# Life-Size

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Jane Benson
Paul Kass
Dominic Kline
Audrius Plioplys

## N.A.M.E.

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**October, 18, 1996 - November, 16, 1996**

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**organized by Michael Hall**

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# Introduction:

*What is Life-Size?* For the purposes of this exhibition its the ability to reference the body without actually representing it. This enables the artists to place the work in relation to the viewer, forcing the scale and placement of the objects to become the key components to understanding the works. This allows the viewer to become the sole figurative aspect, allowing for a more participatory/ experiential reading of the work.

Today representation is no longer a portrayal of life, but a subjectively experienced reality. Objects (Art) are blurring into our daily lives, simultaneously becoming functional and irrational. The true and the false are continually collaged into our daily lives by a variety of new and evolving media, our abilities to focus on the normal everyday and find the uncanny within, has sharpened our perceptual faculties. For both artists and viewers, procedures and practices have moved into real-time, real space.

The destruction of the apparatus* is a constant and consuming theme in a vast majority of contemporary works, and its apparent in varying degrees in this exhibition. Trashing the apparatus underscores the gap between form and content...and that gap must be the fundamental content and also the form. These days allegory is endlessly replayed where structural failure is a new kind of success in its own right. This structural failure is endemic to understanding our contemporary condition.

Michael Hall

* see Fredric Jameson. The Geopolitical Aesthetic: (Cinema and Space in the World System) B.F.I. London/ Indiana University Press, Bloomington, IN. 1992

**Audrius Plioplys** is both an artist and a Doctor of Neurology at Mercy Hospital in Chicago. Plioplys' thinking has always fed-off of both disciplines, making art that concentrates on thinking and the relationship between conceptual thought and neurology. His art is professional and academic but not overtly theoretical (like art theory), more phenomenological (like the physical sciences). Good art inherently has an abstract language and contains its own logic. Therefore, it would not be unreasonable to assume that other professions do as well. Of course I've only been discussing this work as text, but its a little bit more complicated then that... I'm not even sure if I'm supposed to be reading all these papers. Because this text (academic papers) has been objectified by Plioplys' re-authoring of the text, of which he originally authored (and/or co-authored) are now from my perspective sculpture. Folded and stapled these papers hang on the wall and even though their depth is shallow, it has depth and weight and it's still about the space of the page. The narrative running from the front-side of the page to the backside of which you generally can't read, so in a literal sense the text is unreadable/ illegible, only the object nature of the work can be read. At this point Plioplys' project successfully blurs disciplines to an even greater length than the doctor/ artist relationship one naturally infers. The line between theory and practice has dissolved into his trademark thinking about thinking.

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# Immunoglobin Reactivity in Autism and Rett's Syndrome

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**Key Words.** Autism · Immunoglobulins · Neuroimmunology · Rett's syndrome

**Abstract.** Blood samples were obtained from 17 patients with autism (8 – 23 years of age; 16 males and 1 female). B cell numbers as measured by anti-B1 antibodies were normal. B cell function (proliferation and in vitro IgG and IgM synthesis in response to pokeweed mitogen) was normal. Quantitative serum immunoglobulins (IgG, IgA and IgM) were normal. When tested against Western blots prepared from normal, human cerebellar tissue, there was an increased incidence of IgG anti-210K neurofilament subunit reactivity (41 vs. 7% in 348 controls; $p < 0.001$). IgM anti-210K reactivity occurred in 53% of the patients (22% in 111 controls; $p < 0.05$) with an overall incidence of anticerebellar Western blot banding of 88% (23% in controls; $p < 0.001$). IgG or IgM reactivity against front cortex Western blots was not observed. Similar investigations performed on 8 girls with Rett's syndrome failed to reveal any abnormalities.

## Introduction

Autism is a syndrome characterized by social and communicative deficits of early onset accompanied by abnormal behaviors. There are many biomedical causes underlying autistic symptomatology [1], but in the majority of cases no clear etiology is ascertained.

Immune system abnormalities have been associated with autism. Lymphocyte abnormalities have included inhibition of macrophage migration in response to human myelin basic protein [2], reduced mitogen-induced lymphocyte blastogenesis [3 – 5], decreased numbers of T lymphocytes with altered ratios of helper to suppressor T cells [5], and decreased natural killer cell activity [6].

Abnormalities in the circulating immune system have also been described in autism. There have been reports of defective antibody response to rubella vaccine [7] and the presence of circulating antibodies to serotonin receptors [8] and to neurofilament axonal proteins [4].

This study was undertaken in an attempt to better define possible circulating antibody abnormalities in autism. We specifically investigated B cell function and searched for the presence of circulating anticentral nervous system (CNS) antibody reactivity. For comparison, girls with Rett's syndrome were also investigated.

## Materials and Methods

Blood samples were obtained from a total of 17 patients with autism. There were 16 males and 1 female. The age range was from 8 to 23 years with a mean age of 17. The diagnosis of autism conformed to the DSM III-R criteria for autism. There were no identified biomedical causes of autism in any of the studied population. Parental signed consent was obtained prior to phlebotomy. This study was approved by hospital ethics review committees. Simultaneously drawn blood samples from healthy young adults served as controls for the lymphocyte stimulation studies.

Blood samples were obtained from 8 Rett's syndrome girls with an age range of 2 – 15 years and a mean age of 8. The heparinized blood samples were obtained at different geographic areas in the United States and Canada and courier delivered to the laboratory for analysis. In all cases, a blood sample from a healthy young adult accompanied the Rett's syndrome sample, in the same package, to control for handling and shipping differences. In all cases, blood samples were received and processed less than 24 h from the time when they were drawn. Peripheral blood lymphocytes (PBL) were separated on a Ficoll-Hypaque density gradient [9]. After washing, 200 $\mu$l of cells were plated at a concentration of $5 \times 10^5$ cells/ml in 96-well microplates in RPMI-1640 media with 10% fetal calf serum and *L*-glutamine. Triplicate wells were cultured in the presence or absence of pokeweed mitogen in concentrations of 1:10 and 1:40 at 37 °C in 5% $CO_2$. After 7 and 14 days, the supernatants were collected and quantitative IgG and IgM determinations performed using a Pandex nephelometer.

PBL cell surface phenotype was determined by indirect immunofluorescence. Briefly, $10^6$ isolated PBL were incubated with saturating amounts of murine monoclonal antibody. After washing, cells were then incubated with FITC-conjugated goat anti-mouse, isotype-specific immunoglobulin. The percentage of fluorescent positive cells was determined from a 2-parameter analysis of at least $10^4$ lymphocytes on a gated lymphocyte population. The green fluorescence intensity was detected at 488 nm with a laser power of 500 mW using a Coulter Epics V flow cytometer (Coulter Electronics, Hialeah, FL, USA). Murine monoclonal antibody B1 (pan B cell marker) was obtained from Coulter Immunology (Hialeah).

Quantitative serum immunoglobulins were performed in the biochemistry laboratories of The Hospital for Sick Children using a Beckman array nephelometer. Immunoglobulin concentration normative data from the biochemistry laboratories was used for comparison.

Brain samples were obtained at the time of autopsy from neurologically normal young adults who had died from non-neurologic causes. They were kindly provided by Dr. J. Deck of the neuropathology service at the Toronto General Hospital. The time of autopsy was no later than 12 h after the time of death. Routine neuropathologic examination was normal. The brain samples were stored at – 80 °C until being used.

Western blots were made by standard techniques [10]. Homogenates of frontal cortex or cerebellum (taken from the cerebellar hemispheres) were homogenized and boiled for 2 min in 2.5% sodium dodecyl sulphate (w/v), 7% 2-mercaptoethanol (v/v) in TBS (50 m*M* Tris-HCl, 200 m*M* NaCl, pH 7.4) and the proteins separated as a curtain by polyacrylamide gel electrophoresis through a 15% acrylamide gradient. The gel loading was 10 $\mu$g protein/mm track width. The separated polypeptides were electrophoretically transferred to a cellulose nitrate sheet. To detect specific antibody binding 3 mm wide strips from the blot were first incubated 30 min in 10% normal horse serum (NHS) in phosphate-buffered saline (PBS; 0.1 *M* phosphate buffer, 0.15 *M* NaCl, pH 7.4) to block nonspecific binding sites, then overnight in the serum sample diluted 1:100 gave optimal visualization of immunoreactive bands without significant background staining. After two 15-min washes in PBS, the blot strips were incubated for 2 h in horse radish peroxidase conjugated rabbit anti-human IgG or anti-human IgM (Dako Inc.) diluted 1:100 in 10% NHS. Antibody binding was detected by washing the blot twice for 15 min in PBS and then for 15 min in 0.5 mg/ml 4-chloro-1-naphthol-0.01% (v/v) hydrogen peroxide [11]. The apparent molecular weights of antigenic polypeptide bands in kiloDaltons (K) were estimated from prestained molecular weight standards (BRL Inc.) which were blotted concomitantly. Frontal cortex and cerebellar blots in which the serum sample was replaced by 10% NHS revealed no bands. MabN210 is a murine monoclonal antibody which recognizes the 210K subunit of neurofilaments [12]. Frontal cortex and cerebellar blots in which mabN210 was substituted for the serum, and the second antibody replaced by horseradish peroxidase-conjugated rabbit anti-mouse immunoglobulin (Dako Inc.) diluted 1:100 in 10% NHS, consistently revealed an immunoreactive band at 210K.

For statistical analysis, $\chi^2$ and Fisher's exact probability tests were used.

Simultaneously drawn blood samples from healthy young adults served as controls for the pokeweed mitogen stimulations. For comparison of IgG anti-CNS reactivity the results from a study of 248 children were used [13]. For the IgM results a comparison group of 111 normal young adults was used.



## Results

In all cases of autism and Rett's syndrome, B cell numbers as measured by anti-B1 antibodies were normal. B cell function (proliferation and in vitro IgG and IgM synthesis in response to two different concentrations of pokeweed mitogen) was also normal. Quantitative determinations of serum IgG, IgM and IgA concentrations were normal.

When tested against Western blots prepared from normal, human cerebellar tissue, there was an increased incidence of IgG anti-210K neurofilament subunit reactivity in the autistics (41 vs 7% in 348 controls; $p < 0.001$). Representative Western blots are illustrated elsewhere [13, 14]. Immunoreactive IgG banding against other cerebellar molecular weight epitopes was not observed. Western blots prepared from frontal cortex revealed no IgG-reactive banding. In a previously reported investigation of anti-CNS antibody reactivity in adults using identical techniques, the incidence of IgG anti-210K cerebellar reactivity in 18 patients with cerebellar ataxia was 17% [14].

IgM anti-210K cerebellar reactivity occurred in 53% of the autistics and in only 22% of 111 controls ($p < 0.05$). IgM banding at other molecular weights was also observed with an overall incidence of 88% (23% in controls; $p < 0.001$). IgM reactivity against frontal cortex Western blots was not observed. No IgM immunoreactivity was detected in the Rett's syndrome patients.

Of the autistic patients 6 (35%) had both IgG and IgM anti-210K cerebellar reactivity. These were all males with ages of 8, 12, 17, 18, 20, and 22 years (mean age of 19 years) and only 1 was taking a medication (methylphenidate). One (6%) had only IgG anti-210K cerebellar reactivity. This was a 14-year-old male who was taking pimozide. Three (18%) had only IgM anti-210K cerebellar reactivity. These were all males of ages 10, 16 and 18 years (mean age of 16 years) and none were taking medications. Seven (41%) had neither IgG or IgM anti-210K cerebellar reactivity. These included one female of 19 years of age and the remainder were males of 9, 14, 16, 17, 22 and 23 years of age (mean age of 17 years). Of these 4 were taking medications (1 was taking haloperidol, 1 carbamazepine and 2 thioridazine).

There was no correlation between any of the positive results and medication intake or age distribution. There was no correlation between the positive results and the presence of epilepsy since only 1 of the 17 autistics was being treated for seizures. In no case was there any clinical indication of cerebellar dysfunction.

No IgG or IgM immunoreactivity was detected in the Rett's syndrome patients when the serum samples were screened against blots prepared either from frontal cortex or cerebellum.

## Discussion

Although antibodies recognizing serotonin receptors have been reported in 1 autistic child [8], a screening investigation of 20 patients with autism did not detect anti-CNS antibody reactivity [15]. However, the techniques that were used in this study were substantially different from those that we used. A membrane preparation made from human frontal cortex was used, not whole CNS tissue homogenates. Immunoreactivity against many CNS antigenic determinants, including cytoskeletal components such as neurofilaments, was not screened for.

Our results indicate that there is a significantly increased incidence of circulating anti-210K neurofilament immunoreactivity in autism. This finding is not specific for autism since it has been described in Creutzfeldt-Jakob disease [16, 17], Kuru [16], Parkinson's disease [18], the opsoclonus-myoclonus syndrome of childhood [19], and in normals [13, 14]. Furthermore, claims have been made that anti-210K immunoreactivity for both IgG and IgM classes of antibodies can be detected in virtually all normal individuals [20]. However, in our hands consistently the incidence of IgG anti-210K reactivity is low. In a study of 257 adults the incidence was 6% [14]. In a subsequent investigation of 358 children, the incidence was 3% when screened against Western blots prepared from frontal cortex, and 7% when screened against blots prepared from cerebellum [13]. For IgM, in 111 normal adults, the incidence of anti-210K reactivity was 22%. Thus our results of anti-210K reactivity in autism are statistically highly significant, but not specific for autism. It should be noted that none of our autistic patients had any clinical evidence of cerebellar dysfunction.

We did not detect immunoreactivity against frontal cortex blots which are also rich in neurofilaments. It is possible that there may be another substance in cerebellar tissue comigrating at the same molecular weight as the 210K neurofilament subunit. Alternatively, antigenic epitopes on the 210K neurofilament subunit may be revealed in processing cerebellar tissue, an event which may not take place in preparing frontal cortex immunoblots. Nevertheless, a consistent finding was the fact that there was a high incidence of anticerebellar immunoreactivity.

The cerebellar specificity of our findings is particularly intriguing in light of a report suggesting cerebellar abnormalities in autism using brain-imaging techniques [21, 22]. These results are controversial and have not been confirmed by other investigators [23 – 25]. None of our studied autistic patients had brain MRI scans performed. It is possible that subsets of autistics may have differing neuropathologic findings on imaging studies. Ongoing anticerebellar immunoreactivity may play a role in the genesis and/or modification of cerebellar circuitry in autism.

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# Uli Aigner / Jane Benson/Paul Kass/ Dominic Kline/Audrius Plioplys *in Life-Size* @N.A.M.E. Chicago

## Life-Size

**organized by Michael Hall**
**reception: Friday, Oct. 18th @ 6-8pm**
**Oct.18- Nov.16.1996**

## N.A.M.E.

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ELSEVIER

Brain & Development 1994; 16: 146–9

Case Report

# L-Carnitine as a treatment of lethargy in children with chronic neurologic handicaps

Audrius V. Plioplys [a,b,c], MD, FRCPC, Susan Bagherpour [a], RN, Irene Kasnicka [b], RN

**We present five cases of children with severe neurologic handicaps whose management was complicated by excessive lethargy. Treatment with L-carnitine in a dosage range of 35–50 mg/kg/day resulted in a marked improvement in alertness and arousability. In four cases, when L-carnitine was discontinued for a month, they all promptly became lethargic. When L-carnitine was re-started, the lethargy resolved and the improvement has been maintained for up to 14 months. In three children who were tested, serum carnitine levels (total and free) were normal before starting L-carnitine treatment.**

*Key words:* L-Carnitine; Lethargy

## 1. INTRODUCTION

Carnitine is essential in mitochondrial energy metabolism. It has two principal functions: (i) to transport long-chain fatty acids into the mitochondrion; (ii) to help regulate the intramitochondrial ratio of acetylcoenzyme A (CoA) to free CoA (reviewed in [1]). Carnitine deficiency conditions may be primary, such as those associated with inborn errors of metabolism, or secondary, such as those associated with inadequate intake or those that are induced by medications. Clinical symptoms of carnitine deficiency may include: myopathy, cardiomyopathy and Reye syndrome-like encephalopathy. In a child with Rett syndrome, with normal total and free serum carnitine levels, L-carnitine treatment resulted in improved neurologic functioning, especially in improvement in her level of alertness [2]. We decided to treat four children who were developmentally disabled and who were excessively lethargic, with L-carnitine to see if their level of alertness could likewise be improved.

## 2. MATERIALS AND METHODS

### 2.1. Case 1

This is a 16-year-old female. At the age of 4 months, after receiving a DPT and oral polio immunization, she developed seizures and respiratory insufficiency. Her spinal fluid analysis revealed pleocytosis (30 lymphocytes per $mm^3$) with normal chemistries and negative cultures. She was treated with ampicillin, isoniazid and streptomycin. EEG tracings revealed hypsarrythymia. She eventually developed microcephaly, spastic quadriparesis and an ongoing seizure disorder which was controlled with valproic acid and carbamazepime. Psychologic evaluation revealed a Bayley Scale of Infant Development IQ of below 10 (profound mental retardation) and Vineland Adaptive Behavior Scales of between 0 and 1 months in communication, daily living skills and socialization. The medications that she was taking were 2,100 mg per day valproic acid, 450 mg per day carbamazepime, and 30 mg per day clorazepate di-potassium for spasticity. Her routine blood chemistries, thyroid function tests, liver function tests,

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# Expression of a Neural Cell Adhesion Molecule Serum Fragment Is Depressed in Autism

**Audrius V. Plioplys, M.D., F.R.C.P.(C)**
**Susan E. Hemmens, M.Sc.**
**Ciaran M. Regan, Ph.D.**

*The level of a neural cell adhesion molecule (NCAM) serum fragment in autism was determined by using an antiserum prepared with immunoaffinity purified mouse NCAM. Autistic patients (N=16) had statistically significantly decreased serum NCAM levels compared with age-matched controls ($p<0.0005$). This observation could not be attributed to a medication-induced effect. Depressed serum NCAM levels in autism are distinct from schizophrenia, in which serum NCAM levels are elevated.*[1]

(The Journal of Neuropsychiatry and Clinical Neurosciences 1990; 2:413–417)

Autism is a syndrome characterized by social and communicative deficits of early onset, accompanied by abnormal behaviors. There are many different biomedical causes underlying autistic symptomatology, including genetic, metabolic, and infectious ones, as reviewed by Coleman and Gillberg 1985.[2] However, in the majority of autistic patients no clear etiology is ascertainable.

In the past, autism was considered to be a form of schizophrenia. Indeed, the term *autism* itself was coined by Bleuler[3] in 1911 to designate a category of thought disorder present in schizophrenia. In 1943, Kanner[4] described infantile autism as a distinct diagnostic entity, but still closely related to schizophrenia. Subsequently, diagnostic criteria for infantile autism have been developed that clearly distinguish it from schizophrenia and other psychoses.[5–8] However, accurate distinctions in disturbed young children are frequently difficult to make.

It has been suggested that schizophrenia comprises two potentially overlapping syndromes: type I and type II.[9] Type I schizophrenia is characterized by positive symptoms, which include delusions, hallucinations, and thought disorders. Type II schizophrenia is associated with negative features, such as loss or absence of affect, poverty of speech, and loss of volition; it is more closely associated with intellectual impairment and structural brain changes.[10,11]

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# Lymphocyte Function in Autism and Rett Syndrome

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**Abstract**

Peripheral blood lymphocytes from 17 patients with autism were separated on a Ficoll-Hypaque density gradient. Patients had normal numbers of T and B cells and T cell subsets. Although CD4:CD8 ratios were normal for the whole group (2.09 ± 0.97), 6 patients had elevated ratios (>2.2) and 5 had decreased ratios (<1.5). Mitogen-induced proliferation (concanavalin-A and phytohemagglutinin) was normal as was the autologous mixed lymphocyte reaction for the whole group. There was an abnormally increased percentage of DR+ (activated) T lymphocytes in 11 patients. With increasing age percentage of DR+ lymphocytes decreased. No patient had interleukin-2 (IL-2) receptor+ cells. Similar investigations performed on blood samples from 8 girls with Rett syndrome produced normal results. 11 of 17 autistic patients had an abnormally increased percentage of DR+ but not IL-2 receptor+ lymphocytes suggesting 'incomplete' activation, a finding which is seen in autoimmune diseases. The decrease in activated cells with increasing age suggests that there may be an autoimmune process which is more active earlier in life in a subset of autistics.

**Key Words**
Autism
Lymphocytes
Neuroimmunology
Rett syndrome

### Introduction

Autism is a syndrome characterized by social and communicative deficits of early onset accompanied by abnormal behaviors. There are many biomedical causes underlying autistic symptomatology [1]. However, in the majority of autistic patients no clear etiology has been ascertained.

Immune system abnormalities have been associated with autism. These have included inhibition of macrophage migration in response to human myelin basic protein [2], reduced mitogen-induced lymphocyte blastogenesis [3, 4], decreased numbers of T lymphocytes with altered ratios of helper to suppressor T cells [4], decreased helper T cell and B cell numbers [5], deficiency of suppressor-inducer T cells [6], decreased natural killer cell activity [7], and the demonstration of circulating antibodies to serotonin receptors [8]. In another study of 14 patients with autism, 8 had an abnormal lymphocyte proliferative response to mitogens and to autologous lymphocytes and monocytes [9].

This study was undertaken in an attempt to help to better define immune system abnormalities in autism.

For comparison, girls with Rett syndrome were also investigated. In Rett syndrome, following normal early development, there is cognitive and functional decline frequently associated with autistic symptomatology [10, 11]. It is possible that cellular immune system abnormali-

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