to controls. Moreover, the severity of aggression correlated inversely with cortical glucose metabolism in these brain areas.

Ferrie et al. (1997) also examined behaviour ratings and cerebral glucose metabolism in epilepsy. The participants were children with epileptic encephalopathies of idiopathic origin. The index used for adaptive behaviours was the Adaptive Behavior Composite score from the Vineland Adaptive Behavior Scales (Sparrow, Balla, & Cicchetti, 1984). Findings from the study showed that adaptive behaviours correlated

with the degree to which frontal lobe functioning deviated from control levels. Specifically, lower adaptive composite scores were associated with more abnormal frontal lobe metabolism. The majority of the frontal metabolic abnormalities were characterized as hypometabolic. It is of interest that IQ did not correlate with glucose metabolism in these children.

In sum, seizure frequency appears to be a reliable predictor of psychosocial functioning. There is also evidence of better psychosocial functioning in partial compared to generalized epilepsy. The PET studies validate the use of this technique to study the neurobiological bases of specific behaviours in children with epilepsy. One important caveat to these PET studies concerns the nature of the samples studied. Both Juhász et al. (2001) and Ferrie et al. (1997) studied a small sample of low functioning children with epilepsy. It is thus unclear to what extent these findings will hold for children with epilepsy who are of normal intellectual functioning. Nonetheless, these studies raise interesting questions concerning the link between brain metabolism and psychosocial behaviours.

A Neuropsychological Approach to Studying Psychosocial Functioning

A neuropsychological model of psychosocial functioning has been established in the learning disabilities literature. Rourke and colleagues have maintained that specific profiles of neuropsychological assets and deficits (i.e., learning disabilities) can lead to specific problems in academic functioning, psychosocial functioning, or both (Rourke, 1995; 1999; Rourke, & Fuerst, 1992; 1995; 1996; Tsatsanis, Fuerst, & Rourke, 1997). It is noteworthy that this view does not imply that learning disabilities cause psychosocial disturbances. Rather, the research shows that some subtypes of learning disabilities are prone to psychosocial maladjustment, whereas other subtypes are not. The nature of psychosocial maladjustment can be very specific. Rourke and Fuerst (1991) described a series of studies through which seven reliable subtypes of psychopathology (i.e. psychosocial difficulty) were identified in children with learning disabilities.

Two studies have examined psychosocial typologies in epilepsy. Mungas (1992) used cluster analytic techniques to study behavioral profiles of adults with epilepsy based on their responses on the Minnesota Multiphasic Personality Inventory (MMPI). This resulted in a five-cluster solution that classified 94% of the sample. The clusters were

interpreted as the following: absence of psychopathology, generalized psychopathology, severe psychopathology, mild depression/introversion, and internalized psychopathology. No relation was found between epilepsy type or seizure focus and any of these derived profiles. Because no such study has been conducted in children, the question of whether similar psychosocial subtypes are present in these children remains an empirical one.

More recently, King et al. (2002) used cluster analytic techniques to investigate profiles of psychosocial functioning in adults with epilepsy. They examined MMPI-2 cluster profiles in a sample of adults with primarily complex partial seizures. Their findings indicated a three-cluster solution. The average MMPI-2 profiles for the identified clusters suggested that 45% of the sample had minimal or no psychological complaints, 30% had generalized clinical elevations, and 25% had primarily elevated somatic complaints. No specific demographic or patient variables were associated with a given MMPI-2 profile.

The typologies identified by Mungas (1992) and King et al. (2002) in adults do not seem to correspond closely to those identified in the learning disabilities literature (Rourke & Fuerst, 1991), although there are similarities. These studies differ in obvious ways, the foremost being the measures used and the nature of the informant. There is not enough data to conclude whether or not children with epilepsy might show distinct psychosocial profiles that are similar to those in children with learning disabilities. However, as in children with learning disabilities, behavioural and emotional disturbances in children with epilepsy appear to be linked to cognitive deficits (Camfield et al., 1984; 1993; Kokkonen et al., 1997; Schoenfeld et al., 1999).

Camfield et al. (1984) studied children with apparent pure left or right temporal lobe epilepsy on a variety of cognitive and personality measures. Overall, most of the children performed in the average range on neuropsychological and behavioural measures, and there were no significant differences between these two groups. However, a small sample of children identified as "maladjusted" on the Personality Inventory for Children (PIC; Wirt, Lachar, Klinedinst, & Seat, 1984) showed significantly more cognitive deficits than the other children. Moreover, the "maladjusted" group comprised an equal number of left- and right-sided epilepsy cases. Because of methodological

restrictions, it could not be determined whether brain areas outside the temporal lobes were commonly affected in the "maladjusted" group.

Schoenfeld et al. (1999) studied children with complex partial epilepsy with a comprehensive battery of neuropsychological and behavioural measures. They found that frequency of seizures in the last year and overall neuropsychological status were both related to psychosocial functioning. Specifically, higher seizure frequency and more impairment in overall neuropsychological status were related to a greater number of behavioural problems, characterized as internalized (e.g., social withdrawal, anxiety, depression). Other researchers have also shown a relation between cognitive deficits and poor psychosocial functioning (Camfield et al., 1993; Kokkonen et al., 1997). Dodrill and Clemens (1984) and Hermann (1982) found that measures of cognitive abilities were fairly good predictors and discriminators of adjustment and behavioural functioning, and more useful in this regard than basic clinical seizure characteristics. It is also suggestive that when children with epilepsy are screened for behavioural problems, no cognitive impairments are found (Williams et al., 1996).

Taken together, these aforementioned findings suggest a strong link between neuropsychological status and psychosocial functioning in children with epilepsy. The interaction between these two domains of functioning and brain function is less clear. Returning to the learning disabilities literature, it has been posited that some patterns of neuropsychological and psychosocial functioning arise from particular brain abnormalities. Specifically, the profiles of cognition and behaviour associated with the nonverbal learning (NLD) syndrome are thought to arise from dysfunctional white matter systems (Rourke, 1995). Moreover, this interplay between brain and behaviour is couched within a developmental framework. The presenting behavioural phenotype is thought to result from the interaction between brain, neuropsychological functioning, and development. The question thus arises whether cognitive and psychosocial dysfunction in children with epilepsy is a function of specific brain anomalies.

There is intriguing evidence from studies of children with new onset epilepsy linking neurological status to behaviour problems. Dunn, Austin, and Huster (1997) collected parental behaviour ratings in children with epilepsy within 6 weeks of first seizure onset. Parents were instructed to rate the child's behaviour in the 6 months

preceding the child's first seizure. Behavioural ratings were made using the CBCL. The results showed that children who later developed recurrent seizures had higher baseline behaviour problem ratings than children who had no further seizures. The authors hypothesized that neurological dysfunction might be a causal factor in both seizure development and psychosocial disturbances.

Austin et al. (2001) examined rates of behavioural disturbances in a larger sample of children with epilepsy before their first recognized seizures. The behaviours were assessed using the parental ratings on the CBCL shortly after the first seizure onset. The findings revealed higher rates of behaviour problems in children with epilepsy compared to sibling controls in the six months before the first recognized seizure. Specifically, children who would later develop seizure disorders were rated as having more anxiety and depression, more difficulty with inattention, and more total number of problems on the CBCL than sibling controls.

The results from Dunn et al. (1997) and Austin et al. (2001) provide support for the view that neurodevelopmental dysfunction might underlie both seizure manifestation and behavioural disturbances. The traditional view of psychosocial problems in epilepsy assumes that behavioural problems begin after epilepsy is diagnosed. However, an explanation for behavioural problems in terms of the social burden of epilepsy cannot account for such problems before any formal diagnoses are made. Instead, epilepsy may best be viewed as a pervasive neurological condition that includes both seizures and behavioural problems.

A more precise categorization of brain and behavior profiles in children with epilepsy is key to a better understanding of the etiological, prognostic, and treatment issues of this disorder. One reason that brain-behaviour relations in epilepsy have been elusive is that brain variables are not typically examined. The neurobiological variables most often under study are those that define the characteristics of the seizure disorder. These typically include etiology, age of seizure onset, seizure frequency, and seizure type. It is unclear, however, to what extent epilepsy variables can be considered brain variables. While seizure characteristics clearly reflect some features of the underlying brain, they may not suffice as indices of overall brain functioning. Perhaps a more brain-focused as opposed to seizure-focused approach is in order. It has been suggested that

measures of cerebral metabolism may be important correlates of psychological and social problems in epilepsy (Hermann et al., 1992). Although there have been some attempts to investigate the relation between brain metabolism and psychosocial behaviours in epilepsy (Ferrie et al., 1997; Juhász et al., 2001) this area of research remains largely unexplored.

From the preceding review it is clear that psychosocial functioning is an area of great concern in children with epilepsy. There is a paucity of research in neuropsychology investigating the psychosocial aspects of this disorder in children. It is presently argued that a more multidimensional classification of psychosocial functioning in these children may prove more fruitful than the typical contrasting-group comparisons. No study to date has examined psychosocial subtypes in children with epilepsy. The advantages of multidimensional taxonomic systems of psychosocial functioning have been established in children with learning disabilities (Rourke & Fuerst, 1991; 1995), children with traumatic brain injury (Butler, Rourke, Fuerst, & Fisk, 1997), and in a general neuropsychological paediatric population (Saunders, Hall, Casey, & Strang, 2000). The question remains to what extent children with epilepsy will show similar typologies.

The following studies were conducted to investigate typologies of psychosocial functioning in children with epilepsy. The first experiment examined psychosocial subtypes in a population of children with epilepsy. Because little is known concerning the relation between neurology and psychosocial functioning in these children, a second experiment was conducted to examine the relation between brain metabolism and the empirically derived typologies of psychosocial functioning derived from the first experiment.

Specific hypotheses

Hypothesis 1: A PIC-R typology of psychosocial functioning in children with epilepsy

Previous research of PIC-R typologies in paediatric neuropsychological populations have established a limited number of subtypes. It was hypothesized that a PIC-R typology in children with epilepsy would be similar. A well-established empirical PIC-R psychosocial typology was developed for children with learning disabilities (Rourke & Fuerst, 1991). It was hypothesized that subtypes similar to those in the LD

typology would be identified in children with epilepsy. Additional subtypes that differ from those previously identified were also expected.

Hypothesis 2: Seizure-related variables and psychosocial difficulties

Based on prior research, it was expected that seizure frequency would be related to the degree of psychosocial impairment. Specifically, it was expected that the children with the highest seizure frequency would show the highest PIC-R profile elevations within any given subtype. In addition, because research has shown that individuals with localized forms of epilepsy typically show better social development than those with other forms, it was expected that children with generalized epilepsy would show greater psychosocial difficulty than those with partial epilepsy.

Because past research has failed to demonstrate a link between psychosocial difficulties and either site of seizure focus or age of seizure onset, neither of these seizure variables was expected to be associated with psychosocial outcome.

Hypothesis 3: Cerebral glucose metabolism and psychosocial subtype

Previous research has shown that dysfunctional brain metabolism is not limited to the site of seizure focus in individuals with epilepsy. It was expected that PET indices of abnormal brain metabolism would covary with psychosocial subtype. Based on the links made between right hemisphere dysfunction and psychosocial functioning in the LD literature (e.g., Rourke, 1995), it was expected that right hemisphere metabolic dysfunction would be associated with poorer psychosocial outcomes compared to left hemisphere metabolic dysfunction.

Study 1: Cluster Analysis

Method

Participants

The sample consisted of children and adolescents selected from a group of more than 150 children examined through the neurology clinic at a large children's hospital. All participants selected were diagnosed with intractable epilepsy. In addition, the selected participants met the following criteria: a) chronological age between 6 and 16 years, b) a Wechsler Intelligence Scale for Children Full Scale IQ (WISC-III FSIQ) score greater than 75, and c) complete PIC-R scores obtained prior to any surgical intervention for epilepsy (if applicable). Exclusion criteria included: a) history of premorbid head injury, b) a history of ADHD, and c) invalid PIC-R scores.

One-hundred and twenty-six participants (66 males, 60 females) met the inclusion criteria. Following initial screening of participants, PIC profiles that contained significant elevations on any of the validity scales (L >70; F > 110, DEF > 70) were eliminated from the analysis. These profiles were eliminated because they may not accurately reflect the child's clinical presentation (Wirt et al., 1984). Eleven cases were excluded from all analyses because of an incomplete, or invalid PIC-R. An additional 7 cases were excluded because of comorbid head injuries. The remaining 108 participants were included in the analyses.

The neurological records for the participants were reviewed to determine the following clinical variables: type of seizure, frequency of seizure at time of test, and age of seizure onset. Seizure frequency was calculated on a per day basis. For some analyses, the sample was partitioned according to the primary seizure type. Seizures were classified as "partial", "generalized", or "combined" types, according to the nature of the recurring episodes. The "partial" type included both simple and complex seizures, and the "generalized" type included both convulsive and nonconvulsive seizures. The "combined" type referred to those patients who experienced both recurring partial and generalized seizures Demographic and patient variables for the sample are presented in Table 1.

Table 1.

Sample Characteristics

	N	Age	FSIQ	VIQ	PIQ	Age Sz Onset
Overall	108 (60 M, 48 F)	10.9 (3.5)	89.4 (10.1)	91.0 (10.7)	89.4 (12.5)	4.6 (3.5)
Partial	53 (30 M, 23 F)	11.5 (3.5)	89.9 (11.1)	92.1 (12.2)	89.2 (11.4)	5.8 (3.8)
Generalized	28 (18 M, 10 F)	10.9 (3.9)	86.6 (9.1)	89.2 (9.9)	86.0 (8.9)	4.0 (3.1)
Mixed	27 (12 M, 15 F)	12.6 (3.4)	90.2 (11.1)	84.6 (8.9)	91.8 (15.9)	3.9 (3.5)

Note. N = number of cases; Age = mean age at test in years; FSIQ = WISC-III Full Scale IQ; VIQ = WISC-III Verbal IQ; PIQ = WISC-III Performance IQ; Age Sz Onset = mean age of seizure onset in years. The numbers in parentheses under the N column refer to the number of males (M) and females (F). All other numbers within parentheses are standard deviations.

The patients who were classified as having partial seizures were subdivided according to the suspected side (right vs. left) of seizure focus, based on scalp ictal EEG recordings. Table 2 presents patient information for these two groups.

Table 2.

Patient Characteristics According to Side of Seizure Focus for Patients with Partial Seizures.

	N	Age	FSIQ	VIQ	PIQ	Age Sz Onset
Partial (all)	53 (30 M, 23 F)	11.5 (3.5)	89.9 (11.1)	92.1 (12.2)	89.2 (11.4)	5.8 (3.8)
Left sz focus	28 (16 M, 12 F)	10.7 (3.1)	88.6 (10.3)	88.8 (10.4)	90.2 (11.1)	4.7 (3.7)
Right sz focus	25 (14 M, 11 F)	12.3 (3.7)	90.9 (10.6)	93.1 (10.4)	87.4 (11.6)	4.5 (3.2)

Materials

Measure of psychosocial functioning.

The Personality Inventory for Children-Revised (PIC-R; Wirt et al., 1984) is a multidimensional parental rating scale, standardized with age and sex stratified normative data. It comprises 280 descriptive items that are answered "true" or "false" according to the respondent's opinion of the child. It is administered to the child's primary caretaker, usually the biological mother. Sixteen scales are derived from PIC-R: 3 validity scales, 1 general measure of psychosocial adjustment, and 12 clinical scales measuring specific behavioural domains (see Table 3). A child's profile on these scales is expressed in the form of a T-score, where increases in elevation reflect greater levels of psychosocial difficulty. A T-score greater than 70 is typically considered clinically significant in the direction of psychopathology.

Table 3.

Brief Description of the 12 PIC-R Clinical Scales that Measure Specific Behavioural Domains.

Scale	Description
Achievement (Achv)	Identifies children with academic achievement below age expectations.
Intellectual Screening (Int)	Identifies children with impaired intellectual functioning that may contribute to their psychosocial difficulties.
Development (Dev)	A measure of intellectual and physical development. It is most related to retardation in motor coordination, academic achievement, and individual potential.
Somatic Concern (Som)	An index of health related variables, such as somatic complaints, illness, adjustment to illness, eating habits, sleep patterns, general energy and strength, headaches, stomachaches, and other somatic symptoms.
Depression (Dep)	Assesses symptoms of childhood depression, such as brooding, social isolation, crying spells, low energy level, pessimism, anhedonia, poor self-concept, and withdrawal
Family Relations (Fam)	A measure of the family's stability, adaptiveness, happiness, emotional adjustment, and parental effectiveness.

Scale	Description
Delinquency (Dlq)	A measure of delinquent and antisocial tendencies in the child. Elevations indicate a lack of sensitivity for the rights and feelings of others, a disregard for parents and rules, and characteristics such as hostility, intolerance, and frustration.
Withdrawal (Wdrl)	A measure of withdrawal from social contact. It reflects isolation from peers, general social interactions, shyness, fear of strangers, emotional distance, and mistrust of others.
Anxiety (Anx)	Assesses overt manifestations of anxiety, such as irrational fears, nightmares, poor frustration tolerance, exaggeration of problems, and physiological correlates of anxiety.
Psychosis (Psy)	Identifies psychotic symptomatology. Elevations may indicate reality distortion, cognitive disorientation, poor pragmatic skills, social withdrawal, anxiety, and inappropriate affect.
Hyperactivity (Hyp)	Identifies children with characteristics of hyperarousal. Elevations are indicative of emotional instability, hostility, impulsivity, restlessness, poor peer relationships, and discipline problems.
Social Skills (Soc)	Assesses the effectiveness of interpersonal skills and characteristics leading to failure in social situations. Relevant factors include social comprehension, tact, and self-confidence in social situations

General Rationale of Analysis.

Cluster analyses are classification techniques for forming homogenous groups within complex data sets. A set of rules, or algorithm, is used for partitioning a proximity matrix of the data to form groups of similar cases. Two common types of cluster analytic techniques are hierarchical and non-hierarchical.

The characteristic feature of all hierarchical cluster techniques is that they form groups in successive steps, starting with each individual as its own cluster and building into larger nested clusters. Non-hierarchical cluster techniques include a number of popular methods, the most popular of which is iterative partitioning. Iterative partitioning, often referred to as k-means cluster analysis, requires that the user specify the expected number of clusters for the data. On the basis of this initial information, this method calculates centroids for a set of trial clusters, places each case in the cluster with the nearest centroid, and then recalculates the centroids and reallocates the cases. This

process iterates until there is no change in cluster membership. The primary advantage of this method over hierarchical techniques is that it provides multiple opportunities to assign cases to specific clusters, and thus can compensate for poor initial cluster assignment. Because of this, non-hierarchical techniques are much less sensitive to outliers than are hierarchical methods (Lange, Iverson, Senior, & Chelune, 2002).

There are problems inherent with both hierarchical and non-hierarchical cluster techniques. In hierarchical techniques, early ineffective combinations of data may mislead the further analyses and the final results. Non-hierarchical techniques have the advantage of being less susceptible to outliers, but are disadvantaged because the number of clusters must be assigned a priori. Therefore, k-means cluster analysis is not recommended as an exploratory technique when the number of clusters contained within a data set is not known.

A combination of the two techniques has been recommended as the most appropriate means of determining the cluster structure in a data set (Borgen & Barnett, 1987; Lange et al., 2002). First a hierarchical technique is used to identify the number of clusters in a data set. Subsequently, a k-means cluster analysis can then be employed, whereby the number of clusters requested in the analysis is based on the results from the hierarchical analysis. This method of clustering has been found to be superior to hierarchical methodology alone (Hair et al., 1995), and is a procedure that has been validated by researchers in the area of psychology (e.g., Donders, 1996; Fisher et al, 1996).

Proximity Measure

The proximity measure in cluster analysis is a statistic that evaluates the similarity or distance between clusters. Multivariate data sets have elements of elevation, shape, and dispersion. The choice of proximity measure, because of its arithmetic features, directly determines which of these components are the basis of clustering. In this study, squared Euclidian distance was chosen as the proximity measure. Although the squared Euclidian distance reflects all three elements to some extent (Borgen & Barnett, 1987), it is most influenced by elevation and magnitude differences in the data set (Lange et al., 2002). This measure was chosen because the present focus for interpretation of the data

was placed on the individual's level of performance with regard to what is considered normal.

Number of Clusters.

There are no commonly accepted rules or decisions that can be followed to determine the "correct" number of clusters in a given data set. In general, such a determination is somewhat subjective. Previous work with children with LD has suggested that reliability and clinical interpretability are superior to specific quantitative methods for evaluating the adequacy of specific cluster solutions (Fuerst et al., 1989, 1990; Fuerst and Rourke, 1993). As such, replicating solutions across different subtyping techniques is an important step in determining the validity of subtypes generated with cluster analysis.

The number of clusters in the present data was determined by both subjective inspection of graphic representations (e.g., inverse scree plots) and non-graphical methods (e.g., subtype replication with different methods). An inverse scree plot is a visual representation of the change in amalgamation coefficients corresponding to each merging cluster in a given solution. Small changes in coefficients indicate the merging of more similar cases and are reflected by little change on the slope of the scree plot. Large changes in coefficient values are indicative of the merging of dissimilar cases and are reflected by greater changes in the slope of the scree plot. Further criteria used to determine the appropriate number of clusters included examining pseudo-F values, internal validation of the solution through replication using different methods, and by the interpretability of the resulting mean PIC-R profiles at various partition levels (from 3 to 9 clusters). One additional consideration was the number of cases belonging to each cluster. It has been recommended that any cluster whose membership is less than 5% of the data set under investigation should not be included in the final cluster solution (Lange et al., 2002).

With respect to replication using other clustering techniques, there is little evidence suggesting that any one particular method is superior (Aldenderfer & Blashfield, 1984; Borgen & Barnett, 1987). The most common hierarchical methods include single linkage, complete linkage, average linkage, and Ward's (1963) minimum variance technique. Ward's method is a widely used and accepted technique in the

behavioural sciences and is designed to minimize the variance with clusters at each stage of grouping. Single Linkage and Complete Linkage methods are not recommended because they tend to produce chaining artifacts and overly dense groupings, respectively (Borgen & Barnett, 1987; Lange et al., 2002). The Average Linkage method was designed as a compromise between these two techniques, and as such minimizes the biases in both. Average Linkage methods have two main alternative clustering techniques: within group and between group methods. These methods use a clustering criterion defined as the average distance from all individuals in one cluster to all individuals in another cluster. Miligan (1980) reported that the Average Linkage algorithms have relatively low sensitivity to outliers and other forms of error inherent in a data set compared to other hierarchical clustering techniques. Average Linkage algorithms are considered the most appropriate hierarchical clustering technique to employ (Lange et al.). With respect to non-hierarchical techniques, iterative partitioning, or k-means cluster analysis, is most commonly used.

Procedure

Subtype generation by cluster analysis

All 12 of the PIC-R clinical scale scores were included in the cluster analysis (Achievement, Intellectual Screening, Development, Somatic Concern, Depression, Family Relations, Delinquency, Withdrawal, Anxiety, Psychosis, Hyperactivity, and Social Skills). Previous work with children with LD has shown that the Achievement, Intellectual Screening, and Development scales (collectively referred to as the cognitive triad) to be highly correlated and mutually redundant in that population (e.g., Fuerst, Fisk, & Rourke 1989; Fuerst & Rourke, 1993). However, all three of these scales were included in the present investigation because there was no evidence to suggest that these scales would be equally redundant in an epilepsy population. Moreover, these scales have been included in studies of psychosocial subtyping with non-LD pediatric populations (e.g., Butler et al., 1997).

Data from participants included in the analyses were not screened for the presence of outliers. Each participant's score on the PIC-R scales used to form clusters were standardized across that participant's profile to eliminate profile elevation and dispersion. The data were initially clustered using the Within Group Average Linkage hierarchical

method (Sokal and Michener, 1958). First, preliminary results of the WGAL method were examined and the optimal number of clusters selected using subjective and quantitative criteria described above. Two additional hierarchical clustering techniques were applied to the same data used in the initial analysis, Ward's minimum variance method, and the Between Group Average Linkage Method. A k-means analysis, using seeds determined from hierarchical cluster analysis, was also performed. For all cluster analyses, the participant's scores were standardized to maximize cluster solutions towards profile pattern rather than magnitude. All cluster solutions were compared to determine the reliability of the final solution. The degree of agreement between different cluster techniques was determined using visual inspection of the mean profiles, kappa coefficients to quantify the degree of agreement of individual assignment across techniques, as well as correlating the mean PIC-R profiles of the subtypes generated by k-means analysis with those derived by the hierarchical techniques.

Results

All statistical analyses were conducted using SPSS for Windows Version 10.0 (SPSS Inc., 1999). Means and standard deviations for the 12 clinical PIC scales for the entire sample are presented in Table 4.

Table 4.

Mean PIC-R Clinical Scale Elevations for the Entire Sample (n = 108).

PIC-R Scale	Mean	Std Dev
Achievement	65.9	14.7
Intellectual Screening	88.3	30.9
Development	66.7	16.1
Somatic Concern	65.5	13.5
Depression	62.0	14.6
Family Relations	51.6	10.3
Delinquency	60.0	16.9
Withdrawal	57.6	12.5
Anxiety	56.9	13.6
Psychosis	77.3	21.6
Hyperactivity	52.8	13.9
Social Skills	60.5	14.4

Cluster profiles

Initial visual inspection of the inverse scree plot of the amalgamation coefficients of the WGAL cluster analysis, as well as inspection of the pseudo-F values suggested a three to seven cluster solution. Considerations related to clinical interpretation as well as the number of members in each cluster suggested a five or six cluster solution. The data were subjected to validation by the two other hierarchical cluster techniques and compared. Finally, a confirmatory non-hierarchical (k-means) cluster analysis was performed for the three to seven cluster solutions and compared to the hierarchical methods. The most reliable solution was a six-cluster solution.

A kappa statistic (Cohen, 1960) was calculated for each of the three to seven cluster solutions between the final k-means method and the initial average linkage method. The kappa statistic provides a measure of agreement between two ratings. Kappa values were highest between methods for the six-cluster solution. The values were 0.84, 0.86, and 0.92 between the k-means six-cluster solution and the Between Group Average Linkage, Within Group Average Linkage, and Ward's methods, respectively.

Figures 1 though 6 illustrate the mean PIC-R clinical scale scores for each of the six subtypes. Descriptive labels were assigned to each subtype based on the major elevations within the profile, and were in part adapted from previous research of psychosocial subtyping using the PIC-R (Butler et al., 1997, Rourke & Fuerst, 1991, Saunders et al., 2000).

Figure 1. Mean PIC-R profile for the Cognitive-Somatic subtype.

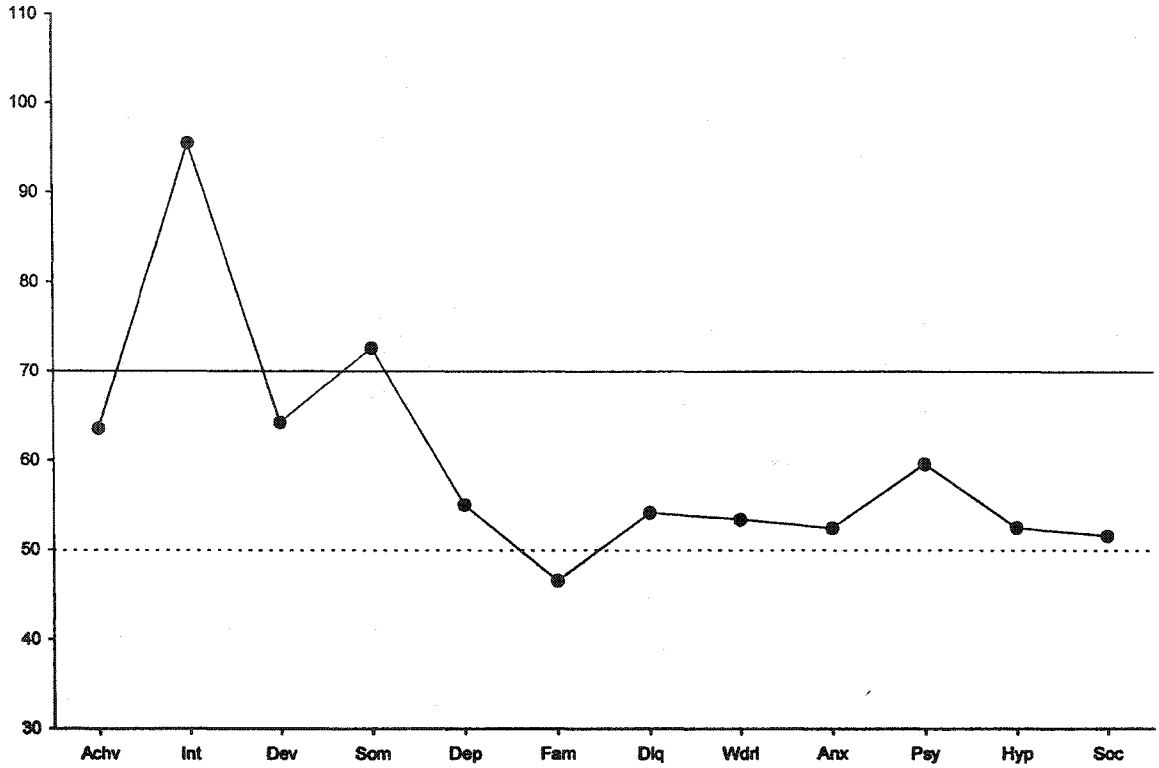


Figure 2. Mean PIC-R profile for the Cognitive-Internalized subtype.

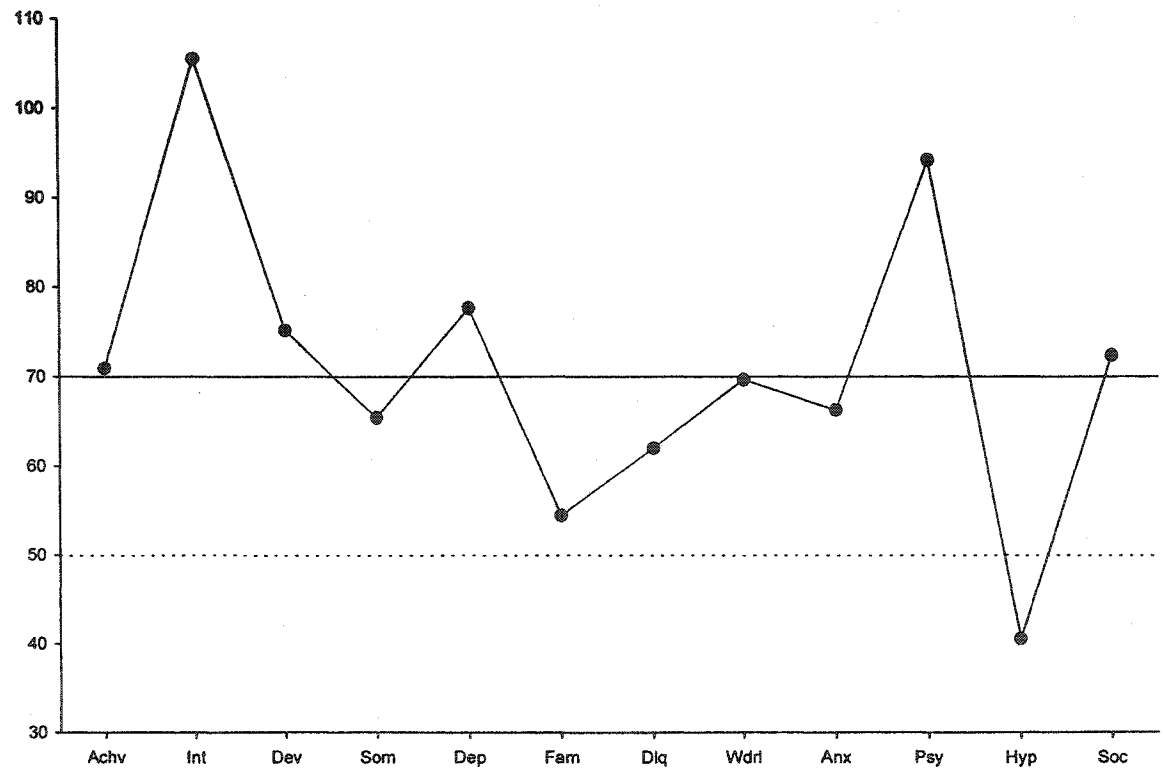


Figure 3. Mean PIC-R profile for the Cognitive-Externalized subtype.

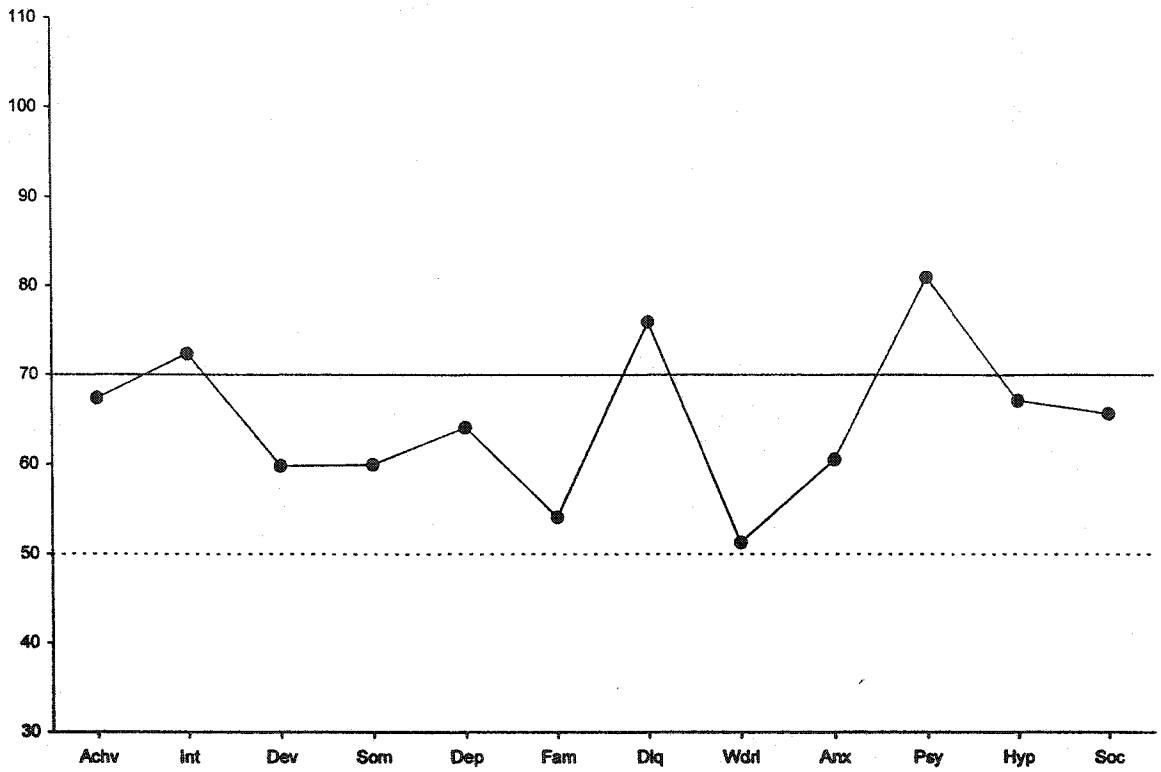


Figure 4. Mean PIC-R profile for the Cognitive-Social Isolation subtype.

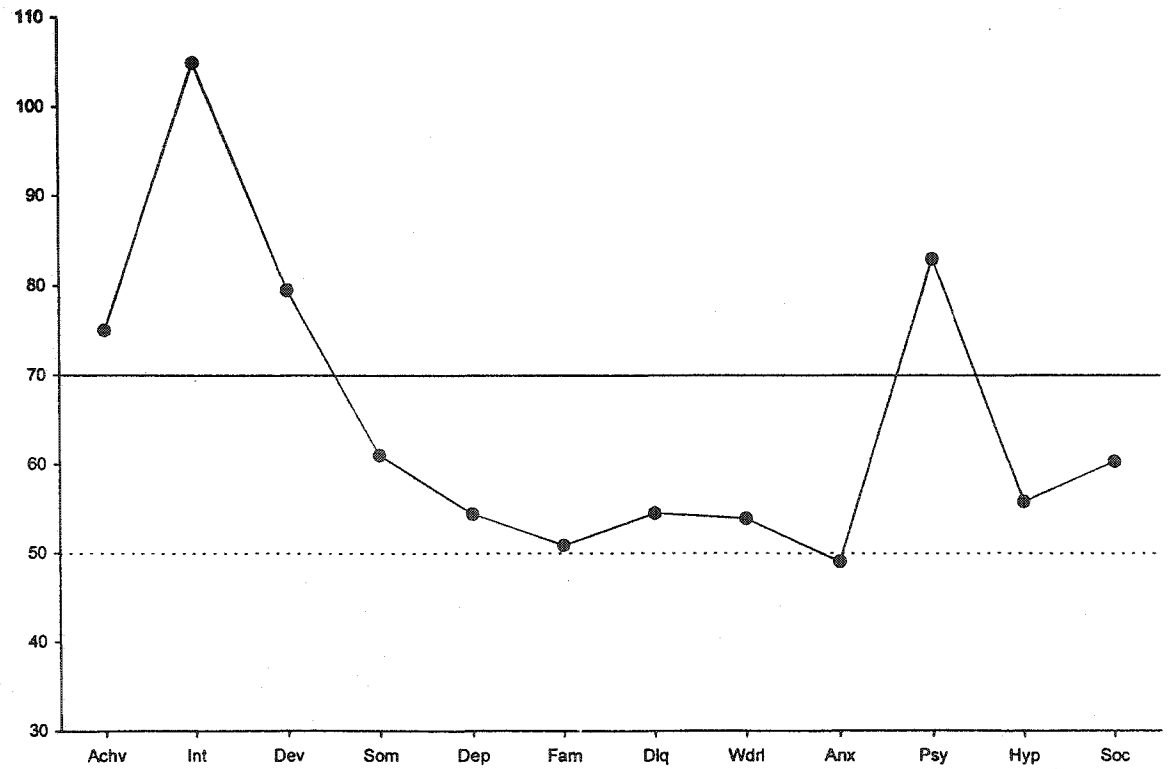


Figure 5. Mean PIC-R profile for the Internalized subtype.

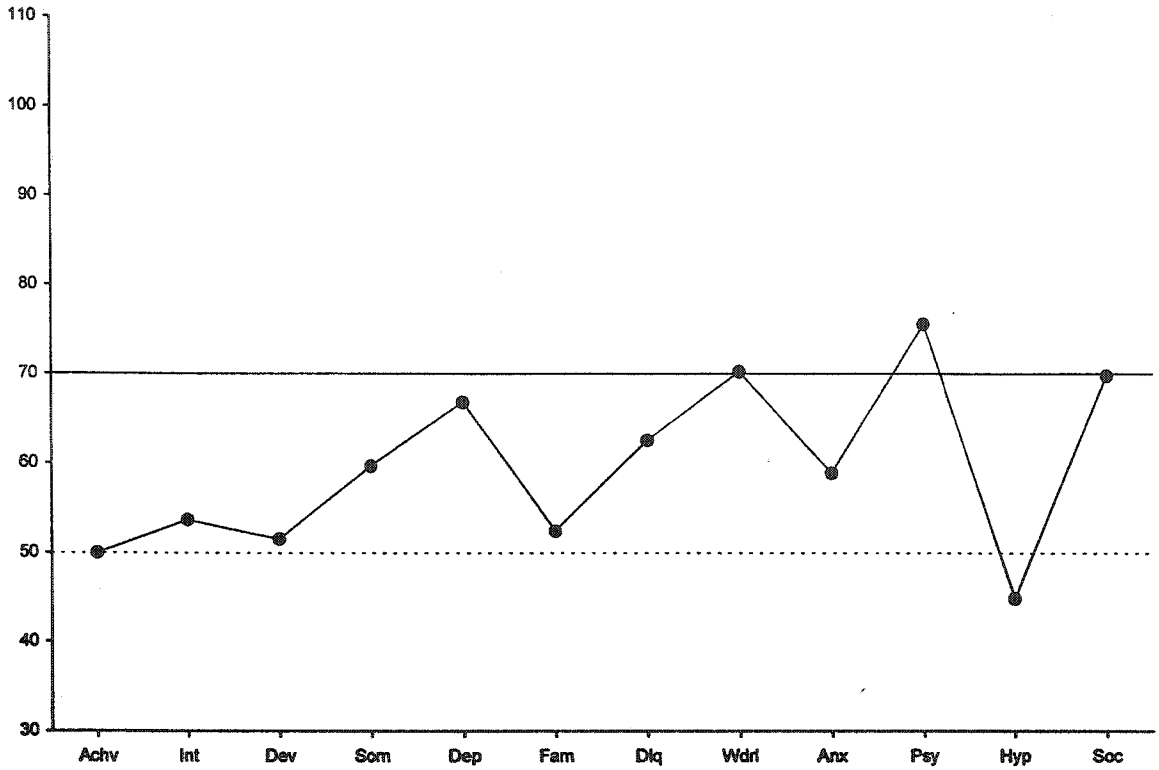
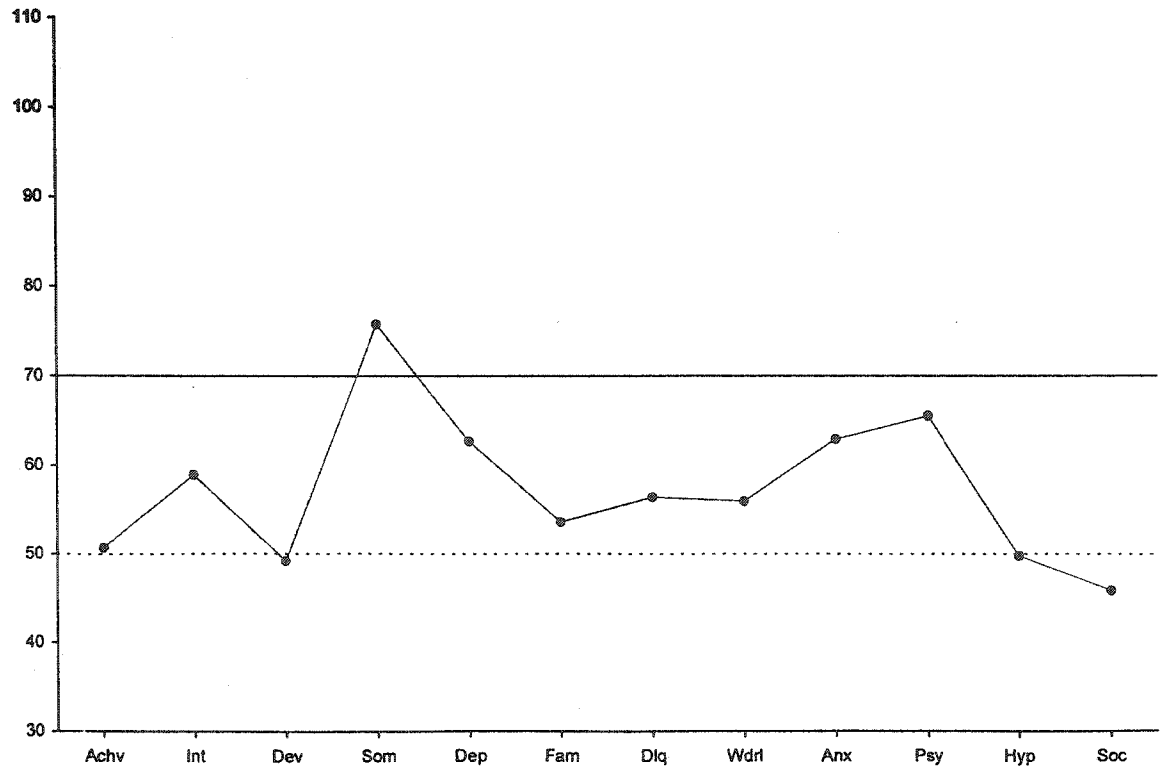
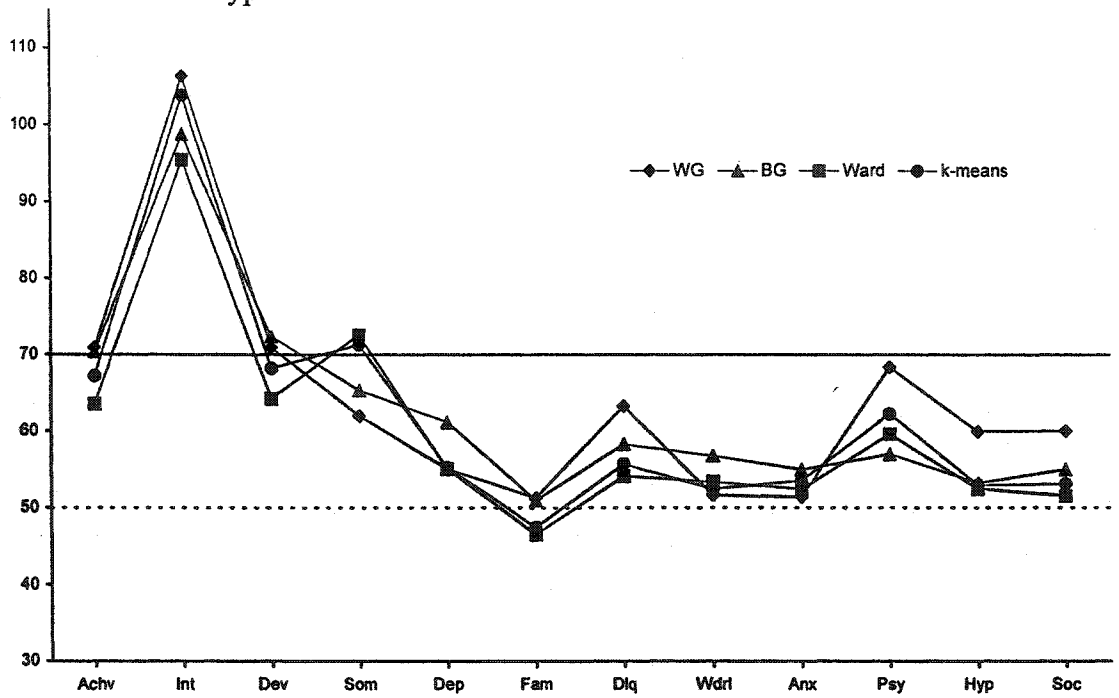


Figure 6. Mean PIC-R profile for the Somatic Concern subtype.



To further compare the different cluster solutions, the mean PIC-R profiles of the clusters derived from Ward's and the Average Linkage methods were compared to the mean PIC-R profiles of the k-means subtype. These profiles are presented in figures 7 through 12.

Figure 7. Mean PIC-R profiles across clustering methods for the Cognitive-Somatic subtype.



WG -Within Group average linkage technique. BG - Between group average linkage technique

Figure 8. Mean PIC-R profiles across clustering methods for the Cognitive-Internalized subtype.

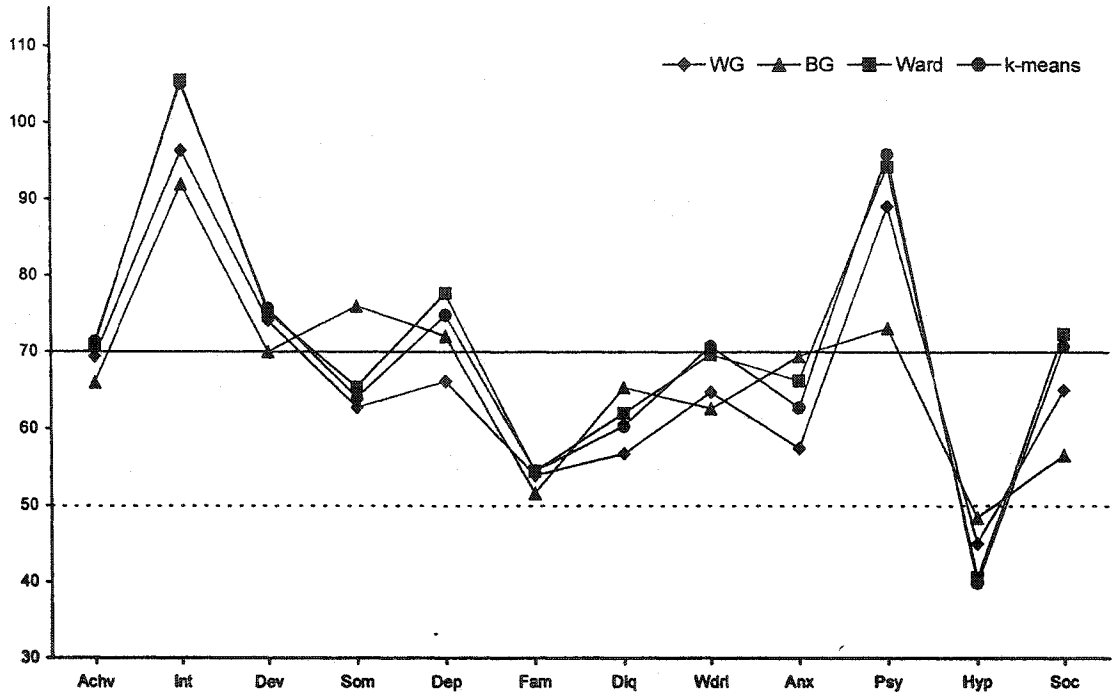


Figure 9. Mean PIC-R profiles across clustering methods for the Cognitive-Externalized subtype.

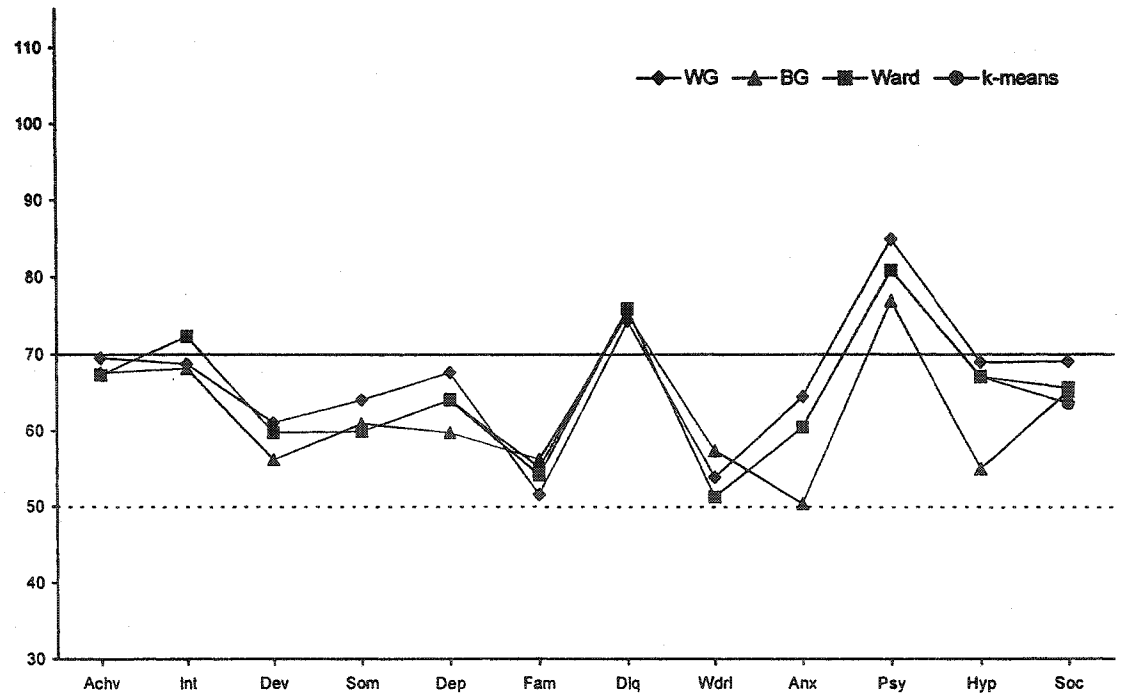


Figure 10. Mean PIC-R profiles across clustering methods for the Cognitive-Social Isolation subtype.

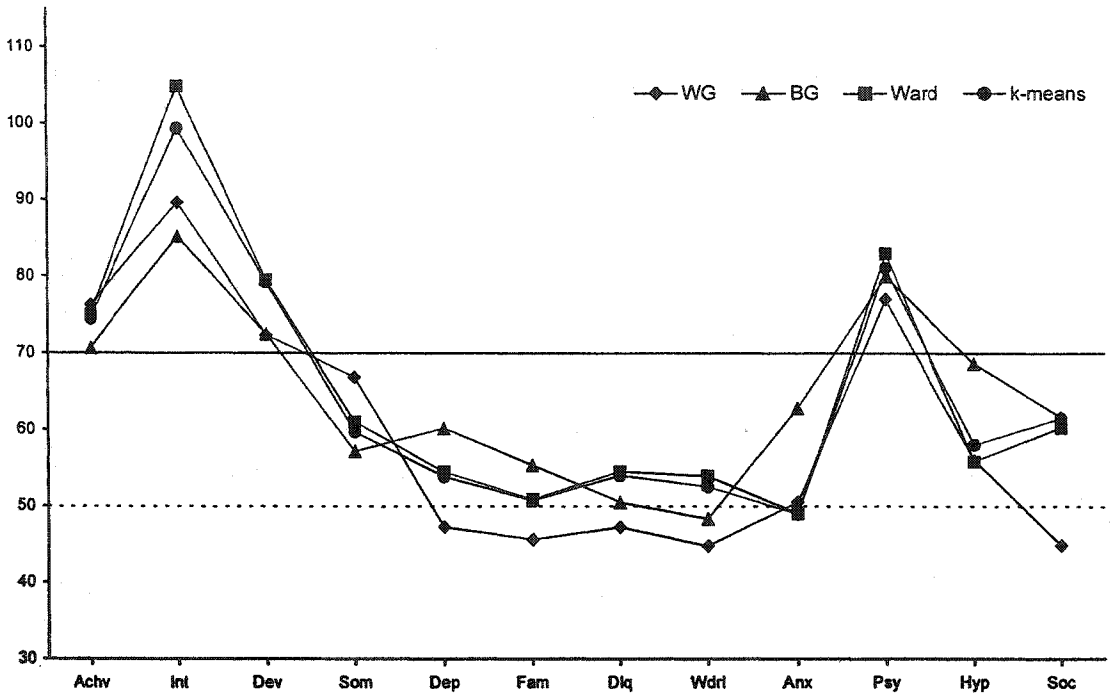


Figure 11 Mean PIC-R profiles across clustering methods for the Internalized Psychopathology subtype.

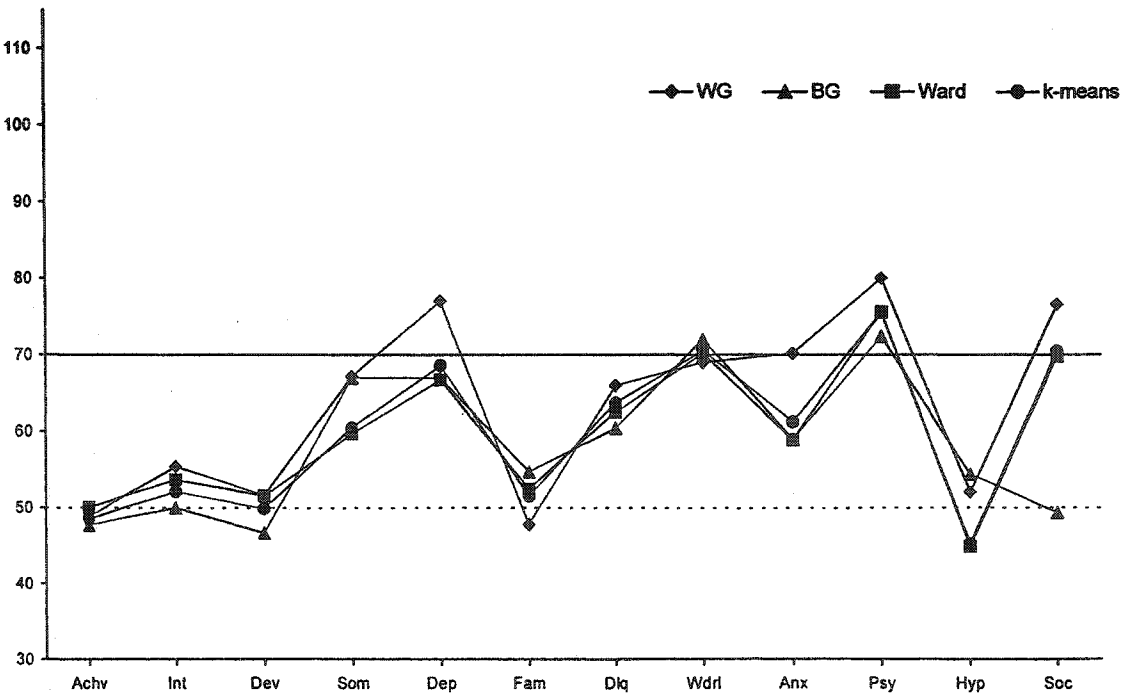
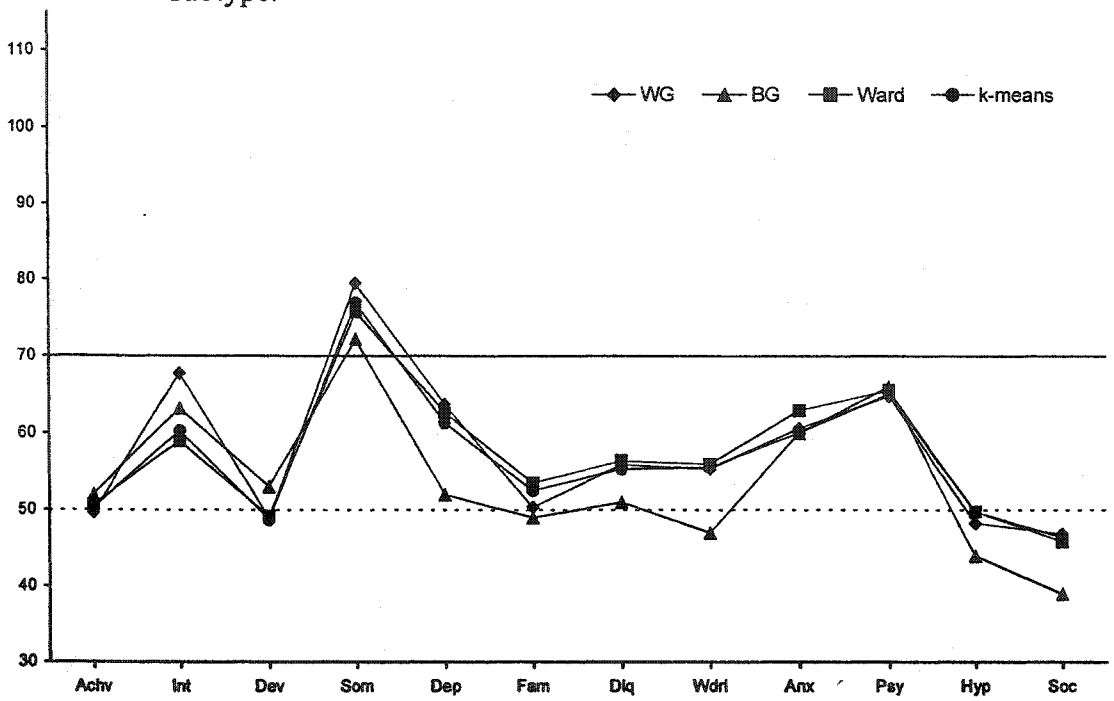


Figure 12. Mean PIC-R profiles across clustering methods for the Somatic Concern subtype.



Confirming visual inspection of Figures 7 through 12, Table 5 shows the correlations between the k-means and hierarchical cluster solutions. All subtypes correlated .71 or greater with their corresponding k-means subtype.

Table 5.

Mean PIC-R Correlations between the K-means Subtype and Corresponding Within Group Average Linkage, Between Group Average Linkage, and Ward's Methods.

	k-means subtype					
	Cog.-Somatic	**Cog.-Internalized**	**Cog.-Externalized**	**Cog. - Social Isolation**	**Internalized**	**Somatic Concern**
	(n = 25)	(n = 20)	(n = 18)	(n = 25)	(n = 9)	(n=11)
Within Group	.94	.98	.93	.92	.94	.97
Between Group	.96	.81	.81	.88	.71	.87
Ward's	.99	.99	.97	.94	.98	.96

Relation of IQ to psychosocial functioning

Table 6 shows the mean VIQ, PIQ, and FSIQ for each psychosocial subtype. A series of one-way analysis of variance (ANOVA) with each IQ measure as the dependent variable and psychosocial subtype as the independent variable were conducted. The results revealed a statistical trend (F (5, 102) = 2.187, p = .07) for differences in FSIQ across psychosocial subtype. No other differences were significant.

Table 6.

IQ and Psychosocial Subtype.

	N	Age	FSIQ	VIQ	PIQ
Cognitive-Somatic	25	11.1	84.8	88.1	84.0
Cognitive-Internalized	20	13.2	86.0	87.2	87.3
Cognitive-Externalized	18	9.7	92.5	93.9	92.5
Cognitive-Social Isolation	25	8.9	82.7	86	82.7
Internalized	9	13.5	95	93	97
Somatic Concern	11	10.7	91.2	94.2	88.9

Relation of seizure variables with psychosocial functioning

A one-way ANOVA with seizure type as the independent variable and the mean PIC-R elevation on the12 clinical scales as the dependent variable revealed a trend (p = .09) for the Partial group to have lower PIC-R elevations than the Generalized and Combined groups. A cross tabulation of seizure type with psychosocial subtype was constructed (Table 7). A Chi-square test of independence of the cross-tabulation presented in Table 7 indicated that there was no association between seizure type and the psychosocial subtype to which participants were assigned (X^2 (10) = 12.09, p > .05). Within the group with partial seizures, a separate Chi-square test of independence was performed for a cross-tabulation of seizure side with psychosocial subtype. The results indicated that there was no association between side of seizure focus and psychosocial subtype (X^2 (5) = 7.239, p > .05).

Table 7.

Number of participants assigned to each PIC-R subtype across seizure type.

	Seizure Type			
	Partial	**Generalized**	**Combined**	**Total**
Cognitive-Somatic	15	3	7	25
Cognitive-Internalized	6	7	7	20
Cognitive-Externalized	6	5	7	18
Cognitive-Social Isolation	15	8	2	25
Internalized	5	2	2	9
Somatic Concern	6	3	2	11
Total	53	28	27	108

To determine whether seizure frequency around the time of testing was related to degree of psychosocial difficulties, the correlation between seizure frequency (per day) and mean PIC-R elevation was calculated. The results indicated that there was no association between number of seizures per day and overall PIC-R elevation ($r = .017$, $p > .05$).

To determine whether age of seizure onset was related to degree of psychosocial difficulty, the age of seizure onset was correlated with the mean PIC-R elevation. The results revealed a significant association between age of seizure onset and mean PIC-R elevation ($r = -.36$, $p < .05$), such that lower age of onset was associated with higher PIC-R elevations. A one-way ANOVA with psychosocial subtype as the independent factor and age of seizure onset was conducted. The results indicated that age of seizure onset was different across subtypes (F (5, 102) = 3.676, $p < .05$). Post-hoc comparisons using Tukey's HSD revealed that participants assigned to the Cognitive-Externalized subtype had a younger mean age of seizure onset than the other groups, and participants assigned

to the Somatic Concern subtype had a older mean age of seizure onset compared to the other groups.

Table 8.

Mean age of seizure onset and mean PIC-R scale elevation by psychosocial subtype.

Subtype	Mean age of seizure onset (years)
Cognitive-Somatic	4.5 (3.2)
Cognitive-Internalized	4.4 (3.6)
Cognitive-Externalized	2.6 (2.9)
Cognitive-Social Isolation	4.5 (3.3)
Internalized	4.9 (3.8)
Somatic Concern	7.1 (4.1)

Comparisons with previous PIC typologies

Previous research using the PIC-R has established typologies of psychosocial functioning in children with LD (Rourke & Fuerst, 1991), children with closed head injuries (Butler et al., 1997), and a heterogeneous sample of children referred to a children's mental health center for neuropsychological difficulties (Saunders et al., 2000). Table 9 presents the various subtypes across studies, according to their verbal descriptions and PIC-R scale elevations.

Table 9. PIC-R typologies across studies.

Primary area of difficulty	Label	PIC elevations												Study[a]	% of sample
		Achv	Int	Dev	Som	Dep	Fam	Dlq	Wdrl	Anx	Psy	Hyp	Soc		
None	Normal													2	27
														3	30
		Achv	Int	Dev										1	28
Somatic	Somatic Concern		Int		Som									1	11
					Som									2	12
					Som									4	10
Cognitive	Cognitive Deficit		Int											2	17
			Int	Dev										3	24
	Cognitive-Somatic		Int		Som									4	23
Hyperactivity	Mild Hyperactive		Int									(Hyp)		1	11
	Cognitive Hyperactive	Achv	Int	Dev				Dlq			Psy	Hyp		3	8
Anxiety	Mild Anxiety		Int			Dep				Anx				1	11
										Anx				2	12
Externalizing	Externalized Psychopathology		Int					Dlq			(Psy)	Hyp	Soc	1	16
	Cognitive-Externalized		Int					Dlq			Psy	(Hyp)	(Soc)	4	17
	Cognitive-Combined Internalized/ Externalized	Achv	Int	Dev		Dep		Dlq	Wdrl	Anx	Psy	Hyp	Soc	3	7

Table 9 (cont.). PIC-R typologies across studies.

Primary area of difficulty	Label	PIC elevations												Study[a]	% of sample
		Achv	Int	Dev	Som	Dep	Fam	Dlq	Wdrl	Anx	Psy	Hyp	Soc		
Internalizing	Internalized Psychopathology	Achv	Int	Dev		Dep			(Wdrl)	(Anx)	Psy		Soc	1	16
		Achv	Int	Dev	Som	Dep			Wdrl	Anx	Psy		Soc	2	7
						(Dep)			Wdrl		Psy		Soc	4	8
	Cognitive Internalized	(Achv)	Int	(Dev)		Dep			Wdrl	Anx	Psy		(Soc)	3	11
		Achv	Int	Dev		Dep			Wdrl	(Anx)	Psy		Soc	4	18
Social problems	Conduct Disorder	Achv	Int	Dev				Dlq						1	8
	Antisocial				Som	Dep		Dlq	Wdrl	Anx	Psy			2	11
	Cognitive-Social Skills Deficit	Achv	Int	Dev		Dep		Dlq			Psy	(Hyp)	Soc	3	10
	Social Isolation	Achv	Int	Dev							Psy			2	13
		Achv	Int	Dev							Psy			4	23
Multiple	Combined Internalized/ Externalized				(Som)	Dep		Dlq		Anx	Psy	Hyp	Soc	3	9
	Cognitive-Combined Internalized/ Externalized	Achv	Int	Dev		Dep		Dlq	Wdrl	Anx	Psy	Hyp	Soc	3	7

Note. Scales in parentheses indicate elevations slightly below 70 T.

[a]1 = Rourke& Fuerst, 1991; 2 = Butler et al., 1997; 3 = Saunders et al., 2000; 4 = present study.

Study 2: Brain Metabolism and Psychosocial Functioning

Method

Patterns of brain dysfunction underlying the psychosocial profiles obtained in Study 1 were examined with PET (FDG) in a subset of participants.

Participants

Neuroimaging PET data was available for 48 individuals from Study 1. Three participants were excluded because of incomplete or corrupt PET data. Demographic and clinical variables for the 45 individuals given PET examinations compared to the overall sample are presented in Table 10.

An adult control group previously validated in a PET study of children (Muzik et al., 2000) was used in Study 2. The control group consisted of 14 normal adults (7 males, 7 females), mean age 27.6 years. The controls were all screened for history of medical and/or psychiatric conditions by physical examinations, blood workup, and structured psychiatric interview.

Table 10.

Sample Characteristics for the PET group and the overall sample.

	N	Age	FSIQ	VIQ	PIQ	Age of Sz Onset	Sz Frequency (mean # / day)
Overall	108 (60 M, 48 F)	10.9 (3.5)	89.4 (10.1)	91.0 (10.7)	89.4 (12.5)	4.6 (3.5)	3.6 (5.1)
PET Group	45 (24 M, 21 F)	10.7 (3.5)	84.2 (9.9)	87.2 (9.5)	83.5 (12.1)	4.7 (3.7)	4.7 (6.6)

Procedure

The PET data was initially obtained as part of a clinical evaluation on the Epilepsy Unit. Participants were fasted for 4 hours prior to the PET analysis. A venous line was established for injection of the FDG (5.3 MBq/kg) produced by a Siemens RDS-11 cyclotron. FDG images were acquired using a CTI/Siemens EX-ACT HR whole-body PET scanner. The scanner has a 15-cm field of view and generates 47 image planes with

a slice thickness of 3.125 mm. The reconstructed image in-plane resolution obtained is 6.0 +/- 0.49 mm in the axial direction. Forty-minutes after FDG injection, patients were positioned into the scanner. Using a low-laser beam system, the patient's head was adjusted so that the imaging planes were parallel to the canthomeatal line. Subsequently, a static 20-min emission scan in 2D mode was initiated collecting approximately million net true counts per plane. Calculated attenuation corrections were performed on all images using the CTI-Siemens reconstruction software. The outline of the head was derived directly from the raw data by threshold fits to the sinograms.

The pattern of glucose metabolism derived from the children with epilepsy was compared to those obtained from a control group using Statistical Parametric Mapping (SPM). The SPM method of analysis requires no a priori assumptions about anatomical regions that may differ between groups, and provides overall information about changes in the pattern of glucose metabolism throughout the brain. This technique relies upon an accurate spatial normalization of image volumes to a standard image template. Muzik et al. (2000) have shown that spatial normalization of PET image volumes using an adult template is feasible for children older than 6 years and that such a comparison does not produce artifacts as a result of SPM analysis.

The analysis involved a one-way analysis of variance with cluster membership as the independent variable and brain glucose metabolism as the dependent variable. The SPM statistic (F or t) was transformed to a normal distribution (z), with threshold at P = 0.0001. In addition, only regions of more than 50 voxels attaining a corrected p value of less than .05 were considered. The SPM maps were analyzed using two corrected levels of statistical significance: a voxel level (Z) and a cluster level (k, Z). The voxel level represents the probability of (corrected for multiple comparisons based on the number of resolution elements in the image volume) of observing a Z score of Z or higher, whereas the cluster level represents the probability of observing a cluster size k or larger with a maximal Z score of Z or higher. The corrected significance level was chosen at $p < .05$.

The resulting significant differences in 3D image space were displayed collapsed into three orthogonal planes ("glass brain"). The Talairach coordinates (Talairach & Tournoux, 1988) are given in millimeters, describing the location of significant voxels: x defining the lateral displacement from midline (negative = left), y the anteroposterior

position relative to the anterior commissure (negative = posterior), and z the vertical position relative to the line connecting the anterior and posterior commissure (negative = down). Figure 13 illustrates the Talairach coordinate system as well as the glass brain orthogonal planes.

Results

Visual inspection of Table 10 indicated that participants involved in the PET study were closely matched to the overall sample with respect to age at testing, mean age of seizure onset, and mean seizure frequency. There was a statistical trend for the PET group to have a lower FSIQ compared to the non-PET group (t (106) = 1.9, p = .07). However, no differences were found between the PET and non-PET group with respect to PIC-R scale mean elevations or seizure variables. Table 11 shows the number of participants and IQ scores for each psychosocial subtype, as well as the mean FSIQ for each of these groups for the entire sample.

Table 11.

Number of Participants with PET Data by Psychosocial Subtype.

	N	FSIQ	VIQ	PIQ	FSIQ entire sample (N = 108)
Cognitive-Somatic	9	81.2	85.7	79.5	84.8
Cognitive-Internalized	7	84.7	86.3	84.7	86.0
Cognitive-Externalized	8	80.1	84.0	79.0	92.5
Cognitive-Social Isolation	12	84.6	87.6	84.6	82.7
Internalized	3	88.7	91.7	86.7	95
Somatic Concern	6	90.4	91.8	89.6	91.2

A one-way ANOVA was conducted to test for overall metabolic differences between the psychosocial subtype and control groups. The omnibus test was significant for areas of decreased glucose metabolism in the psychosocial subtypes compared to controls (F (6, 52) = 7.24, $p < .05$). Post-hoc comparisons were made to evaluate specific

differences between subtype groupings and controls. Four of the psychosocial subtypes showed statistically significant areas of decreased glucose metabolism compared to controls. Figure 13 presents the coordinate system for stereotaxic space, as well as the "glass brain" used to present the PET data. Figures 14 through 17 show the specific areas of decreased metabolism relative to controls for each of these subtypes. The two subtypes that did not differ significantly from controls were Internalized, and Somatic Concern.

Figure 13. PET data presentation. (A) The x-y-z coordinate system within standardized stereotaxic space. (B) Example of PET data depicted in a "glass brain". The areas of decreased metabolism are shown within sagittal, coronal, and axial planes.

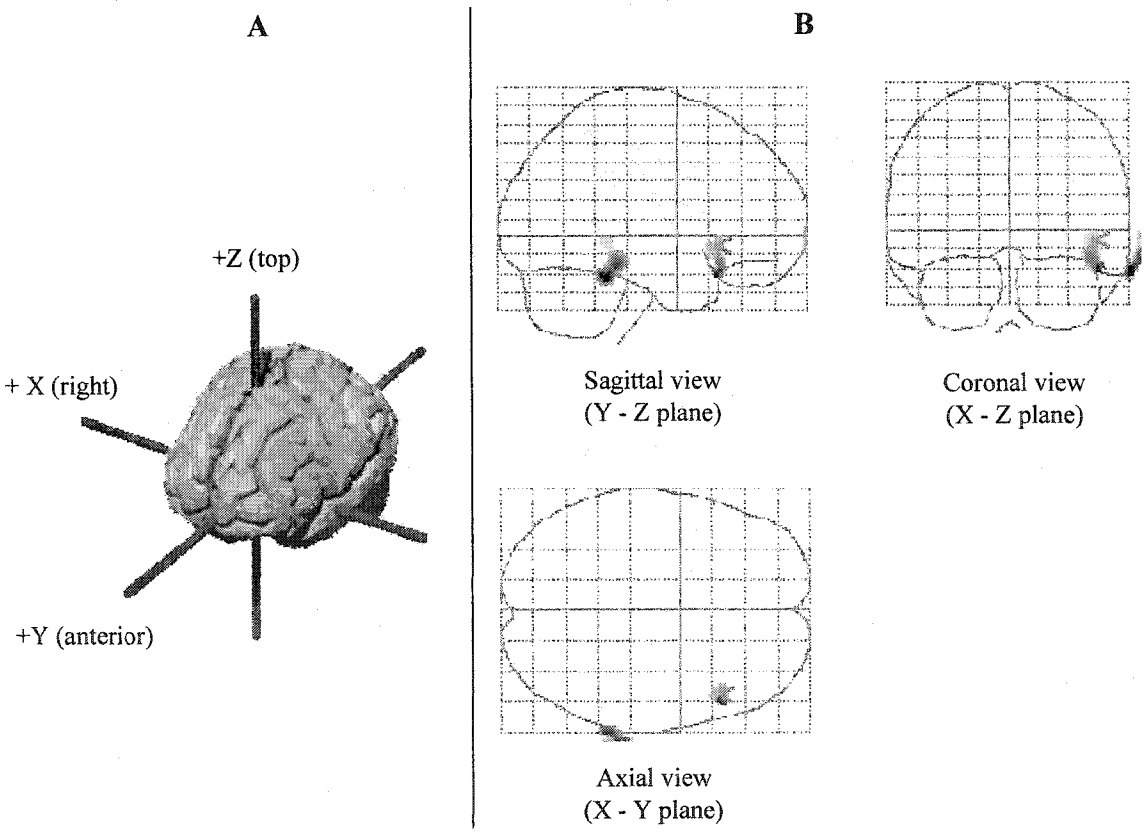
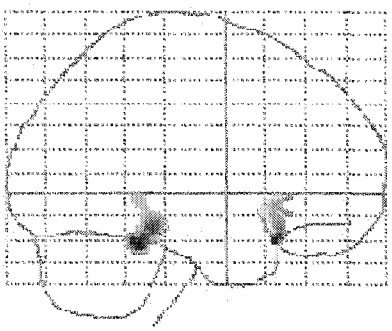
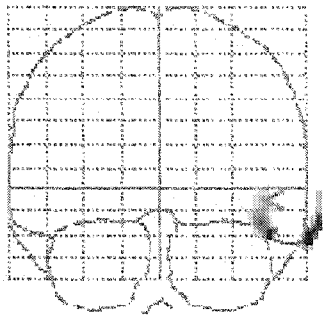


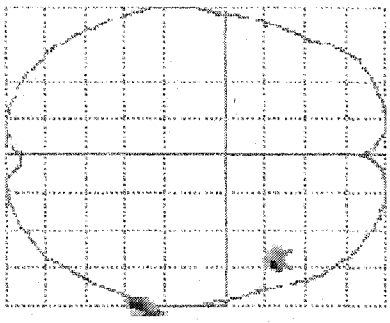
Figure 14. Brain areas of decreased metabolism in the Cognitive-Somatic subtype relative to controls.



Sagittal view



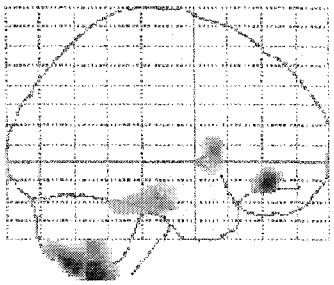
Coronal view



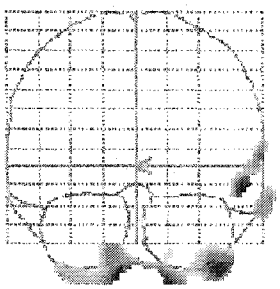
Axial view

P value cluster level	**P value voxel level (Z)**	**Talairach coordinates x, y, z (mm)**	**Brain region**
p = .11	P = .10 (3.19)	50, 22, -22	R temporal
p = .10	P = .10 (3.20)	68, -40, -24	R temporal

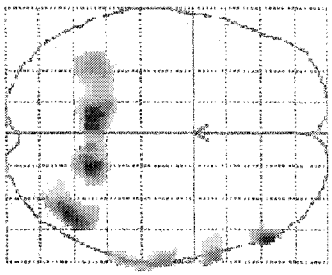
Figure 15. Brain areas of decreased metabolism in the Cognitive-Internalized subtype relative to controls.



Sagittal view



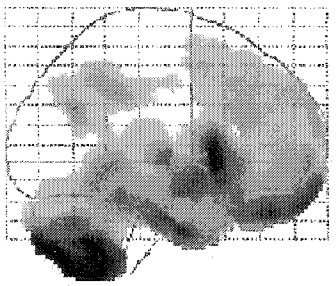
Coronal view



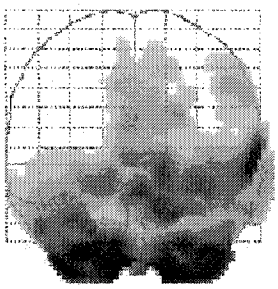
Axial view

P value cluster level	P value voxel level (Z)	Talairach coordinates x, y, z (mm)	Brain region
p = .11	p = .05 (3.47)	56, 40, -12	R frontal
p = .05	p = .06 (3.41)	18, -54, -62	R cerebellum
	p = .06 (3.40)	-12, -54, -46	L cerebellum
p = .09	p = .06 (3.40)	42, -68, -54	R cerebellum
p = .11	p = .08 (3.31)	66, 12, 6	R frontal
p = .10	p = .08 (3.29)	70, -20, -20	R temporal
	p = .09 (3.29)	66, -14, -24	R temporal

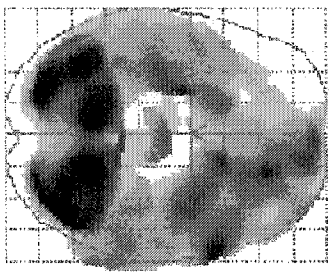
Figure 16. Brain areas of decreased metabolism in the Cognitive-Externalized subtype relative to controls.



Sagittal view



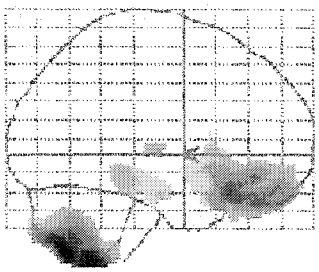
Coronal view



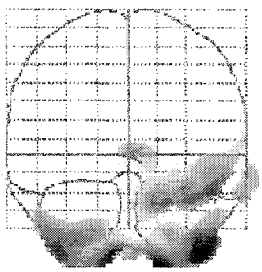
Axial view

P value cluster level	P value voxel level (Z)	Talairach coordinates x, y, z (mm)	Brain region
p < .001	p = .004 (4.25)	18, -56, -58	R cerebellum
	p = .004 (4.24)	42, -68, -54	R cerebellum
	p = .004 (4.23)	-8, -54, -56	L cerebellum
p = .08	p = .01 (3.81)	2, -14, 0	R thalamus
p = .05	p = .03 (3.61)	22, -62, 26	R parietal
	p = .08 (3.28)	8,-70, 38	R parietal
	p = .09 (3.25)	-4, -70, 34	L parietal
p = .07	p = .05 (3.45)	56, 6, 50	R frontal
p = .07	p = .09 (3.25)	2, -32, 34	R cingulate
	p = .09 (3.23)	12, -26, 40	R cingulate
p = .11	p = .10 (3.19)	-34, 26, -2	L insula
p = .10	p = .10 (3.18)	-12, -14, 42	L cingulate

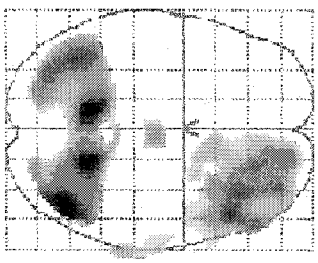
Figure 17. Brain areas of decreased metabolism in the Cognitive-Social Isolation subtype relative to controls.



Sagittal view



Coronal view

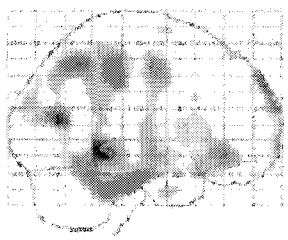


Axial view

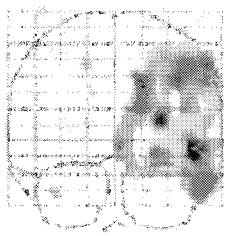
P value cluster level	P value voxel level (Z)	Talairach coordinates x, y, z (mm)	Brain region
p = .09	p = .01 (3.88)	42, -68, -54	R cerebellum
	p = .01 (3.85)	-10, -50,-60	L cerebellum
	p = .01 (3.82)	16, -52, -62	R cerebellum
p = .01	p = .02 (3.64)	48, 26, -22	R temporal
	p = .03 (3.58)	36, 30, -26	R frontal
	p = .03 (3.56)	20, 42, -28	R frontal
p = .10	p = .06 (3.36)	4, -14, 0	R thalamus
p = .08	p = .08 (3.27)	70, -30, -14	R temporal
	p = .08 (3.27)	66, -14, -24	R temporal
p = .11	p = .08 (3.27)	12, 16, -2	R caudate

To determine whether specific brain areas were associated with general psychosocial dysfunction across subtypes, mean PIC-R Adjustment scores were correlated with brain glucose metabolism. Figure 18 shows brain areas where glucose metabolism was inversely correlated with mean PIC-R Adjustment scores.

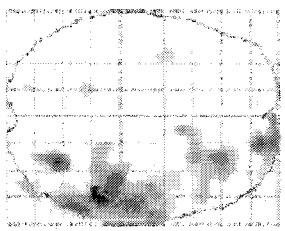
Figure 18. Brain areas where glucose metabolism is negatively correlated with PIC-R Adjustment scores.



Sagittal view



Coronal View



Axial View

P value cluster level	P value voxel level (Z)	Talairach coordinates x, y, z (mm)	Brain region
p = .004	p = .04 (3.52)	48, -42, -6	R temporal
	p = .06 (3.36)	58, -56, 48	R parietal
	p = .07 (3.34)	44, -34, 46	R parietal
p = .07	p = .06 (3.39)	28, -68, 12	R parietal
	p = .10 (3.18)	32, -70, 38	R parietal
p = .08	p = .06 (3.37)	18, 62, 34	R frontal
	p = .07 (3.34)	16, 70, 20	R frontal
	p = .08 (3.29)	4, 70, -6	R frontal
p = .05	p = .07 (3.31)	26, 36, -8	R frontal
	p = .09 (3.22)	26, 22, -16	R frontal

Discussion

The main goal of this study was to investigate a typology of psychosocial functioning in children with epilepsy based on cluster analysis of their PIC-R profiles. The psychosocial subtypes were examined in relation to various seizure variables (i.e., side of seizure focus, seizure frequency, seizure type, and age of seizure onset), and compared to previously established PIC-R typologies in the literature. A second study in a subsample of the participants examined the relation between subtype assignment and patterns of cerebral glucose metabolism using PET.

The present findings provided strong support that children with epilepsy can be meaningfully categorized into six subtypes based on PIC-R profiles. Five of the six subtypes resembled subtypes previously identified in children with LD, TBI or nonspecific neuropsychological deficits. A relation was found between the subtype to which children were assigned and seizure type, as well as with the age of seizure onset. Results from the PET study indicated that four of the subtypes were differentiated from controls by decreased glucose metabolism in specific brain areas, particularly in the right cerebral hemisphere, and cerebellum bilaterally. These findings are discussed in detail below in relation to the initial hypotheses.

Hypothesis 1: A PIC-R Typology of Psychosocial Functioning in Children with Epilepsy.

The results of the present investigation provide support for a PIC-R typology in children with epilepsy consisting of six subtypes. The number of subtypes is much less that the PIC-R typology that was derived using a general clinical sample (12 subtypes; Gdowski, Lachar, & Kline, 1985). However, research conducted with neuropsychological and neurological samples of children have identified a more limited number of PIC-R subtypes (Butler et al., 1997; Rourke & Fuerst, 1991; Ralston, Fuerst, & Rourke, 2003; Saunders et al., 2000). Moreover, a small number of subtypes is not unexpected in samples limited to specific neuropsychological or neurological characteristics, because such groups are unlikely to exhibit the full range of child psychopathology evident in a more general clinical population.

Description of the typology

Descriptive labels were assigned to each subtype based on the characteristics of the clinical scales that were elevated above T = 70 (clinically significant elevation in the direction of psychopathology). Labeling schemes used in prior similar research were also taken into consideration (see Table 12 for an overview of overlapping PIC-R subtypes across studies). Each subtype is discussed in terms of the expected behavioural characteristics given a particular pattern of scale elevations.

The mean PIC-R profiles of two of the subtypes were characteristic of normal psychosocial functioning. The profile of the Somatic Concern subtype consisted of a single elevation (above 70 T) on the Somatic Concern Scale. Children with similar PIC-R profiles are described as having health related complaints such as sustained fatigue, headaches, or aches and pains. Research in adults using similar multidimensional ratings scales has shown that neurological patients tend to endorse somatic items more than other items (Gass & Ansley, 1995). Indeed, half of the present sample (51%) exhibited elevations on the Somatic Concern scale. Therefore, it is likely that somatic complaints consistent with epilepsy and not psychopathology contribute heavily to these high elevations. It is, however, possible that such somatization is maladaptive in nature (i.e., employed to avoid situations or responsibilities). The Somatic Concern subtype accounted for 10% of the present sample. A similar subtype was identified in children with LD, and in children with TBI.

The Cognitive-Somatic subtype also exhibited a PIC-R profile that suggested normal psychosocial functioning, with high elevations only on the Intellectual Screening and Somatic Concerns scales. Elevations on the Intellectual Screening scale reflect parental concerns that the child may have impaired intellectual functioning. This subtype was similar to the Normal subtype identified in children with LD, as well as the Cognitive Deficit subtype identified in children with TBI and in children with nonspecific neuropsychological deficits. In children with LD, elevations on the cognitive triad (i.e., Achievement, Intellectual Screening, and Development) scales in the absence of other clinical scale elevations are considered "normal" because of the presence of a known learning problems. Although such a profile is not considered to be strictly normal in an epilepsy population, given the high rates of academic difficulties associated with

childhood epilepsy, the Cognitive-Somatic profile was considered essentially free of significant psychosocial dysfunction. This subtype accounted for 23% of the present sample.

Collectively, the Somatic Concern and Cognitive-Somatic subtypes accounted for 33% of the present sample. This indicates that only one-third of the population presented without significant psychosocial difficulties. Such findings are consistent with the high rates of behaviour problems typically reported in this population. By comparison, studies of children with LD indicate that more than half of these children exhibit either normal functioning or very mild disturbances (Rourke & Fuerst, 1991). Similar rates have been reported in children with CHI (Butler et al., 1997) and in children with nonspecific neuropsychological difficulties (Saunders et al., 2000). Thus higher rates of psychosocial disturbance are exhibited in children with epilepsy compared to other neuropsychological/neurological populations.

The remainder of the PIC-R subtypes had profiles that suggested high degrees of psychosocial disturbance (i.e., profiles with multiple clinically significant elevations). The mean PIC-R profile of the Cognitive-Externalized subtype was elevated on a number of scales. Children in this subtype have particularly high mean scores on the Intellectual Screening, Delinquency, and Psychosis scales. Although not at a clinically significant level, they also have high mean scores on the Hyperactivity and Social Skills scales. These children are apt to exhibit acting-out behaviours as well as emotional lability. Such children may be aggressive, impulsive, restless, and may exhibit low frustration tolerance. This was the only subtype to be characterized with externalizing psychopathology, and accounted for 17% of the sample. A similar subtype had been reported in children with LD.

The Cognitive-Social Isolation subtype was characterized by significant elevations on the Achievement, Intellectual Screening, Development (i.e., cognitive triad), and Psychosis scales. Parental ratings of these children indicated concerns with cognitive development, academic performance, as well as social adaptation. Elevations on the Psychosis scale may reflect behaviours characteristic of social isolation, emotional lability, inappropriate affect, poor reality testing, and unusual behaviours. Twenty-three

percent of the sample was assigned to this subtype. This subtype was very similar to the Social Isolation subtype identified in children with CHI.

The two remaining subtypes were classified as reflecting internalizing psychosocial difficulties. The Cognitive-Internalized subtype was characterized by elevations on the cognitive triad, Depression, Withdrawal, Psychosis, and Social Skills scales. A high but not clinically significant elevation was also exhibited on the Anxiety scale. Children in this subtype likely display cognitive and academic difficulties in addition to psychosocial difficulties. The ratings suggest that these children have feelings of low self-esteem, sadness, anxiety, poor peer relationships, peer rejection, and solitary activities. This subtype accounted for 18% of the sample, and reflected the greatest degree of psychosocial disturbance in this population, both with respect to scope and magnitude of the difficulties. Similar subtypes have been identified in children with LD, TBI, and nonspecific neuropsychological deficits.

The final subtype, Internalized Psychopathology, exhibited marked elevations on the Withdrawal, Psychosis and Social Skills scales. There was also a high, although not clinically significant, elevation on the Depression scale. Children in this subtype are likely to suffer from significant internalizing psychopathology, including problems with depressed mood, emotional lability, inappropriate affect, poor reality testing, and social isolation. However, they do not appear to have cognitive difficulties. This was the smallest of the subtypes, accounting for 8% of the sample.

Reliability of the typology

Because multivariate subtyping techniques were applied in an exploratory fashion to a data set with unknown or poorly understood structure, the demonstration of reliability is crucial. In this study reliability was demonstrated by replicating the obtained cluster solution with three additional clustering techniques. Good agreement between the four clustering methods suggested that a six-cluster typology described above was reliable.

Although the primary focus of this study was not to compare PIC-R typologies across populations, it was expected that at least some of the present subtypes would be similar to those developed for children with LD (Rourke & Fuerst, 1991). Additional subtypes were also expected in the epilepsy-derived typology. Preliminary support for

this hypothesis was found, based on the finding that three of the epilepsy subtypes (Somatic Concern, Cognitive-Externalized, and Cognitive-Internalized) showed a similar profile of scale elevations to three of the prototypical LD subtypes (see Table 12). These three common subtypes accounted for approximately 43% of the children with LD, and 45% of the children with epilepsy. Moreover, visual inspection of Table 12 reveals that there is a close correspondence across LD and epilepsy populations with respect to the percentages assigned to each of these three subtypes.

Table 12.

Common psychosocial subtypes between children with epilepsy and other child populations: LD (Rourke & Fuerst, 1991), CHI (Butler et al., 1997), and nonspecific neuropsychological deficits (mixed NP; Saunders et al., 2000).

Psychosocial Difficulty	Population	% of sample assigned	Subtype label
Somatic	LD	11	Somatic Concern
	epilepsy	10	Somatic Concern
	CHI	12	Somatic Concern
Externalized	LD	16	Externalized Psychopathology
	epilepsy	17	Cognitive Externalized
Internalized	LD	16	Internalized Psychopathology
	epilepsy	18	Cognitive Internalized
	mixed NP	11	Cognitive Internalized
	CHI	7	Internalized Psychopathology
Cognitive-Social Isolation	epilepsy	23	Cognitive-Social Isolation
	CHI	13	Social Isolation
Cognitive	epilepsy	23	Cognitive-Somatic
	CHI	17	Cognitive Deficit
	mixed NP	24	Cognitive Deficit

Two of the epilepsy derived subtypes, although not present in children with LD, have been reported in other child populations. The Cognitive-Social Isolation subtype has been identified in children with CHI, and a subtype characterized primarily by cognitive deficits has been identified in both children with CHI and children with nonspecific neuropsychological deficits. Overall, five of the six epilepsy subtypes are

similar in nature to those reported in previous PIC-R typologies. Finding similar subtypes across different populations supports the reliability of the subtypes.

The remaining subtype, Internalized Psychopathology appears relatively unique to the epilepsy population. Subtypes characterized by internalized psychopathology have typically been reported to exhibit significant cognitive difficulties. However, the scales that make up the cognitive triad in the epilepsy Internalized subtype are all well below the clinical range. It appears that in children with epilepsy, internalized psychopathology appears both in isolation, as well as accompanied by cognitive deficits. When combined, the two internalized subtypes in the epilepsy population (Cognitive-Internalized and Internalized) accounted for approximately 26% of the sample. However, the pure Internalized subtype was the smallest group, and thus such problems are most likely to co-occur with cognitive difficulties in this population.

Additional support for the reliability of the present typology is provided by its correspondence with the PIC typology derived from a psychiatric sample (Gdowski et al., 1985; LaCombe, Kline, Lachar, Butkus, & Hllman, 1991). The Type 2 profile in the Gdowski et al. typology contains a single elevation, as does the Somatic Concern subtype. The epilepsy Cognitive-Social Isolation subtype is similar to the Type 5 profile, showing elevations on the cognitive triad and Psychosis scales. The cognitive dysfunction profile of Type 6 resembles the Cognitive-Somatic subtype. Cognitive-Internalized and Cognitive-Externalized profiles are identified in both the epilepsy and psychiatric samples. The Type 9 Internalization profile is similar to the Internalized psychopathology profile in children with epilepsy. Overall, there is good correspondence between the six subtypes in this investigation and those identified in children referred to a psychiatric facility.

External Validity of the Typology

All of the subtypes derived in the present investigation were readily interpretable within the framework recommended in the PIC-R manual (Wirt et al., 1984). These subtypes were also consistent with patterns of psychosocial disturbance reported in the literature. However, few studies have employed a measure as comprehensive as the PIC-R, or a sample as large as the present one. Nonetheless, collective findings across

previous studies of psychosocial difficulties in children with epilepsy are in general agreement with the present findings.

Previous research has shown that children with epilepsy appear particularly prone to psychosocial difficulties (Carleton-Ford et al., 1995). The present findings indicated that two-thirds of the children were assigned to subtypes reflecting psychosocial disturbances. More specifically, past research has shown that children with epilepsy tend to show more internalizing than externalizing behaviour problems, and tend to be more socially withdrawn compared to other children (Dorenbaum et al., 1985; Dunn, Austin, Caffrey, & Perkins, 2003; Ettinger, et al., 1998; Huberty, Austin, Risinger, & McNelis, 1992; McDermott, Mani, & Krishnaswami, 1995). Similarly, the present findings identified internalizing behaviours and social difficulties as the main areas of psychosocial difficulty in these children. Collectively, the Cognitive-Internalized, Internalized, and Cognitive-Social Isolation subtypes accounted for approximately 50% of the entire sample, representing 75% of those identified as having significant psychosocial disturbances.

In addition to psychosocial functioning, there was also consistency between the present and previous findings with respect to cognitive difficulties. Although individuals with epilepsy rarely demonstrate significant impairments in general intellectual functioning, past research has demonstrated that children with epilepsy are at a higher risk for academic difficulties compared to other children (Austin et al., 1998; Bennett, 1992; Dodson, 1993; Williams & Sharp, 2000). In the present study, psychometric intelligence across psychosocial subtype fell within the low average to average range, which is generally consistent with the literature. Despite the absence of any significant impairment of overall intellectual functioning in the groups, four of the six subtypes presently identified had clinically significant elevations on the Intellectual Screening or the entire cognitive triad scales. These four subtypes accounted for approximately 81% of the entire sample. It is noteworthy that no significant difference in overall IQ was found between subtypes. The present findings suggest that while low average intellectual functioning may contribute to learning difficulties in these children, poor academic performance may also be related to other factors, such as neuropsychological deficits (e.g., attention, memory) and/or psychosocial difficulties. This is consistent with

previous findings in the literature showing that academic difficulties in children with epilepsy are not typically accounted for by poor psychometric intelligence.

Additional evidence for the external validation of the PIC-R subtypes was provided in Study 2 (discussed below).

Hypothesis 2: Seizure Variables and Psychosocial Difficulties.

The present findings indicated no relation between seizure frequency (at the time of PIC-R data collection) and degree of psychosocial impairment. This was unexpected given previous findings showing higher seizure frequency to be associated with higher levels of psychosocial difficulties. One problem with the present data is that seizure frequency was not recorded in a rigorous or systematic fashion across subjects. It was not possible to evaluate for each subject the exact period covered by the seizure frequency estimates (i.e., estimated over several months vs. an entire year). Therefore, the lack of association in the present findings may reflect errors or variability in the estimates. In addition, for subjects with multiple seizure types, seizure frequency referred to the total number of seizures, regardless of type. A more detailed analysis of seizure frequency by type may yield different findings.

The present findings revealed a statistical trend for children with generalized epilepsy to show higher PIC-R elevations compared to those with partial epilepsy. This is generally consistent with previous reports in the literature. Differences in specific measures used to quantify psychosocial dysfunction across studies may in part account for the lack of a robust effect in the present investigation.

No relation was presently found between side of seizure focus (left vs. right) and psychosocial subtype assignment. This is consistent with previous findings showing that left- and right-sided seizure foci are equally represented in groups of maladjusted children with temporal lobe epilepsy (Camfield et al., 1984). However, grouping methods based on seizure focus may mask important brain differences between groups because they fail to take into account possible brain dysfunction in areas outside the primary seizure foci.

Past research on whether age of seizure onset is related to degree of psychosocial impairment has provided equivocal findings. Some studies have indicated that later age of seizure onset is associated with increased behavioural difficulties, whereas others have

found the age of onset is a greater predictor of cognitive impairment (Hermann et al., 1980; Schoenfeld et al., 1999). An association between early age of seizure onset and higher PIC-R elevations was presently found. Moreover, differences in mean age of seizure onset were found across subtypes, such that the Cognitive-Externalized subtype had the youngest age of onset, and the Somatic Concern subtype had the oldest age of onset. It is noteworthy that the Cognitive-Externalized subtype is the only subtype to likely present with conduct problems, whereas the Somatic Concern subtype is essentially normal both with respect to cognitive and psychosocial functioning. The present results suggest that early age of seizure onset may be predictive of externalized behavioural problems as well as cognitive difficulties.

Hypothesis 3: Patterns of Cerebral Glucose Metabolism and PIC-R Subtype

The findings from Study 2 are important for two main reasons. First, the relation between psychosocial problems and brain functioning is poorly understood, due in part to a paucity of research in this area. Second, the PET findings were a means of providing external validation for the PIC-R typology derived in Study 1. In order for a typology to be meaningful, its relation to measures other than those used to construct it should be demonstrated. Such a demonstration, referred to as concurrent validity, provides a measure of external validation of the typology. In this study, it was expected that the subtypes of psychosocial functioning in children with epilepsy would show unique patterns of cerebral metabolic dysfunction compared to controls. Moreover, it was expected that in general psychosocial dysfunction would be more characteristic of right compared to left hemisphere dysfunction.

A rigorous analysis approach using SPM was employed to compare each PIC-R subtype to controls. Four of the six subtypes showed specific brain areas of metabolic dysfunction compared to controls. All areas of dysfunction were characterized by decreased glucose metabolism, which is consistent with previous studies that have associated behaviour problems with cerebral hypometabolism (e.g., Juhasz et al., 2001). Overall, different patterns of psychosocial difficulty appear to be related to different patterns of decreased brain metabolism.

The Somatic Concern and Internalized subtypes were not differentiated from controls with respect to glucose metabolism. In the case of the Somatic Concern subtype,

it is not surprising that no differences relative to controls were found because this subtype was characterized by essentially "normal" cognitive and psychosocial functioning. With regard to the Internalized subtype, the small number of individuals therein (n=3) calls into question the reliability of any finding involving this group. In theory, a larger sample may have exhibited brain differences relative to controls given the high number of PIC-R elevations in this subtype and the fact that other subtypes with numerous elevations show brain dysfunction.

The four subtypes that showed differences in cerebral glucose metabolism relative to controls were: Cognitive-Somatic, Cognitive-Internalized, Cognitive-Externalized, and Cognitive-Social Isolation. It is noteworthy that not all brain areas of dysfunction showed robust differences between subtype and controls. Table 13 shows the main areas of decreased metabolism in each subtype relative to controls. Because the PET groups had relatively small numbers of individuals in each, areas showing a statistical trend (at the voxel level) for differences were also identified. Whether or not these areas showing trends reflect reliable findings requires additional study with larger samples.

Table 13.

Main areas of decreased cerebral metabolism in PIC-R subtypes compared to controls.

Subtype	**Brain areas of hypometabolism**	
	($p < .05$)	**($.05 < p < .10$)**
Cognitive-Somatic		R temporal
Cognitive-Internalized	R frontal	R/L cerebellum R temporal
Cognitive-Externalized	R frontal R/L cerebellum R thalamus R parietal	L parietal R/L cingulate L insula
Cognitive-Social Isolation	R frontal R/L cerebellum R temporal	R thalamus R caudate

An examination of Table 13 reveals that the main areas of brain differences are localized in the right frontal, bilateral cerebellar, and to a lesser extent right temporal

regions. Although these data are preliminary, such patterns of brain dysfunction are suggestive of specific neural mechanisms underlying psychosocial problems.

Three of the four subtypes showed decreased metabolism in the right temporal regions compared to controls. Although the existence of a "temporal lobe personality" has largely been refuted, temporal lobe lesions have long been associated with altered personality and behaviour. There are some reports in the literature linking dysfunctional temporal lobe functioning to poor social development in the autism literature. Temporal lobes and limbic structures (hippocampus and amygdala) have been called the seat of the "social brain" because damage to these areas can produce autistic symptomatology (i.e., social impairment, language impairment, and restricted interests; Green, Joy, Robins, Brooklier, Waterhouse, & Fein, 2003). Animal models of autism have shown that neonatal lesions to temporal lobe structures produce significant socioemotional dysfunction in monkeys (e.g., Bachevalier, Malkova, & Mishkin, 2001). In humans, postmortem investigations have revealed medial temporal lobe abnormalities in autistic children (Bauman & Kemper, 1994), and decreased brain metabolism has been identified in the temporal areas of autistic individuals (Ohnishi et al., 2000). In one PET study involving children, ratings of aggression correlated with brain glucose hypometabolism in several brain areas, including temporal lobe structures (Juhasz et al., 2001).

Taken together, there is some evidence that intact temporal lobe functioning is important for some aspects of social functioning. However, whereas previous research has pointed to bilateral temporal lobe dysfunction, the present findings implicated right-sided dysfunction in particular. There is some evidence that changes in personality or behaviour may occur more often following right temporal lobectomy than left, although such findings are questionable (Kolb & Wishaw, 1996). Previous research has found that although psychiatric disorders, particularly hypomania, tend to be associated with right-sided foci, depression appears to be more common in those with left-sided foci (Lambert, Schmitz, Ring & Trimble, 2003). Presently, the subtype most reflective of depressive symptomatology, the Cognitive-Internalized, showed only right-sided temporal hypometabolism. Differences between the present study and previous ones may explain some of these laterality discrepancies (e.g., children as participants, use of PIC-R, use of PET versus other neurological investigative techniques).

It may be that some of the psychosocial difficulties in the present study reflect temporal lobe dysfunction. An alternate view is that the temporal lobe hypometabolism reflects cognitive disturbances, possibly in the form of memory impairment, a common cognitive sequelae in children with epilepsy (Aldenkamp at al., 1990; Jambaque wt al., 1993; Milberg et al., 1980; Schoenfeld et al., 1999; Semrud-Clikeman & Wical, 1999). It is of interest that very high elevations on the Intellectual Screening scale were common to the three subtypes that showed right temporal hypometabolism. The Cognitive-Externalized subtype showed a relatively lower, albeit clinically significant, elevation on this scale. Although lateralized, the present temporal hypometabolism may reflect generalized dysfunction in memory systems, reflected in the high Intellectual Screening elevations presently found. Because comprehensive memory testing was not performed on these children, such a link remains open to further investigation.

The most robust finding of brain dysfunction in the subtypes involved hypometabolism in the right frontal lobe region. Frontal lobes are typically regarded as subserving "executive functions", cognitive functions associated with planning and regulating adaptive and goal-directed behaviours such as initiation, planning, cognitive flexibility, abstraction, and inhibitory control. When executive dysfunction is observed, the prefrontal cortex is typically thought to be involved, although dysfunction may reflect disruption in any of the neural pathways connected to this area (D'Esposito, 2003). With respect to laterality, there is evidence that patients with left frontal damage behave similarly to those with right frontal damage on tests of executive functions (Demakis, 2003). However, Seger Desmond, Glover and Gabrieli (2000) have suggested that right frontal systems may be more important for cognitive tasks that require greater self-monitoring of performance.

Executive dysfunction is thought to regulate antisocial and/or aggressive behaviour due to decreased behavioural inhibition and inability to generate socially acceptable responses in challenging situations. Such a view appears most consistent with the Cognitive-Externalized subtype. It is of interest that the Cognitive-Externalized subtype is the only subtype to show brain dysfunction in parietal in addition to right frontal regions, two regions that have been recently associated with successful inhibition behaviours (Nielson, Langenecker, & Garavan, 2002). Thus this subtype may be

particularly prone to inhibitory control problems because of dysfunction in these areas. In addition, this is the only subtype to show dysfunction in the cingulate cortex, which is thought to be involved in regulating responses to stressful emotional and behavioural events, emotional expression, and social behaviour (Davidson, 2003). Thus, the externalized problems that characterize this subtypes may be related to decreased inhibitory control due to prefrontal cortex and parietal dysfunction, as well as dysfunctional affective regulation due to limbic (cingulate) dysfunction.

The remaining two subtypes to show right frontal dysfunction (Cognitive Internalized and Cognitive-Social Isolation) do not appear to be characterized primarily by disinhibition. Rather, they reflect psychosocial difficulties related to social isolation and internalized psychopathology. Frontal lobe dysfunction in these groups may reflect difficulty with initiation behaviours. Patients with frontal lobe dysfunction often have difficulty initiating responses to task, or in producing spontaneous behaviours (Kolb & Wishaw, 1996). It is also of interest that dysfunctional frontal lobe systems have been associated with autistic symptamotology, such as social impairment (Green et al., 2003).

It is noteworthy that frontal dysfunction has been associated with thought disorders, and that all three subtypes with dysfunctional frontal areas are characterized by high elevations on the Psychotic scale. Although the PIC-R Psychosis scale does not indicate the presence of a thought disorder, elevation on this scale may indicate dysfunctional thought processes and poor reality testing. Numerous PET studies of patients with schizophrenia have reported frontal hypometabolism (e.g., Buchsbaum, DeLisi, & Holcomb, 1984). Thus dysfunctional frontal areas in these PIC-R subtypes may reflect systems important for intact thinking processes. Furthermore, such a view may account for the cerebellar dysfunction presently identified in these subtypes.

Until recently, the cerebellum was viewed primarily as a motor coordination centre. Research over the last decade suggests that it may play a role in cognitive function (Katsetos, Hyde, & Herman, 1997). Some researchers have emphasized the importance of connections between the cerebellum and frontal lobes. For example, Schmanmann and Pandya (1997) have argued that the cerebellum is an essential node in distributed corticosubcortical neural circuits subserving cognitive operations. These connections involve the cerebellar dentate and the relay nuclei of the thalamus to the

prefrontal cortex. These anatomical connections may explain reports that cerebellar patients have difficulties with executive functions (Grafman et al., 1992). Similarly, Andreasen (1998) suggested that pathways between the prefrontal cortex, thalamic nuclei, and cerebellum result in the "cognitive dysmetria" of schizophrenia (i.e., impairments in formation processing, retrieval and prioritization of cognitive tasks). The cerebellar dysfunction presently identified in children with epilepsy may thus reflect disturbances in distributed neural system involved in executive functions. Disruptions in this system may be reflected as difficulties in the areas of initiation, behavioural regulation, affective regulation, and/or social withdrawal.

One finding of particular interest was the extent of right hemisphere dysfunction found across subtypes. Moreover, scores on the PIC-R Adjustment scale (a general measure of psychosocial adjustment) were significantly correlated only with right-sided brain areas of glucose hypometabolism. That is, higher Adjustment scale elevations (indicating a greater degree of maladjustment) were associated with a greater degree of hypometabolism in the right temporal, parietal, and frontal lobes. While overall there were slightly more individuals with right-sided seizure foci in the PET group, the Cognitive-Internalized and Social isolation subtypes had approximately the same number of left versus right sided cases, and showed the same pattern of right hypometabolism.

The findings that psychosocial functioning may be particularly sensitive to right hemisphere dysfunction are not novel. Research in adults has shown that individuals exhibit more difficulty with psychosocial adjustment following damage to the right hemisphere compared to the left (e.g., Tellier, Adams, Walker, & Rourke, 1990). Research with children with LD has suggested that right hemisphere dysfunction may be associated with socioemotional deficits such as difficulty adapting to novel situations, deficits in social skills development, and internalized forms of psychopathology (Rourke, 1995; Semrud-Clikeman & Hynd, 1990). In part, this is based on the theory that the right hemisphere specializes in intermodal integration, whereas the left processes in a modality-specific manner (Goldberg & Costa, 1981). It is argued that as a result of this functional asymmetry, socioemotional/adaptational functioning is more sensitive to deficits in right hemisphere systems compared to the left (e.g., Rourke, 1995).

It was hypothesized that right hemisphere dysfunction would be associated with a greater degree of psychosocial difficulty compared to left hemisphere dysfunction. Children with epilepsy in the present study exhibited metabolic dysfunction lateralized almost exclusively to the right hemisphere. Although there appears to be a consensus in the literature that the right hemisphere plays a key role in psychosocial functioning and development, it remains unclear why children with epilepsy as a group would exhibit specific dysfunction in the right hemisphere, regardless of seizure focus. The answer to such a question is beyond the scope of the present investigation, and warrants further study. Future research to address this question may look to laterality differences in the distribution of white matter. The right hemisphere has been reported to contain a larger relative proportion of white matter than the left hemisphere, a difference that is particularly apparent in the frontal lobes (Gur et al., 1980). Although seizures are characterized as sudden discharges of grey matter, they propagate throughout the brain via white matter fibers, and seizure activity has been shown to influence axonal branching (Holmes, 2002). To the extent that seizure activity modulates white matter systems, the right hemisphere may be particularly susceptible to some forms of dysfunction. Accordingly, children with intractable seizures may have a tendency to develop subtle dysfunctions in right hemisphere white matter systems, which may manifest as metabolic dysfunction and contribute to subsequent disturbances in psychosocial functioning.

It is noteworthy that there was presently a statistical trend for lower overall IQ in the PET group compared to the non-PET group. Thus the question arises to what extent the former group may be representative of the latter. However, patterns of glucose metabolism did not appear to be related to IQ across subtypes in the PET study. For example, the Cognitive-Internalized and Cognitive-Social Isolation subtypes showed the same mean overall IQ scores, but exhibited different patterns of metabolic dysfunction compared to controls. In addition, whereas PIC-R Adjustment scores correlated inversely with glucose metabolism, such scores were not significantly correlated with FSIQ in the present study ($r = .20$, $p > .05$). These findings are consistent with previous reports in the literature showing that adaptive functioning but not IQ is correlated with the degree of cerebral glucose metabolism in children with epilepsy (Ferrie et al., 1997). It appears

that differences in cerebral metabolism across psychosocial subtype in the present study may reflect to a large extent differences in psychosocial functioning.

Summary

The primary goal of this investigation, to develop a PIC-R based typology of psychosocial functioning in children with epilepsy was accomplished. Using cluster analysis, a six-subtype solution was derived that overlapped, in part, with typologies previously reported in children with LD, CHI, and non-specific neuropsychological deficits. This overlap was expected, as was an additional subtype that appeared unique to the epilepsy population. Compared to other neuropsychological/neurological populations, children with epilepsy showed elevated rates of psychopathology, particularly of internalizing variety. The PIC-R profiles were also characterized by a high degree of cognitive difficulties. Collectively, these findings are consistent with the literature that children with epilepsy have a high degree of academic and social difficulties.

Contrary to expectations, no relation was found between seizure frequency and degree of psychosocial difficulty. The results provided some support that children with generalized forms of epilepsy are more likely to exhibit psychosocial difficulties than are those with other forms. The findings also indicated that younger age of seizure onset was associated with greater general degree of psychosocial difficulty. In addition, a younger age of onset may be predictive of externalized psychopathology. No relation was found between psychosocial difficulties and side of seizure focus.

The results from the PET study provided external validation for the subtypes derived in Study 1. Four of the subtypes exhibited unique patterns of dysfunctional cerebral glucose metabolism compared to controls. This dysfunction was characterized as decreased glucose metabolism, and was primarily found in right frontal regions, the cerebellum bilaterally, and to a lesser extent right temporal areas. Moreover, increased hypometabolism in the right hemisphere, including temporal, frontal and parietal regions, was associated with increased general psychosocial maladjustment.

General Conclusions

This investigation demonstrated that there is no single, unitary pattern of psychosocial functioning that is characteristic of all children with epilepsy. Thus the

present findings do not support the notion of an "epileptic personality", or specific behavioural profile associated with epilepsy. Rather, the results lead to the conclusion that the psychosocial sequelae of epilepsy during childhood cover a range of patterns, ranging from essentially normal, to relatively circumscribed intellectual problems, to significant disturbances characterized by internalized psychopathology, social isolation, and to a lesser extent externalizing psychopathology. However, as pointed out by Rourke and Fuerst (1991), the classification of children into homogenous subtypes does not imply that the children so classified are identical. Within any given "subtype", children would likely exhibit, together with their similarities, substantial individual differences.

Collectively, children with epilepsy are rated as having a high degree of cognitive difficulties, which may reflect poor academic performance and/or parental concerns that difficulties in other areas are related to impaired intellectual functioning. With respect to psychosocial functioning, these children exhibit a higher general degree of psychopathology than other groups of children with neuropsychological/neurological deficits. However, it is noteworthy that the present sample is made up of individuals with intractable epilepsy, and thus may reflect the extreme range of psychosocial disturbances in this population. The findings also showed that children with epilepsy may be more likely to exhibit more extreme forms of internalizing psychopathology, including social withdrawal. This speaks to the importance of addressing the psychosocial disturbances exhibited by these individuals, including regular assessments for signs of depression, social withdrawal, and/or emotional lability. It appears that children with epilepsy are less likely to exhibit psychopathology of the externalizing type (e.g., hyperactivity, conduct disorder), although early age of seizure onset may be a predisposing factor to such disturbances.

The results from the PET study are considered preliminary, and should be interpreted with caution. Further study in this area is needed before firm conclusions can be established. Given this consideration, it appears that psychosocial difficulties in children with epilepsy are associated with specific patterns of cerebral metabolic dysfunction, characterized by decreased glucose utilization. Brain areas of decreased metabolism vary as a function of psychosocial subtype. In general terms, the brain areas that are dysfunctional in these subtypes have been associated with poor social skills

development, poor behavioural and emotional regulation, and thought disorders. Frontal systems, and by association cerebellar systems, appear to be important markers of specific patterns of psychosocial difficulties. However, general maladjustment appears to be associated with broad areas of metabolic dysfunction in right hemisphere systems.

Although tentative, findings from the PET data are consistent with the notion of neurological dysfunction as an etiology for both seizures and behaviour problems in children with epilepsy (e.g., Dunn et al., 2003). Thus, psychosocial difficulties in children with epilepsy may arise as a result of both environmental factors (e.g., stigma, social isolation) and neurological dysfunction. Whether or not the nature of such neurological dysfunction is accurately reflected by decreased cerebral metabolism awaits further study. However, the present findings of decreased activity in right hemisphere systems are consistent with links made between right hemisphere dysfunction and psychosocial functioning in the LD literature (e.g., Collins & Rourke, 2003; Rourke, 1995).

Limitations and Suggestions for Future Research

Because multivariate subtyping techniques such as cluster analysis will always provide groupings even on random data, the internal validity (reliability) of the present solution should be assessed by applying the subtyping technique to different sets of participants. Replication of the present results in a different sample of children with epilepsy would provide additional support for the reliability of the typology derived. In particular, it would be of interest to study psychosocial functioning in children with well-controlled epilepsy, to determine the extent to which the present typology is applicable to a broader range of epilepsy severity.

The validity of the typology was demonstrated in part by its overlap with the PIC typologies derived from other samples, in particular children with LD (Rourke & Fuerst, 1991). Visual inspection revealed that three of the epilepsy subtypes closely matched those derived from children with LD. The overlap between the two typologies could be examined more quantitatively by using profile-matching techniques (e.g., Ralston et al., 2003).

The present findings provide a rationale for the inclusion of the PIC-R in prospective studies of psychosocial sequelae of epilepsy. Such studies would eliminate

some of the biases associated with retrospective analyses (e.g., selective survival). In addition, such studies could address the question of whether psychosocial functioning changes over time in children with epilepsy.

One limitation of the current study concerns the nature of the PIC-R. The PIC-R is completed by the primary caregiver (usually the biological mother), and thus reflects parental perceptions of the child's areas of difficulty. It may not necessarily reflect the child's actual level of functioning and/or areas of psychosocial difficulty. Reliance on only parental reports of behavioural problems in children has been discouraged (Dunn et al., 2002). For example, Najman et al. (2000) have shown that depressed or anxious parents are more prone to report behavioural problems compared to controls; Cantwell et al (1997) reported that using only a single source of information could lead to some problems being overlooked. Therefore, it would be of interest to employ teacher ratings of psychosocial functioning in children with epilepsy, both as a means of providing external validation for the parental ratings subtypes, and/or to determine whether psychosocial difficulties are manifested to the same degree across different settings.

The inclusion of measures of neuropsychological functioning in the study of psychosocial functioning could address many questions presently left unanswered. Research in children with LD has linked specific profiles of psychosocial dysfunction with unique profiles of neuropsychological functioning (Rourke & Fuerst, 1991). The question arises whether such links are present in children with epilepsy. Measures of neuropsychological functioning could also be compared to patterns of brain dysfunction, to determine the extent to which brain differences may reflect neuropsychological differences between groups.

A related question concerns the extent to which combined elevations on the Psychosis and cognitive triad scales are related to neuropsychological deficits. Butler et al. (1997) reported that in children with TBI, the lowest neuropsychological scores were obtained by those who exhibited elevations on both the Psychosis and cognitive triad scales (i.e., the Social Isolation subtype). Moreover, these lower scores on neuropsychological measures were not due solely to elevations on the cognitive triad. Rather, elevations on the cognitive triad and Psychosis scales in combination were important determinants of neuropsychological deficits. Whether children with epilepsy

who exhibit elevations on both the cognitive triad and Psychosis scales will show greater neuropsychological deficits than those with only cognitive triad elevations remains in question.

It is of interest that Byrne, Backman, Gates, and Clark-Touesnard (1986) have argued that PIC-R Psychosis scale elevations in preschoolers with cognitive difficulties are related to language delays rather than psychopathology. The question thus arises whether language deficits, a common neuropsychological sequelae in seizure disorders, may also contribute to elevated Psychosis scales in children with epilepsy. According to this view, children with epilepsy who have language deficits may, in addition to performing poorly at school, have few friends, talk infrequently, and be difficult to understand. Such symptoms, which contribute to elevated Psychosis scales, may be related to ineffectual language or communication skills as well as psychopathology.

Because the present PET findings are considered preliminary, further study in larger samples of children is needed. With respect to future investigations of the neurophysiological substrate of psychosocial functioning, it would be of interest to study the links between measures of psychosocial functioning and brain activity using less invasive methods (e.g., functional MRI). Overall, the current findings call into question the practice of using a seizure-focused approach to studying brain-behaviour relations in epilepsy. The clear advantage of a more brain-focused approach, such as the use of functional neuroimaging techniques, is that functioning of the entire brain is taken into consideration. While knowledge of seizure variables is important to a full understanding of brain-behaviour relations in epilepsy, such variables cannot capture the full extent of underlying brain function.

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Vita Auctoris

David Wesley Collins was born and raised in Ottawa, Ontario. He earned his Bachelor of Arts Degree (with Honours) from the University of Ottawa, and his Masters of Arts degree from the University of Western Ontario. In 1998 David married Julie Anne Perry, and enrolled in the doctoral program in Clinical Neuropsychology at the University of Windsor. He anticipates graduating with a doctorate in Clinical Psychology in the Fall of 2003.