قسم الكيمياء الحيوية
Biochemistry Department
College of Science - King Saud University

OMICS Group Conferences
Accelerating Scientific Discovery

Gut-brain axis-based biomarkers as predictive tools in testing efficacy of carnosine and carnitine in rodent model of autism

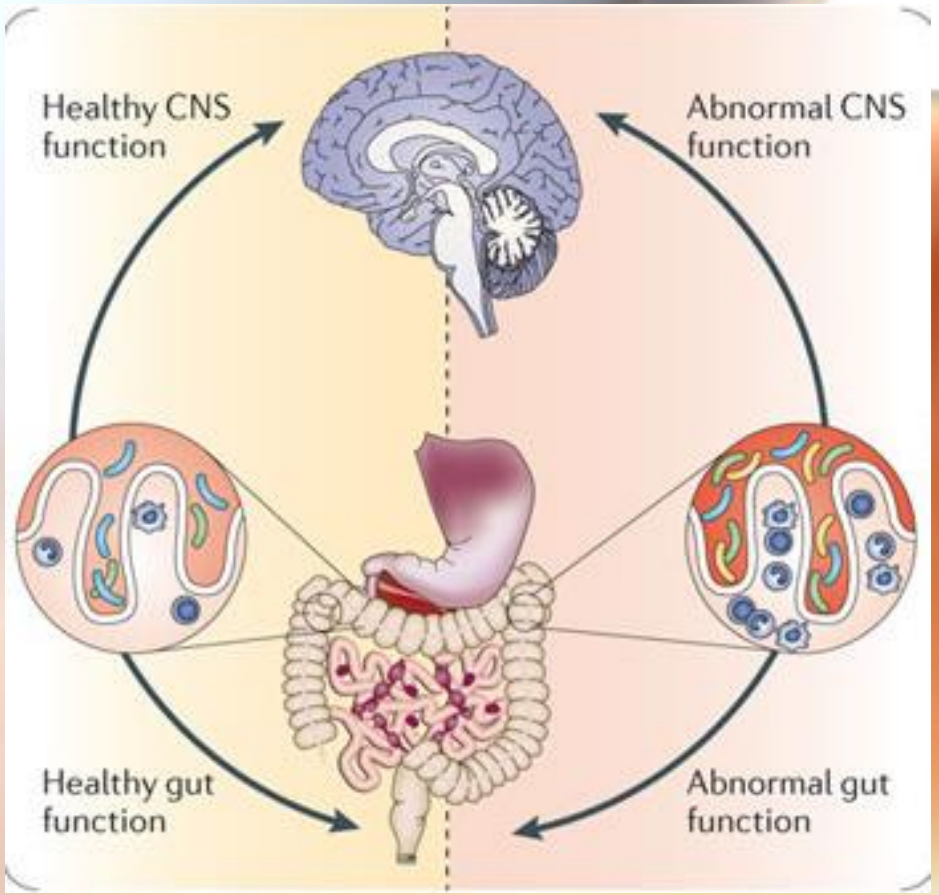
By

Prof. Afaf El-Ansary

The Gut-brain Axis

- Within the first few days of life the human gut is colonized by commensal intestinal microbiota.

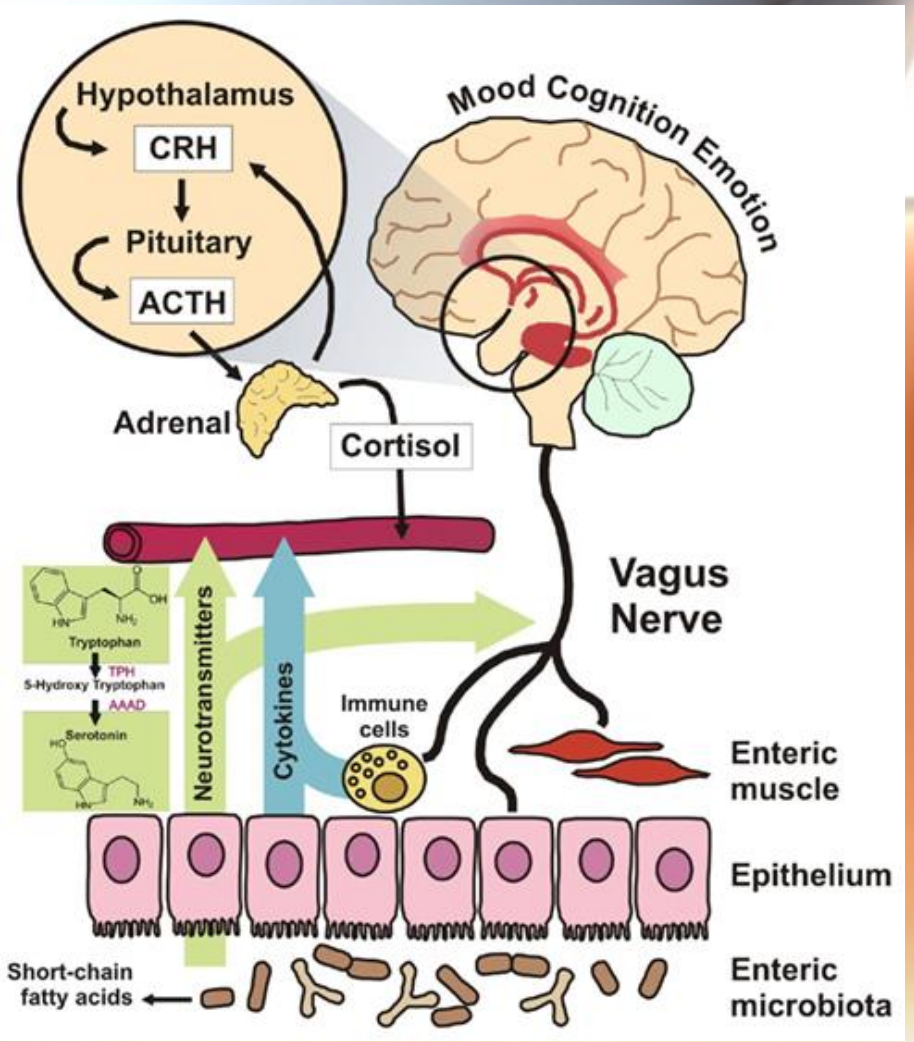
- Studies show that commensal, probiotic, and pathogenic bacteria in the gastrointestinal tract can activate neural pathways and central nervous system signaling systems.



Gut and Brain Tissue

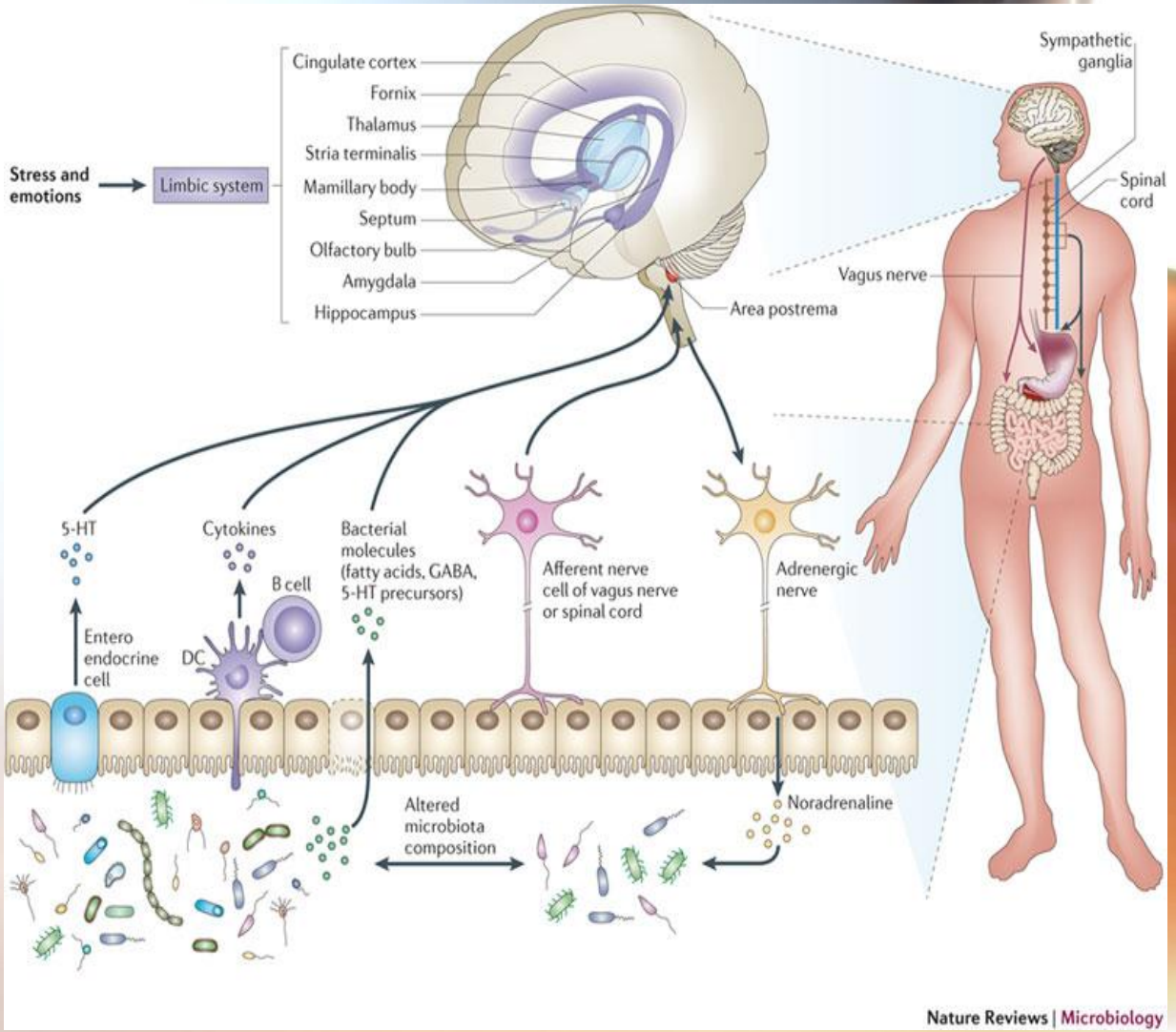
- The brain and the gut both develop from the same tissue – during foetal development one part becomes the central nervous system, while the other develops into the enteric nervous system. They are connected via the Vagus nerve.

- The gut has a large, semi-autonomous brain, and its endocrine signaling to the entire body is very elaborate.



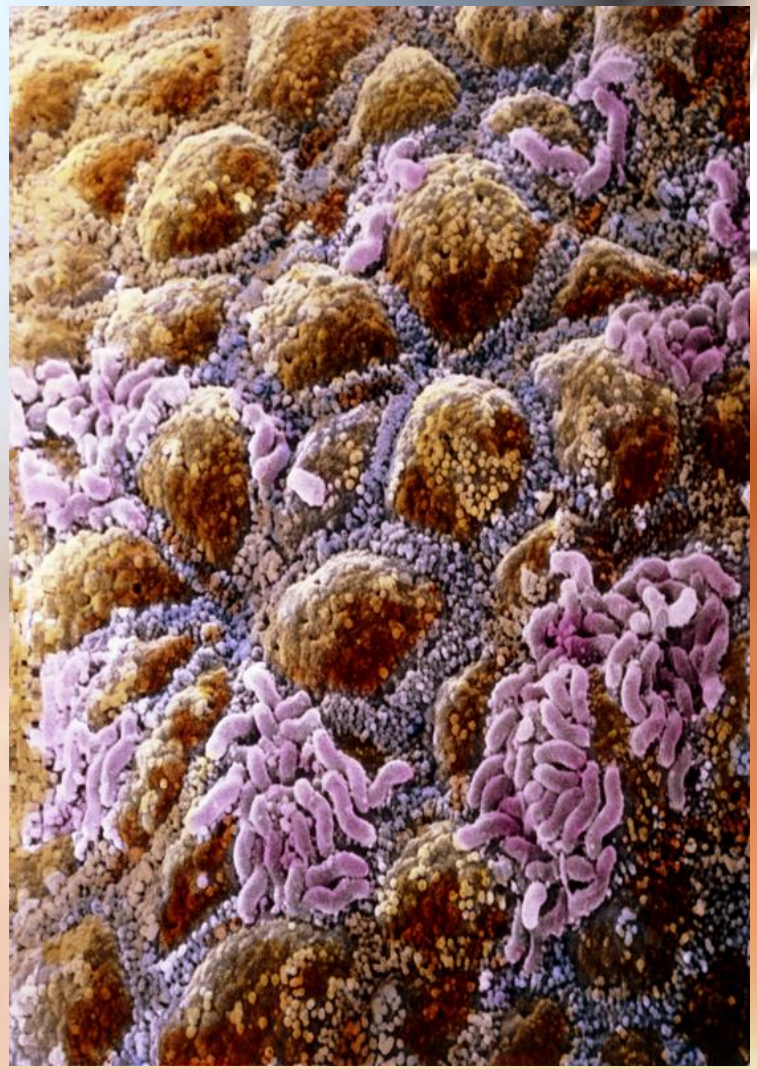
How the Gut-brain Axis works

- ✓ The microbiome is affected by our experiences and emotions.
- ✓ In turn microbes in the gut send chemical signals (including neurotransmitters) affecting memory, emotions and behaviour in important parts of the brain.
- ✓ Gut microbes even alter gene expression in the gut.

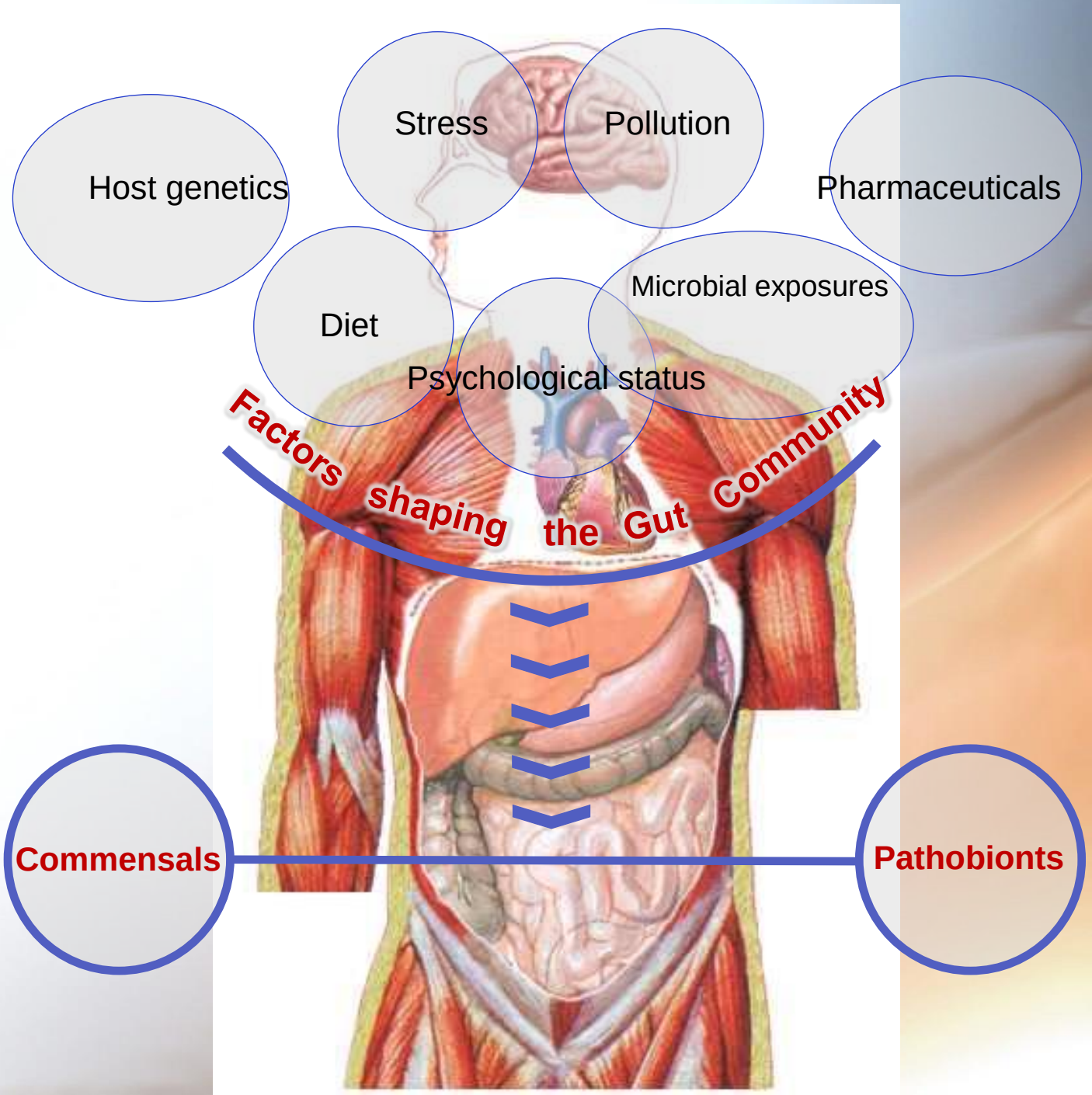


Functions of our digestive microbiome

- Aid digestion, synthesize vitamins
- Detoxify foreign compounds and help metabolize indigestible compounds
- Defend against opportunistic pathogens.
- Help programme the functioning of immune cells.
- Compounds produced by the microbiome are found throughout the body, where they continue to signal disease.



Major factors affecting our digestive microbiome?



- Every day, our brains understand the things we see, smell, hear, taste, touch, and experience. But when someone's brain has trouble interpreting these things, it can make it hard to talk, listen, understand, play, and learn.

Autism

- Autism is a disorder of neural development characterized by impaired social interaction and communication, and by restricted and repetitive behavior.
- The prevalence of autism in Saudi Arabia is 18 per 10,000, (Al-Salehi et al.,2009).

The Centre for systems Change

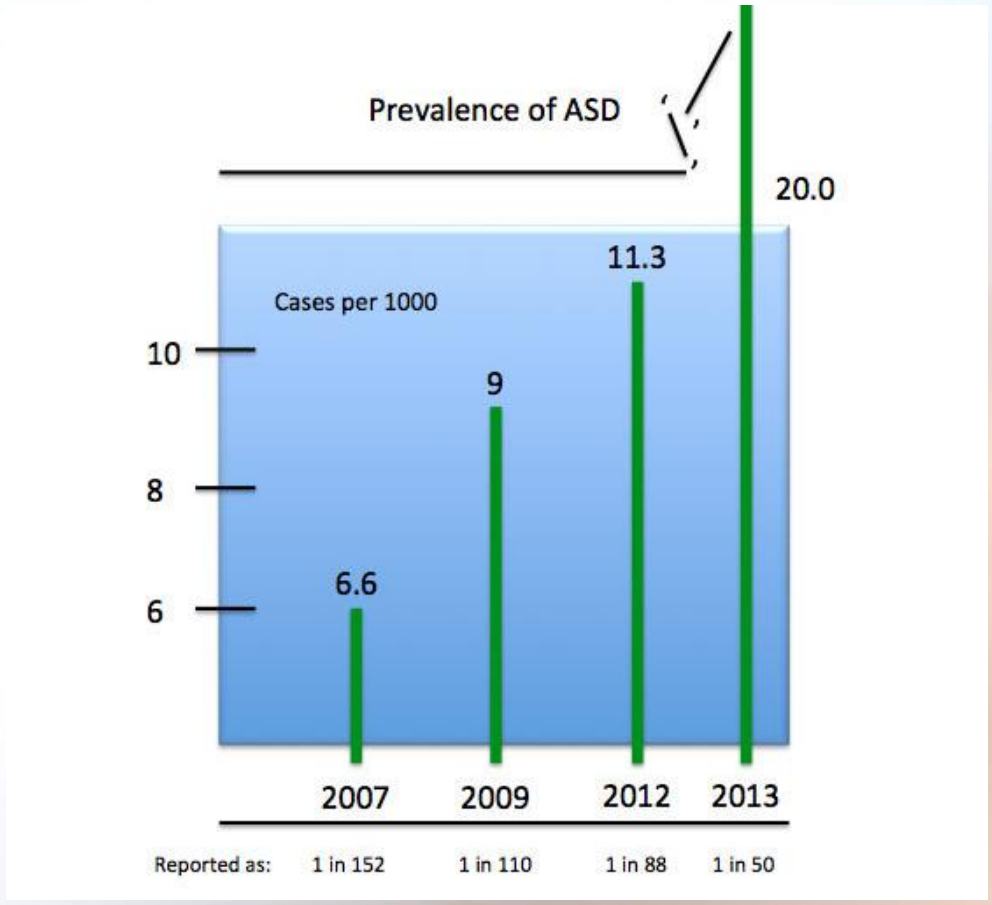
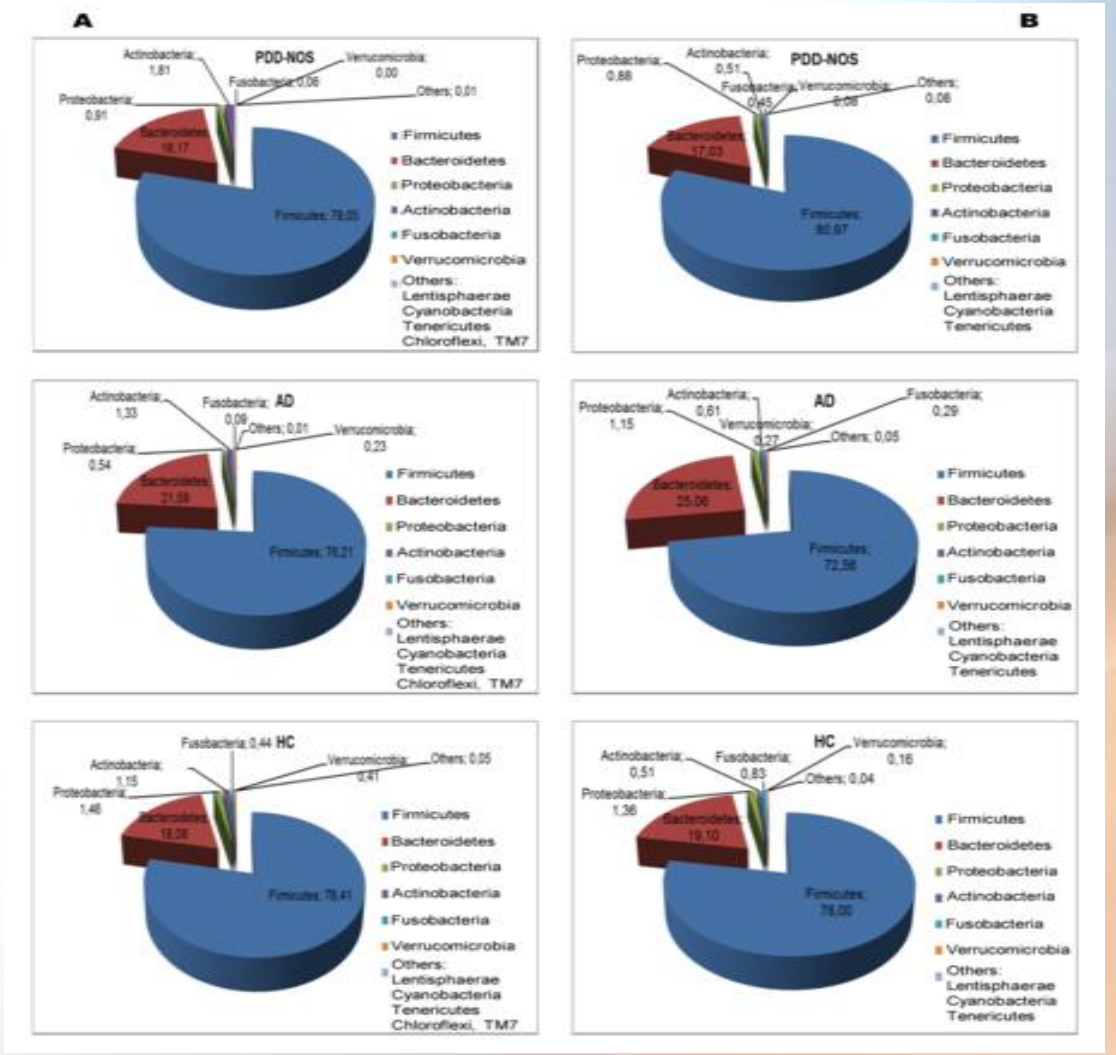


Figure 1. Total and active bacteria found in feces of children.



De Angelis M, Piccolo M, Vannini L, Siragusa S, et al. (2013) Fecal Microbiota and Metabolome of Children with Autism and Pervasive Developmental Disorder Not Otherwise Specified. PLoS ONE 8(10): e76993. doi:10.1371/journal.pone.0076993
http://www.plosone.org/article/info:doi/10.1371/journal.pone.0076993

PLOS | ONE

Brain Complexity

- The complexity of the brain itself presents a severe roadblock to identification of useful biomarkers.
- In the brain, transcriptomes, proteomes, morphological phenotypes, and interactive connections vary widely within the neurons and glia, while most organs (eg, liver, muscle), cells are more homogenous in their phenotypes, transcriptomes, proteomes, and cellular interactions.
- Many attempts at bypassing the problem of tissue availability have used in vitro and animal models of neurological disease. However, given the complexities of human neurological disorders, which often contain significant behavioral components, these models are often imperfect.

Animal Models

- Animal models are essential for translation of drug findings from bench to clinical use. Hence, critical evaluation of the face and predictive validity of these models is important.
- Proper design, and reporting of animal model results help to make preclinical data more reproducible and translatable to the clinic.
- Design of an animal model strategy is part of the translational plan rather than (a) single experiment(s).
- Data from animal models are essential in predicting the clinical outcome for a specific drug in development.

Animal Models

- Animal models of neurological disease have successfully and accurately recreated many aspects of human illness in a variety of organisms, from mice to primates, allowing for in-depth study of neuropathophysiology.

- The development and testing of therapeutic interventions for diseases that affect the (CNS)often begin in animal models.

- Progress in understanding and treating autism will require translational research efforts to transfer knowledge through successive fields of research from basic scientific discovery to public health impact.

Gut microbiota and autism

- A developmentally abnormal gut microbiota may in turn affect both the gut-brain axis and brain development and contribute to the etiology of autism.
- Propionic acid (PA) found as a metabolic product of gut bacteria has been reported to mimic/ mediate the neurotoxic effects of autism.
- Results from animal studies may guide investigations on human populations toward identifying environmental contaminants that produce or drugs that protect from neurotoxicity.

Study Objectives

- In a three successive independent experimental design, we tested the neurotoxic effect of PA either orally administered or biologically induced in clindamycin-treated hamsters.

The Kilee Patchell-Evans
Autism Research Group
THE UNIVERSITY OF WESTERN ONTARIO

"Scientists Listening to Parents"

- The paradigm of understanding Autism is changing
- Autism is a whole body disorder with many potentially treatable features
- We are an international multi-disciplinary team of neuroscientists working towards a cure

Autism Model Rodents – Propionate- behaviour/EEG

PBS

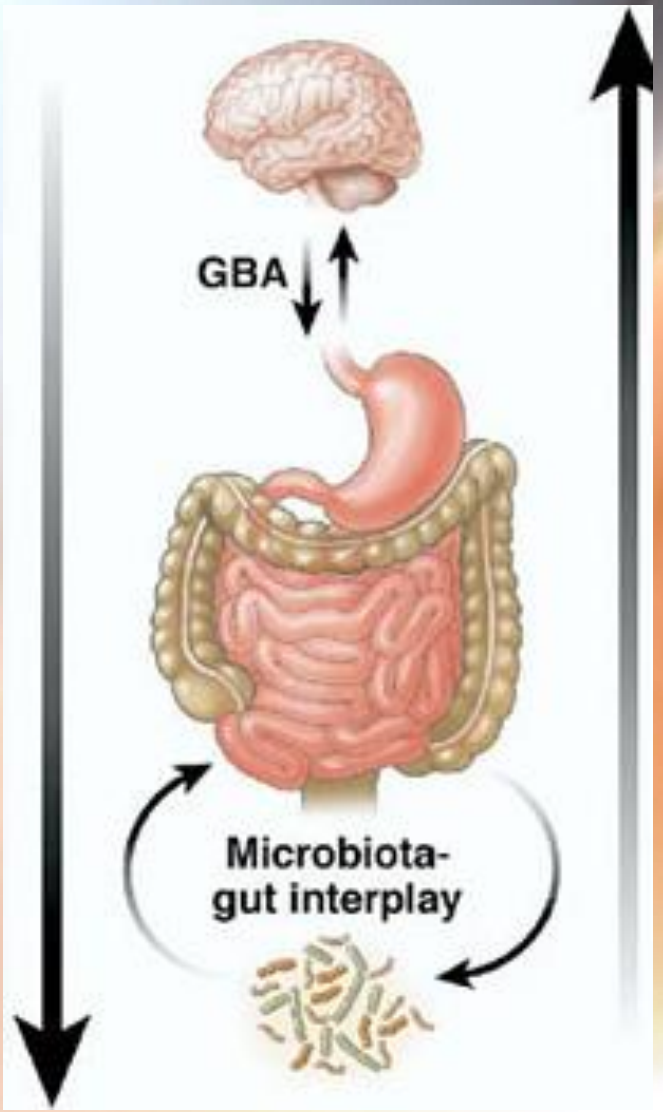
-Injected into cerebral ventricles
-NB buffered to pH 7.5
- Reversible repetitive behaviour
-Fixation on objects
-Seizure +/behaviour cortex
-Subcortical spiking

Propionate Autism Model

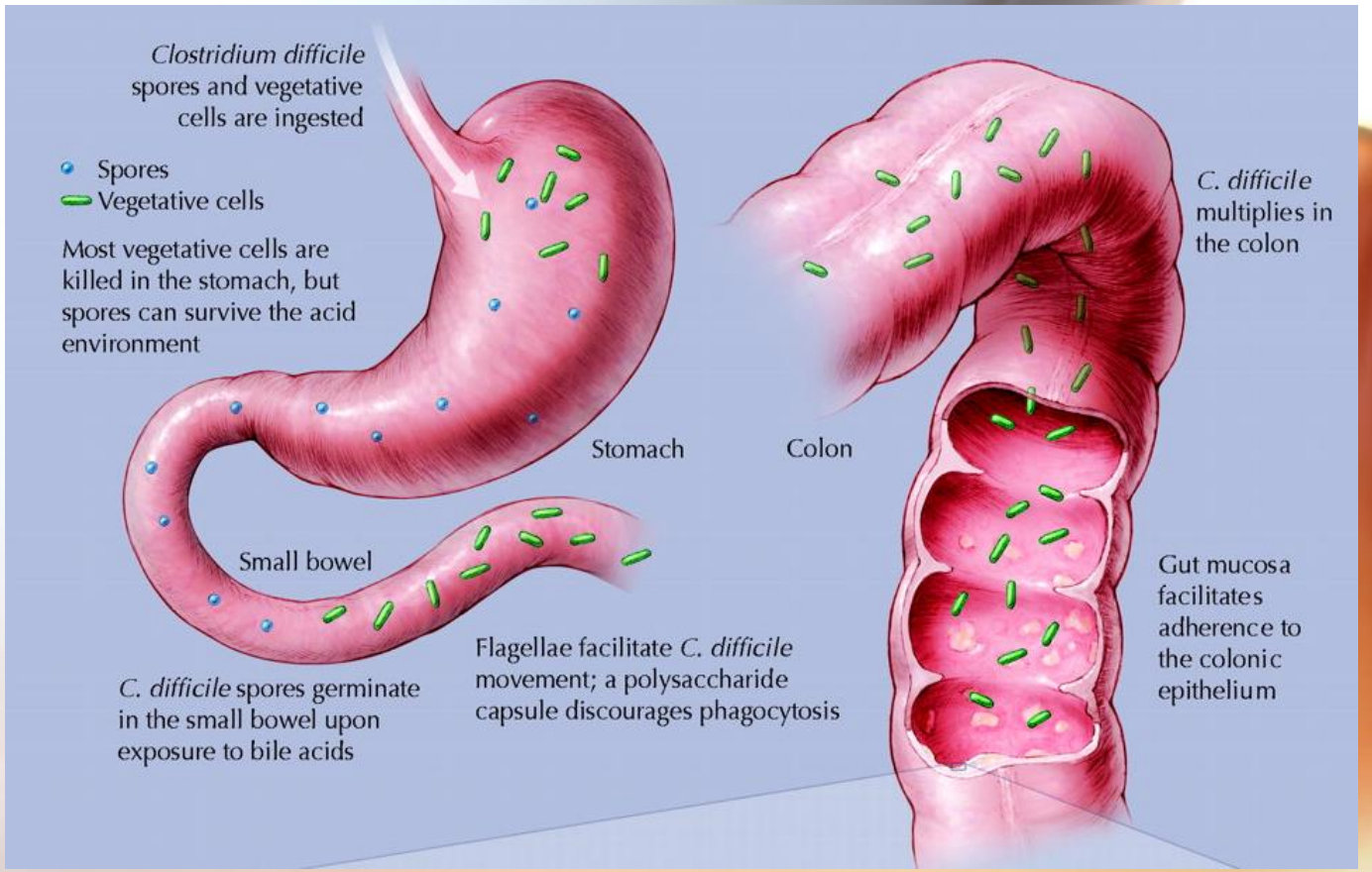
Effect immediate, transient (45min) but some permanent

Why oral adminstration was selected???

- The oral administration was used to confirm the role of gut-brain axis in the induction of autistic features probably found in treated rats. Additionally, Clindamycin was used to ascertain the role of overgrowth of Clostridia species as PA producer in inducing autistic features in animals.



- Additionally, clindamycin was used to ascertain the role of overgrowth of Clostridia species as PA producer in inducing biochemical autistic features in animals.



Experimental

- A total of 54 young male golden Syrian hamsters weighing approximately 80–100 g (8 weeks of age) were used in the present study.

- Animals were randomly allocated to 9 groups of 6 animals each:

- a control group that received only phosphate buffered saline;
- an oral buffered PA-treated group that was given a neurotoxic dose of 250 mg/kg body weight/day for 3 days.
- a clindamycin-treated group that received a single dose (orogastrically) of 30 mg/kg on experiment day 0;
- a carnosine-treated group that received a dose of 10 mg/kg body weight/day orally (daily for one week);
- a carnitine-treated group that received 50 mg/kg body weight/day orally (daily for one week) and;
- four protected groups were given the same doses of carnosine or carnitine for one week followed by PA for 3 days or a single dose of clindamycin as described above.

- All groups were kept at a controlled temperature (21 ± 1°C) with ad-libitum access to food and water.

- Quantitative stool cultures were collected and tested both aerobically and anaerobically on groups of hamsters receiving clindamycin and the untreated controls. All experiments were performed in accordance with national animal care guidelines and were pre-approved by the faculty ethics committee, King Saud University.

- The brain was removed from the skull, homogenized and tissue homogenates were used for the biochemical analyses.

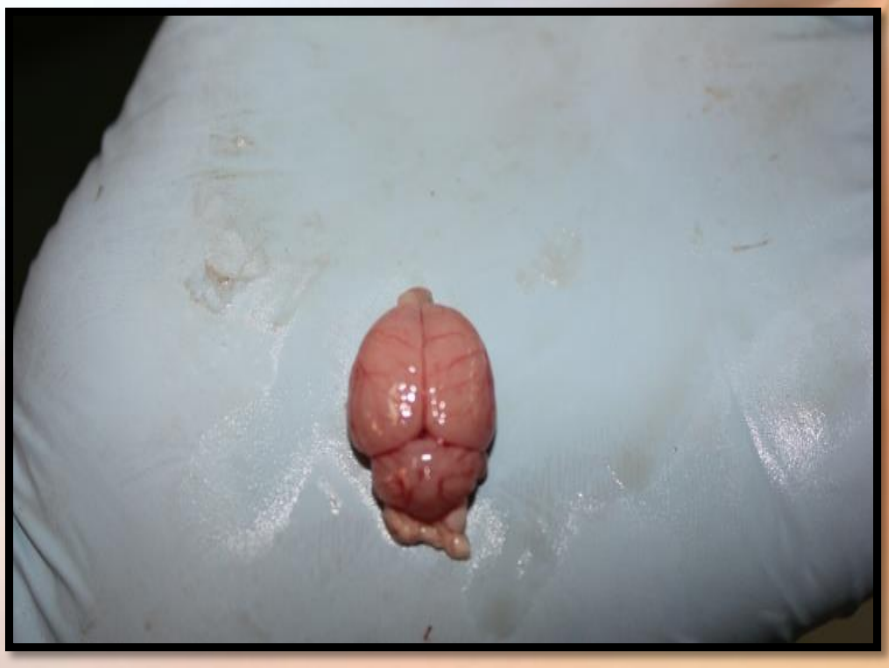


Table 1. Estimation of microorganisms recovery in hamster`s intestinal tract before and after treatment with clindamycin antibiotic.

Organisms isolated	Media used and incubation condition	Control hamster	Clindamycin recipient
Staphylococci, group of gram-positive bacilli	MHA/ aerobic: 37°C/24 h	++	+++
Enterobacteriacaea (lactose fermentor)	MCA/aerobic: 37°C/24 h	0	+++
Group β streptococci	BAP/aerobic: 37°C/24 h	+	++
Candida albicans	SDA/aerobic: 25°C/48 h	+	++
Clostridia	CCFA/anaerobic; 37°C/ 72 h	0	++

MHA, muller hinton agar; MCA, Macconkey agar; BAP, 5% sheep blood agar; SDA, sabouroud dextrose agar (yeast media); CCFA, modified cefoxitin cycloserine fructose agar.

Table 2. Mean ±S.D of INF- γ (ng/100 mg), MD (UM/100 mg), and HSP70 (ng/100 mg) levels and GPX activity (U/100 mg), in the cortex and medulla homogenates of hamsters.

Group	Homogenate	Parameter			
		INF- γ	GPX	MD	HSP70
Control	Cortex	90.01 ± 5.14	5.17 ± 0.86	21.91 ± 2.15	32.66 ± 2.53
	Medulla	81.26 ± 1.95	6.11 ± 0.42	18.56 ± 1.43	29.69 ± 2.88
PA	Cortex	141.59 ± 6.28**	2.49 ± 0.32**	46.69 ± 3.06**	57.69 ± 2.57**
	Medulla	98.57 ± 3.49**	3.26 ± 0.40**	36.55 ± 1.91**	59.14 ± 2.38**
Clindamycin	Cortex	84.44 ± 3.55	3.34 ± 0.39**	31.52 ± 1.98**	35.70 ± 1.99
	Medulla	84.09 ± 4.37	3.65 ± 0.54**	21.66 ± 1.41**	34.14 ± 2.17*
Carnosine	Cortex	86.79 ± 1.72	6.59 ± 0.21*	17.64 ± 2.18*	30.90 ± 1.20
	Medulla	83.59 ± 2.56	5.84 ± 0.75	17.72 ± 2.13	31.08 ± 3.46
Carnitine	Cortex	85.88 ± 1.82	7.08 ± 0.18**	18.45 ± 2.07*	31.27 ± 1.95
	Medulla	79.10 ± 3.84	5.62 ± 0.34	16.11 ± 1.16*	33.62 ± 3.85
PA +Carnosine	Cortex	117.07 ± 4.12**	3.39 ± 0.31**	36.98 ± 1.68**	43.66 ± 2.10**
	Medulla	87.94 ± 1.27**	4.03 ± 0.31**	26.19 ± 0.79**	48.19 ± 2.61**
PA +Carnitine	Cortex	119.04 ± 2.79**	3.20 ± 0.31**	37.82 ± 3.77**	44.95 ± 0.94**
	Medulla	88.78 ± 2.46**	4.39 ± 0.42**	28.71 ± 2.12**	44.14 ± 3.68**
Clindamycin+	Cortex	76.51 ± 4.03**	3.61 ± 0.20*	23.95 ± 1.99	35.99 ± 2.17*
Carnosine	Medulla	78.59 ± 4.03	3.56 ± 0.33**	23.96 ± 1.11**	34.03 ± 2.74*
Clindamycin +Carnitine	Cortex	79.49 ± 1.71**	3.42 ± 0.28**	24.16 ± 3.27	37.68 ± 1.38**
	Medulla	83.27 ± 0.71	4.34 ± 0.37**	23.66 ± 1.67**	35.66 ± 1.10**

*Significant at 0.05 level; ** significant at 0.01 level.

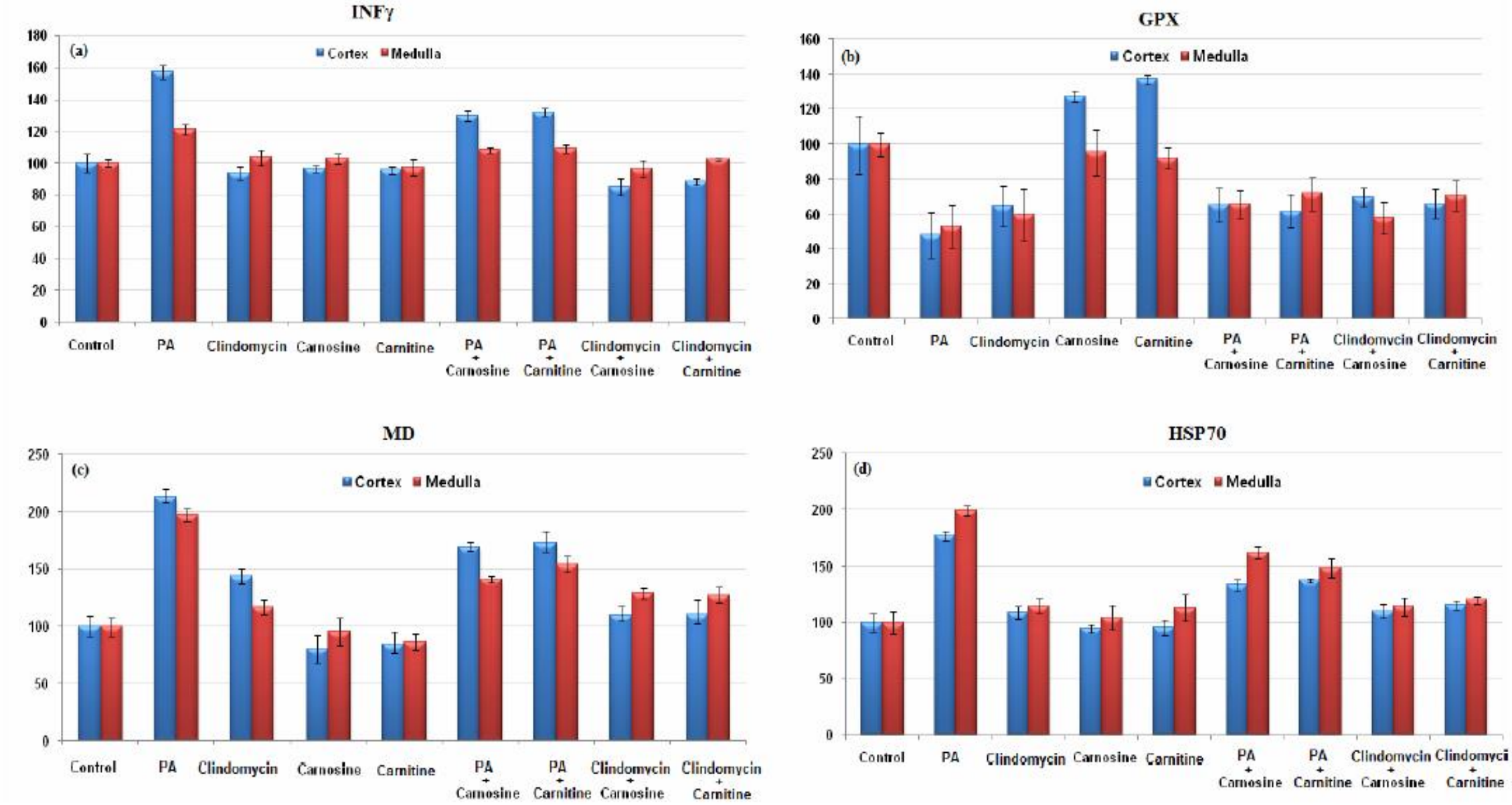


Figure 1. Levels of the parameters measured in the cortex and medulla homogenates of the nine groups of hamsters. Mean ± S.D of INF-γ (a), GPX (b), MD (c), and HSP70 (d) measured in treated hamsters compared to the control groups.

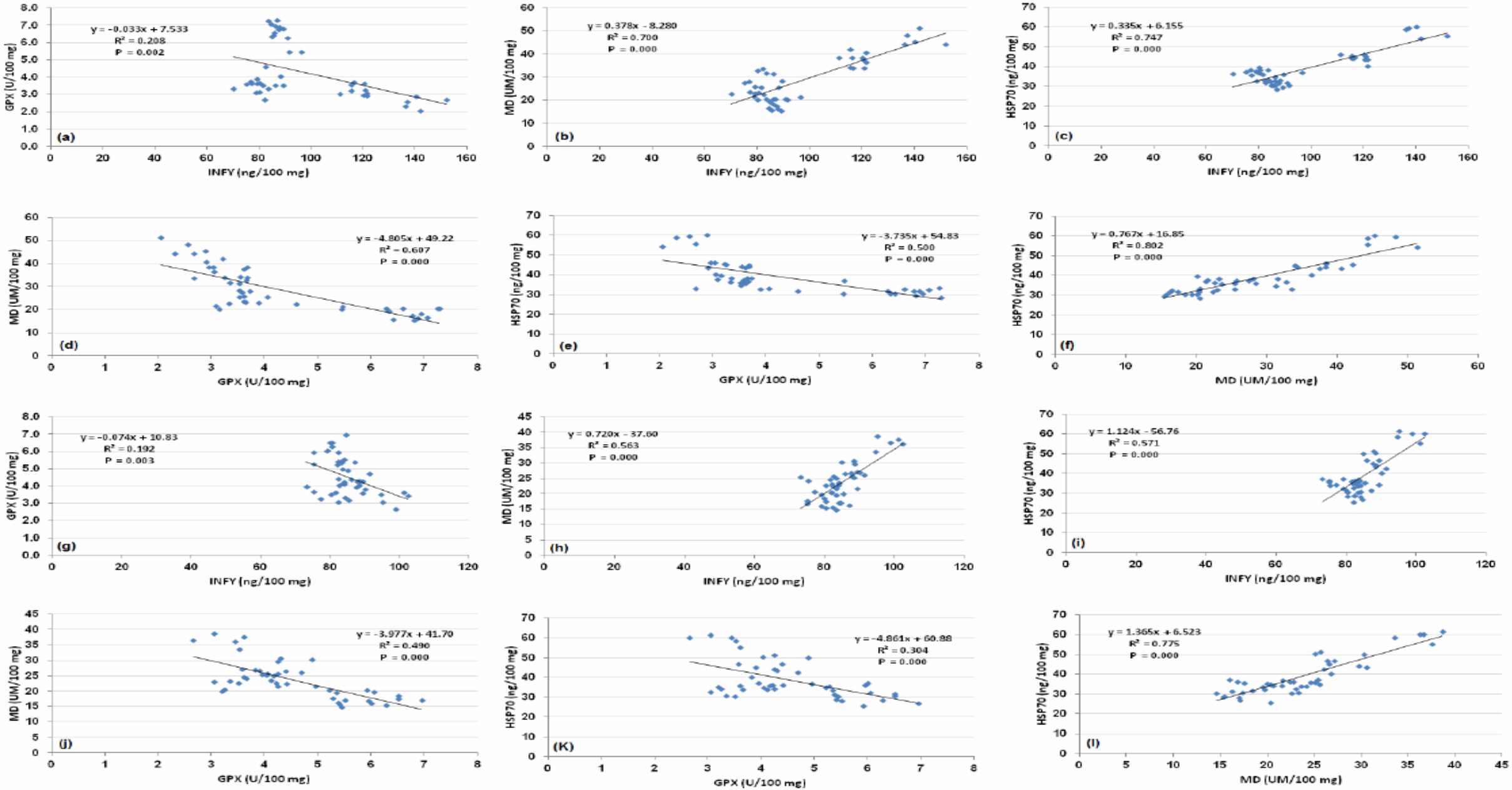


Figure 2. Pearson's correlations of the most significant positive and negative correlated variables with best fit line/curve.

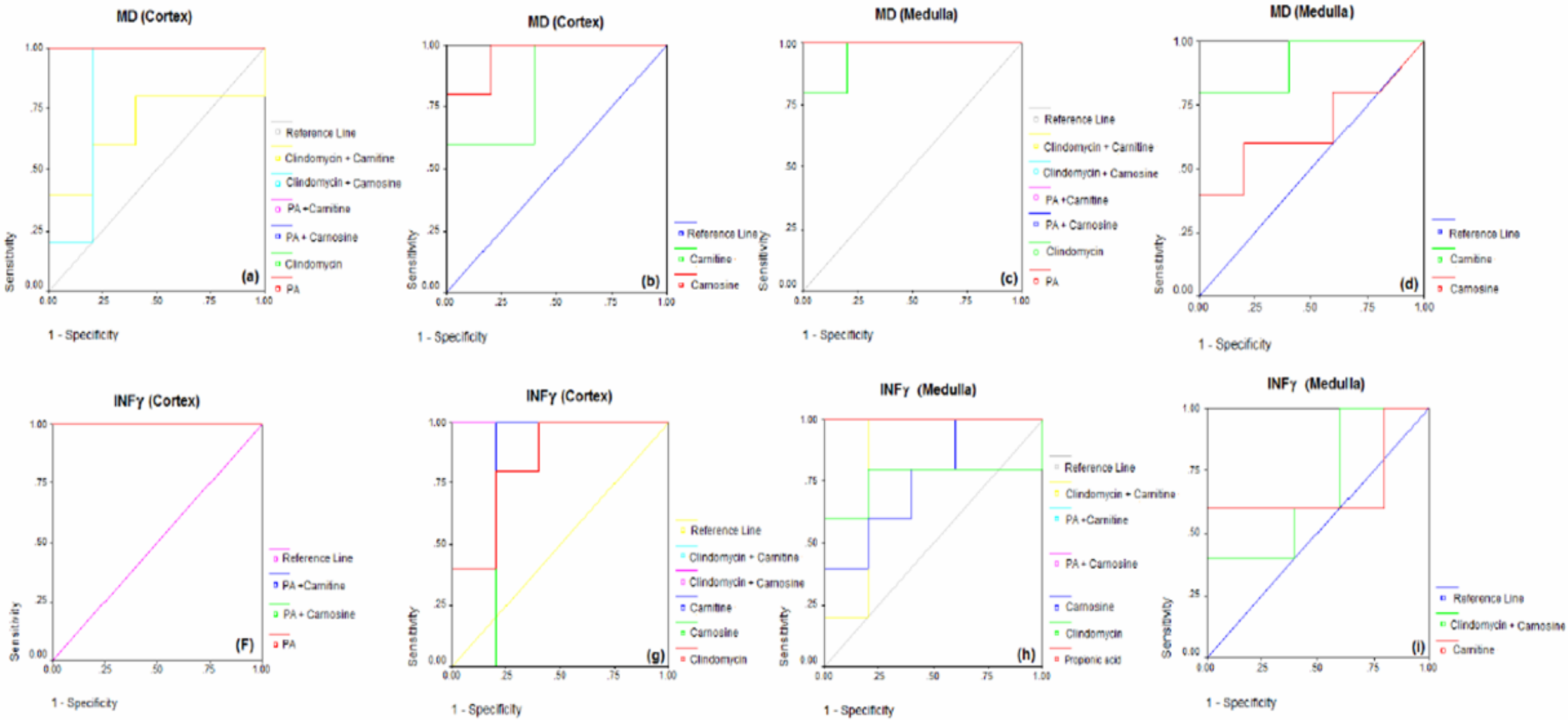
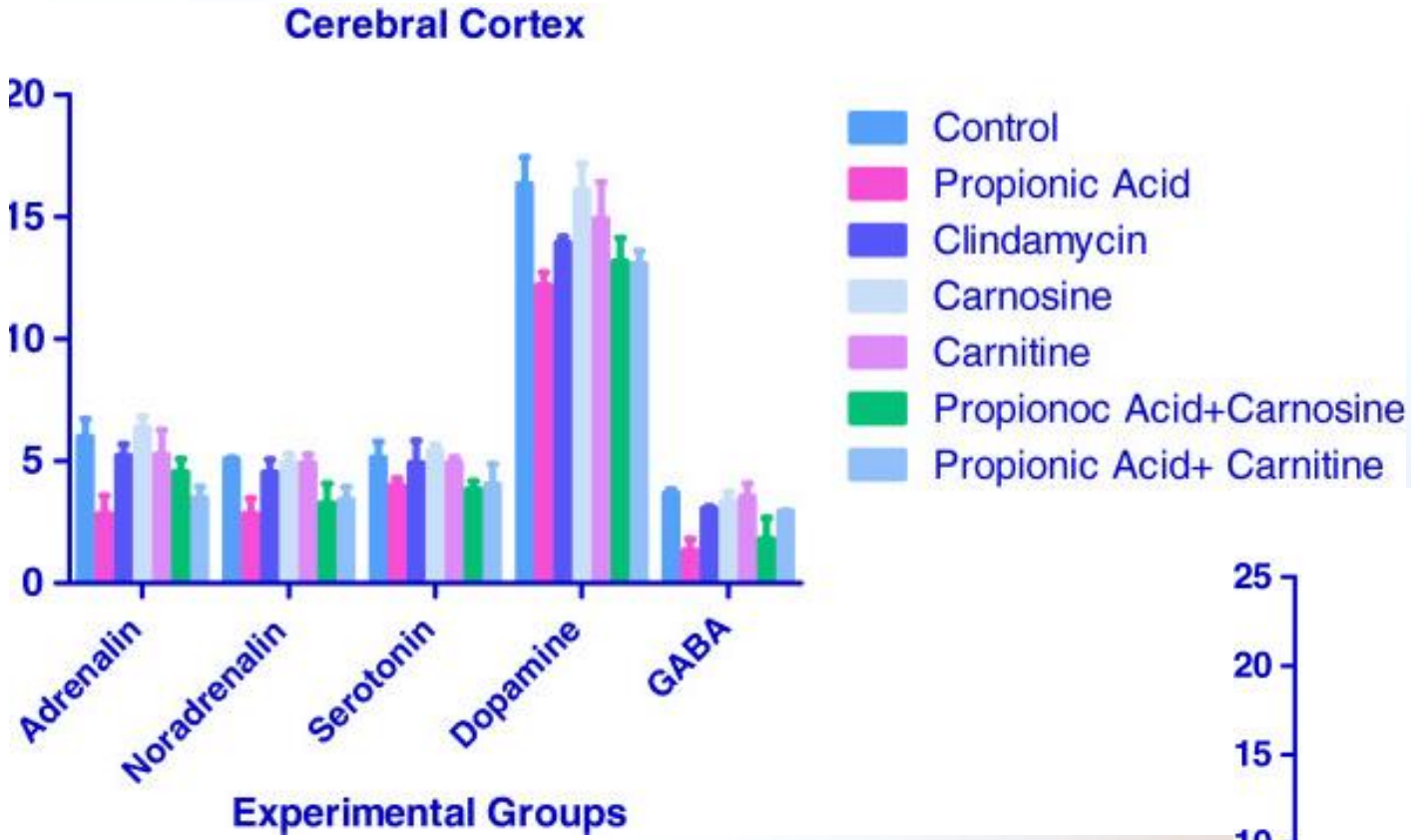
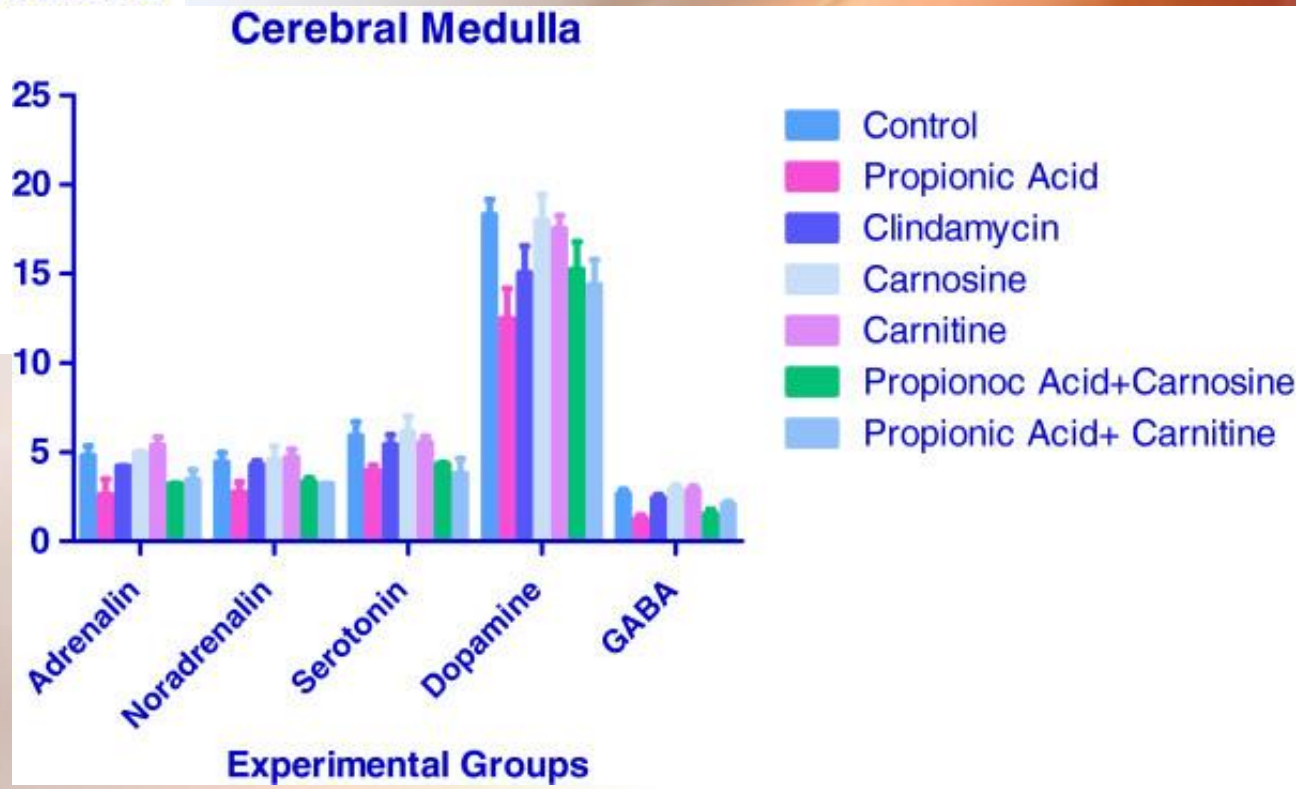


Figure 3. Analysis of receiver operating characteristics of selective parameters measured in the cortex and medulla homogenates of the nine groups of hamsters.


Cerebral Cortex
20
15
10
5
0
Adrenalin
Noradrenalin
Serotonin
Dopamine
GABA
Experimental Groups
Control
Propionic Acid
Clindamycin
Carnosine
Carnitine
Propionoc Acid+Carnosine
Propionic Acid+ Carnitine


Cerebral Medulla
25
20
15
10
5
0
Adrenalin
Noradrenalin
Serotonin
Dopamine
GABA
Experimental Groups
Control
Propionic Acid
Clindamycin
Carnosine
Carnitine
Propionoc Acid+Carnosine
Propionic Acid+ Carnitine

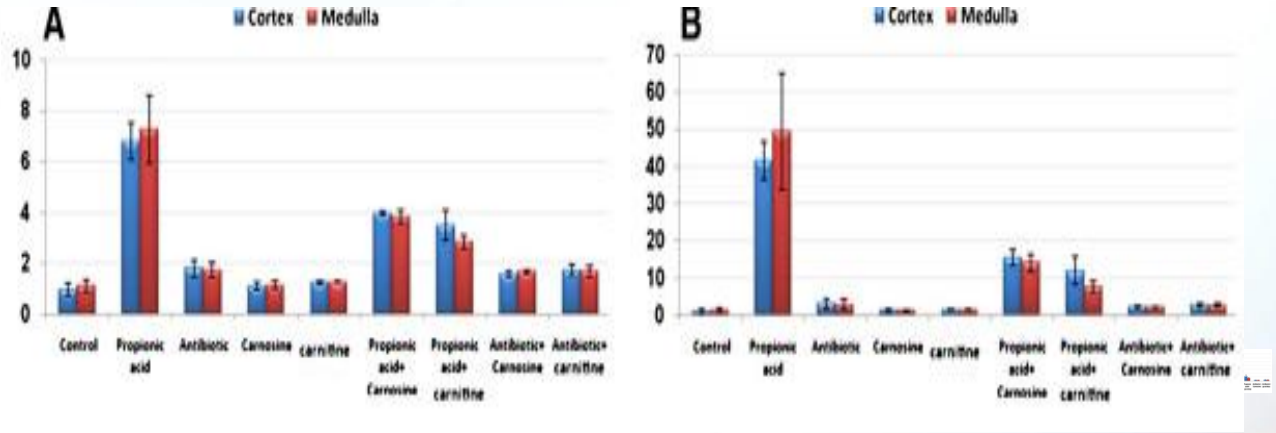
- The results of this study lead us to suggest that PA may play a role in ASD by interfering with the neurotransmitters.

- Carnosine and carnitine which are known antioxidants cause no significant changes in the levels of neurotransmitters when administered alone to hamsters.

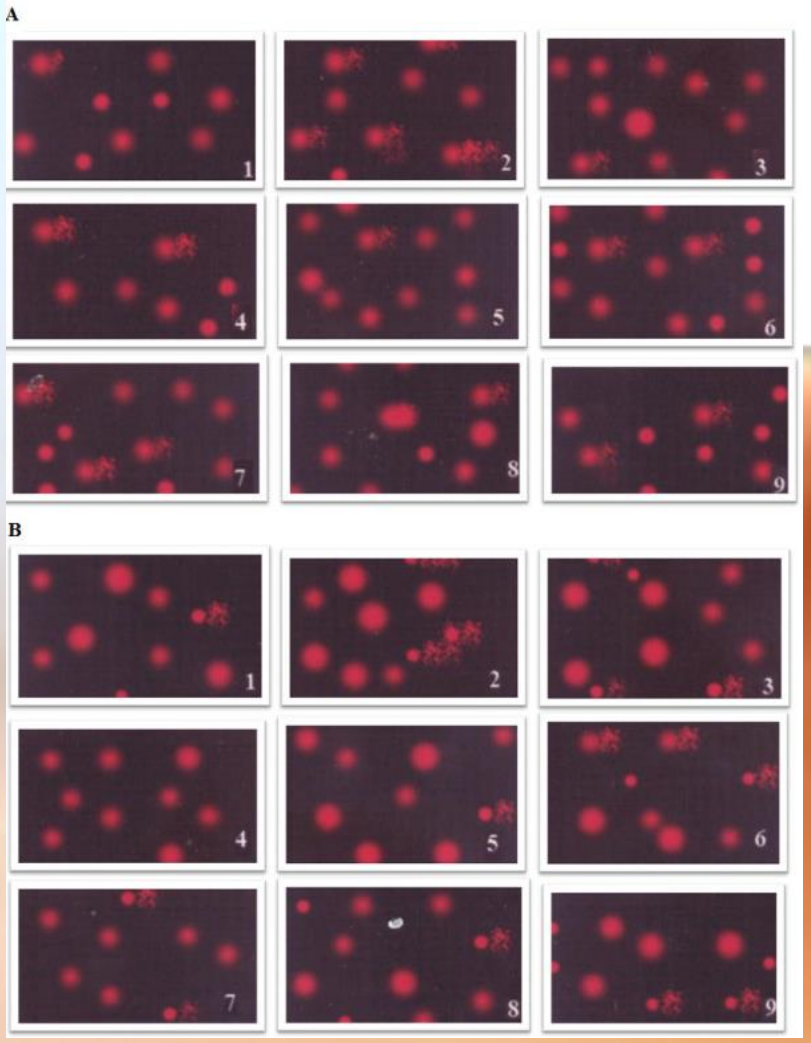
- However when administered with PA both carnosine and carnitine tended to restore the altered levels of neurotransmitters to near normal levels.

- Therefore carnosine and carnitine may be used as antioxidants as supplements to protect against PA neurotoxicity.

DNA damage (Comet assay)



- DNA damage induced in hamster brains (cortex and medulla) by PA or clindamycin-induced bacterial overgrowth together with the protective effects of carnosine and L-carnitine.
- Neurotoxic effects of PA, bacterial overgrowth and ameliorating effects of both the supplements could be seen as significant changes in tail length (µm) and tail moments (Arbitrary units) (A &B respectively) It is clear that orally administered PA was more neurotoxic than induced bacterial overgrowth. Carnosine was more protective than carnitine.



- Measure of PA or clindamycin-induced DNA damage by comet assay. (A) Photograph showing comet tailing in PA and clindamycine treated hamsters together with the protective effects of carnosine and carnitine in cortex; (B) Photograph showing comet tailing in PA and clindamycine treated hamsters together with the protective effects of carnosine and carnitine in medulla.

Causes & Prevalence

OA Autism
Open Access

Detoxification mechanisms in auti

A El-Ansary*

Abstract

Introduction

Xenobiotics are neurotoxins that dramatically alter the health of a child. A three-phase efficient mechanism is involved in detoxifying these toxins. Autism spectrum disorders are neurodevelopmental disorders that result from a combination of genetic or biochemical susceptibilities in the form of a reduced ability to excrete heavy metals and/or increased envi-

substances from the body. It
the major functions of t
kidney and gastrointestin
Additionally, it is the bio
process that transforms no
soluble toxins and metabol
water-soluble compounds th
excreted in urine, sweat, bile
Endogenous toxins are those
generated internally as end
of metabolism, bacterial by
and other complex molec

Review

El-Ansary *et al. Journal of Neuroinflammation* 2012, **9**:74
http://www.jneuroinflammation.com/content/9/1/74

JNI JOURNAL OF NEUROINFLAMMATION

RESEARCH Open Access

Etiology of autistic features: the persisting neurotoxic effects of propionic acid

Afaf K El-Ansary[1*], Abir Ben Bacha[1] and Malak Kotb[2]

Abstract

Background: Recent clinical observations suggest that certain gut and dietary factors may transiently worsen symptoms in autism. Propionic acid (PA) is a short chain fatty acid and an important intermediate of cellular metabolism. Although PA has several beneficial biological effects, its accumulation is neurotoxic.

Methods: Two groups of young Western albino male rats weighing about 45 to 60 grams (approximately 21 days old) were used in the present study. The first group consisted of oral buffered PA-treated rats that were given a neurotoxic dose of 250 mg/kg body weight/day for three days, n = eight; the second group of rats were given only phosphate buffered saline and used as a control. Biochemical parameters representing oxidative stress, energy metabolism, neuroinflammation, neurotransmission, and apoptosis were investigated in brain homogenates of both groups.

Results: Biochemical analyses of brain homogenates from PA-treated rats showed an increase in oxidative stress markers (for example, lipid peroxidation), coupled with a decrease in glutathione (GSH) and glutathione peroxidase (GPX) and catalase activities. Impaired energy metabolism was ascertained through the decrease of lactate

El-Ansary et al. Gut Pathogens 2013, 5:9
http://www.gutpathogens.com/content/5/1/9

Gut Pathogens

RESEARCH Open Access

The neurotoxic effect of clindamycin - induced gut bacterial imbalance and orally administered propionic acid on DNA damage assessed by the comet assay: protective potency of carnosine and carnitine

Afaf El-Ansary[1,2,4*], Ghada H Shaker[5], Amina R El-Gezeery[1] and Laila Al-Ayadhi[2,3,4]

Abstract

Background: Comet assay is a quick method for assessing DNA damage in individual cells. It allows the detection of single and double DNA strand breaks, which represent the direct effect of some damaging agents. This study uses standard comet quantification models to compare the neurotoxic effect of orally administered propionic acid (PA) to that produced as a metabolite of bacterial overgrowth induced by clindamycin. Additionally, the protective effect of carnosine and carnitine as natural dietary supplements is assessed.

Methods: Single cell gel electrophoresis (comet assays) were performed on brain cortex and medulla samples after removal from nine groups of hamsters including: a control (untreated) group; PA-intoxicated group; clindamycin treated group; clindamycin-carnosine group and; clindamycin-carnitine group.

Results: There were significant double strand breaks recorded as tail length, tail moment and % DNA damage in PA and clindamycin-treated groups for the cortex and medulla compared to the control group. Neuroprotective effects of carnosine and carnitine were observed. Receiver Operating Characteristics curve (ROC) analysis showed satisfactory values of sensitivity and specificity of the comet assay parameters.

Conclusion: Percentage DNA damage, tail length, and tail moment are adequate biomarkers of PA neurotoxicity due to oral administration or as a metabolite of induced enteric bacterial overgrowth. Establishing biomarkers of these two exposures is important for protecting children's health by documenting the role of the imbalance in gut microbiota in the etiology of autism through the gut-brain axis. These outcomes will help efforts directed at controlling the prevalence of autism, a disorder recently related to PA neurotoxicity.

Keywords: Propionic acid, Clindamycin, Tail length, Tail moment, Carnosine, Carnitine, Autism, Neurotoxicity

Introduction

The investigation of the environmental contribution towards developmental neurotoxicity is fundamental to identifying the effects of environmental contaminants on humans. Exposure to environmental chemicals may contribute to the development of neurological disorders, especially in children. Animal studies may help identify the etiology of neurotoxicity due to some of these environmental chemicals. Additionally, animal studies can help understanding the protective effects of some dietary supplements against neurotoxicity. Due to the high number of reports of antibiotic exposure, hospitalization, and gastrointestinal disturbances [1-3] in many children with autism spectrum disorders (ASDs), the neurobiological effects of microbiota-produced short-chain fatty acids (SCFAs), such as propionic acid (PA), has been

*Correspondence: elansary@ksu.edu.sa
[1]Department of Biochemistry, College of Science, King Saud University, P.O Box 22452, Riyadh 11495, Saudi Arabia

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Full Length Research Paper

Comparative study on the protective effect of carnosine and carnitine against pro-inflammatory/pro-oxidant effects of clindamycin and propionic acid administrations to hamsters

Afaf K. El-Ansary[1,2,3]*, Sooad Al-Daihan[1], Abir Ben Bacha[1], Ghada H. Shaker[4] and Laila Y. Al-Ayadhi[2,3,5]

[1]Biochemistry Department, Science College, King Saud University, P.O Box 22452, Zip code 11495, Riyadh, Saudi Arabia.
[2]Autism Research and Treatment Unit, King Saud University, Riyadh, Saudi Arabia.

El-Ansary et al. Gut Pathogens 2013, 5:32
http://www.gutpathogens.com/content/5/1/32

Gut Pathogens

RESEARCH Open Access

Possible ameliorative effects of antioxidants on propionic acid / clindamycin - induced neurotoxicity in Syrian hamsters

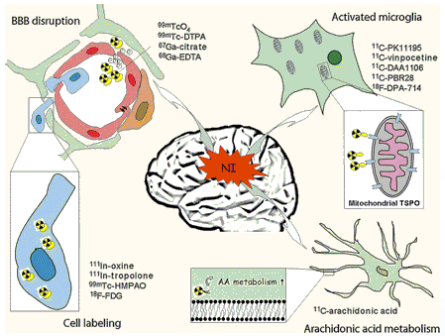
Afaf El-Ansary[1,4,5,6*], Ghada Shaker[2], Nikhat J Siddiqi[1] and Laila Y Al-Ayadhi[3,4,5]

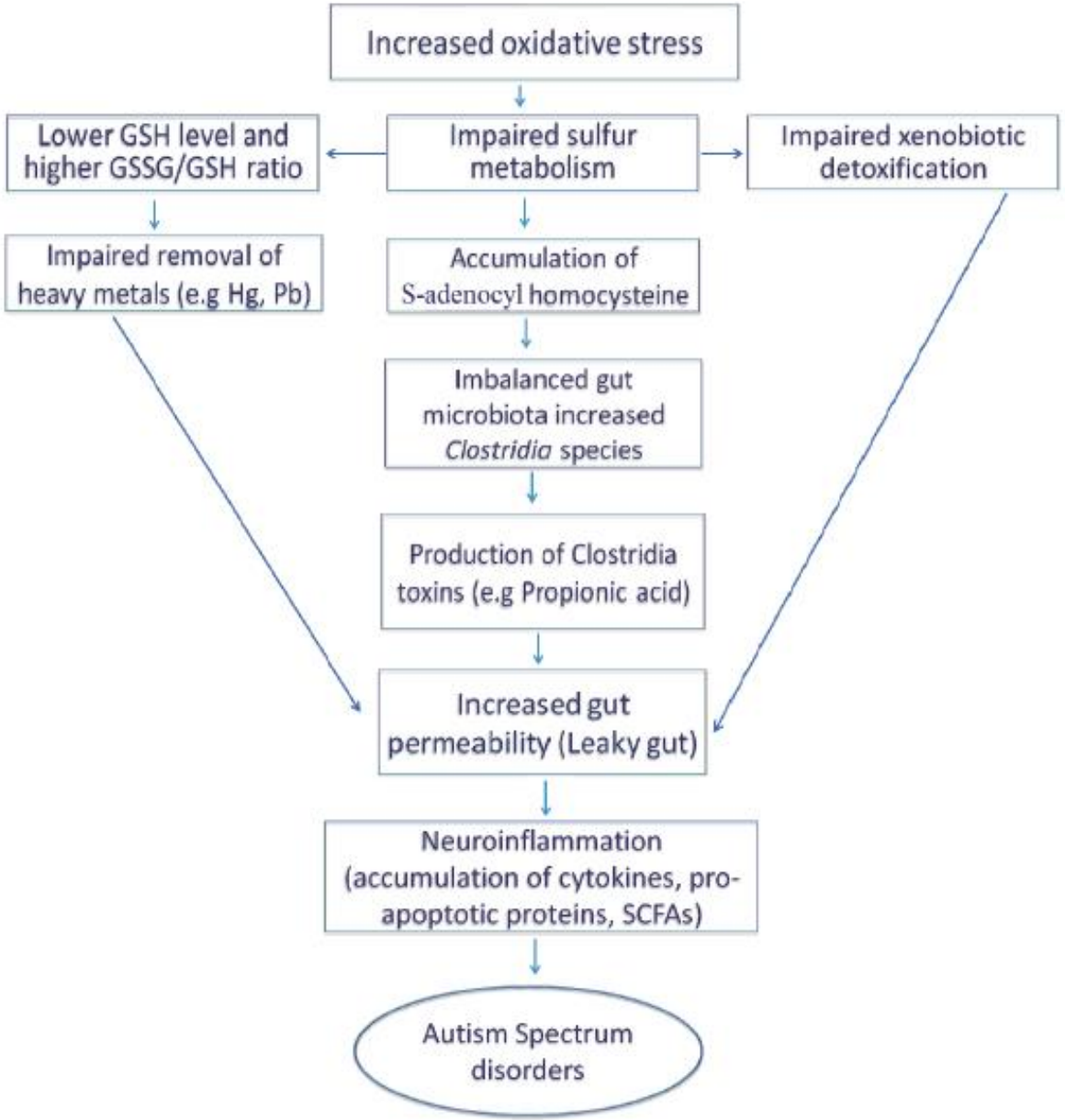
Abstract

Background: Propionic acid (PA) found in some foods and formed as a metabolic product of gut bacteria has been reported to mimic/mediate the effects of autism. The present study was undertaken to compare the effect of orally administered PA with that of clindamycin-induced PA-microbial producers in inducing persistent biochemical autistic features in hamsters. The neuroprotective potency of carnosine and carnitine supplements against PA toxicity was also investigated.

Methods: The following groups were studied. 1. Control group, which received phosphate buffered saline orally,

Propionic acid





Where do probiotic come from ??

- The micro biota of a newborn develops rapidly after the birth .

  It is initially dependent mainly on :

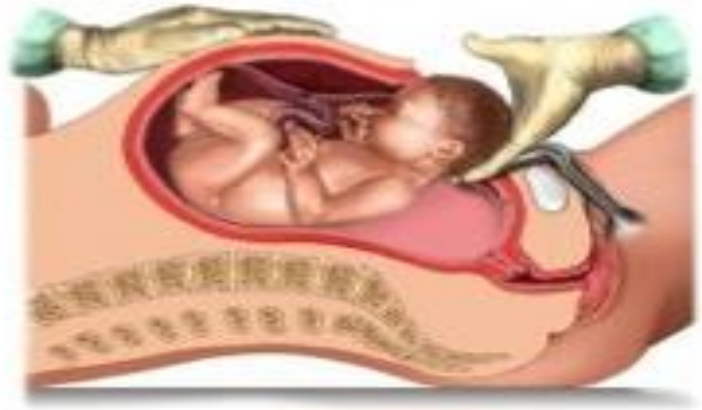
  - the mother's micro biota,
  - mode of delivery,
  - birth environment
  - and rarely genetic factors .
- The maternal vaginal and intestinal flora constitutes the source of bacteria, which colonizes the intestine of the newborn.
- After infancy probiotics are supplied to us by raw foods; lactic acid fermented foods such as yogurt and cheese; and probiotic supplements.

Vaginal delivery and C-section

Vaginal Delivery

vs.

Cesarean Delivery



Introduced to Vaginal Microbes: Lactobacillus

Introduced to Skin Flora: Staphylococcus

Normal Introduction of Gut Microbes

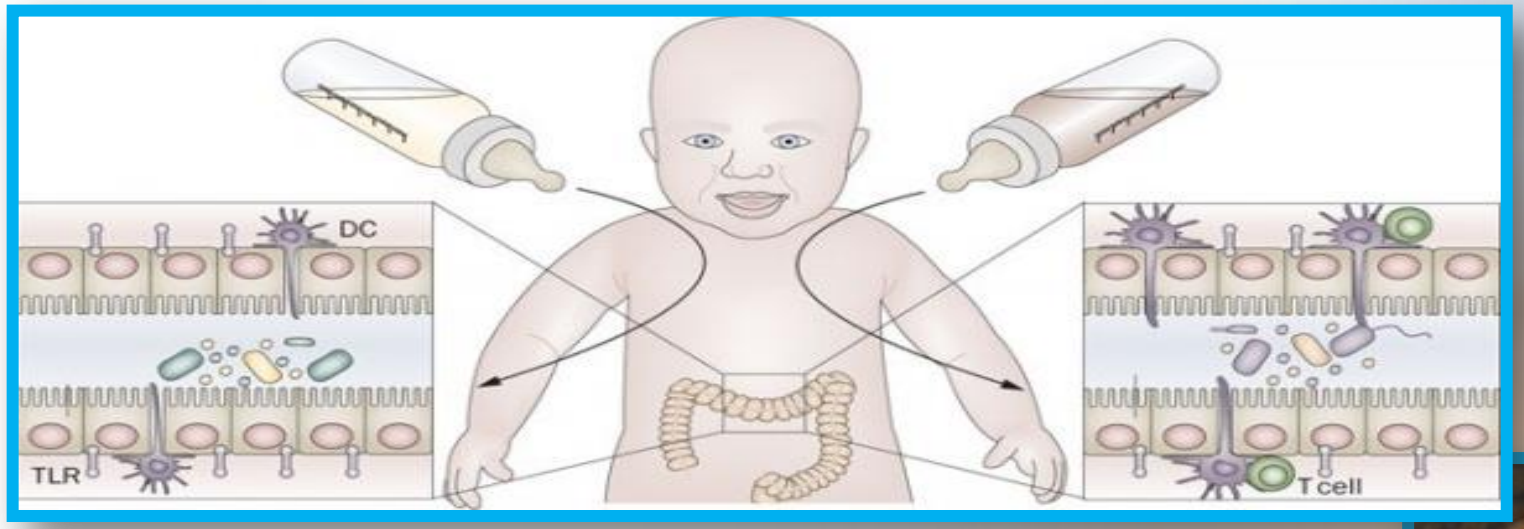
Abnormal Microbial Introduction

Normal Development of the Immune System
- Production of specific cytokines for proper immune system development

Richardson; 2013

Disrupted Intestinal Microbial Colonization
- Increase risk for Atopic Diseases, Asthma, Allergic Rhinitis, and Celiac Disease
- Association: Delayed Onset of Lactation
  - Lack Breast Milk Support for Gut Flora

Balanced at birth microbiota



Factors affecting the intestinal microbiota

- Any action taken to kill ‘bad’ bacteria essentially kills ‘good’ bacteria as well.

- Antibiotics and other drugs intake
- Microbial infections
- Diet (highly processed, low-fiber foods)
- Chronic diarrhea
- Stress

Selection of probiotic organism

- Safety
- Origin
- Functional aspects
- Survival
- Adherence, colonization
- Anti-microbial products
- Immune stimulation
- Genetic stable
- Prevention of pathogens

Major pre-requisite properties for a microbe to be accepted as a probiotic are:

- It should be non-pathogenic, non-toxic and non-allergic.
- It should be capable of surviving and metabolizing in upper G.I. tract secretion in the gut environment e.g. Resistant to low pH, organic acids, bile juice, saliva and gastric acid.
- It should be human in origin, genetically stable and capable of remaining viable for long periods.
- It should be able to modulate immune response and provide resistance to disease through improved immunity or by the production of antimicrobial substance in the guts.

Contd....

- It should have a good adhesion/ colonization to human intestinal tract and influence on gut mucosal permeability.
- It should be antagonistic against carcinogenic/ pathogenic organism.
- It should posses clinically proven health benefit, e.g. gastrointestinal disorders, persistant diarrhoea, clostridium difficle colitis, antibiotics associated diarrhoea, acute infantile gastroenteritis.
- It should have technologic properties for commercial viability such as stability of desired characteristics during processing, storage and transportation.

Advantages of a probiotic

- ✓ Produce lactic acid- lowers the pH of intestines and inhibiting bacterial villains such as *Clostridium, Salmonella, Shigella*, *E. coli,* etc.
- ✓ Decreases the production of a variety of toxic or carcinogenic metabolites.
- ✓ Aid absorption of minerals, especially calcium, due to increased intestinal acidity.
- ✓ Production of β- D- galactosidase enzymes that break down lactose .

Contd....

Probiotics in Pregnancy:

- Bacterial vaginosis , increases the risk of preterm labour and infant mortality .
- Probiotics decrease the risk of bacterial vaginosis and maintain normal lactobacilli vaginal flora

Prebiotics

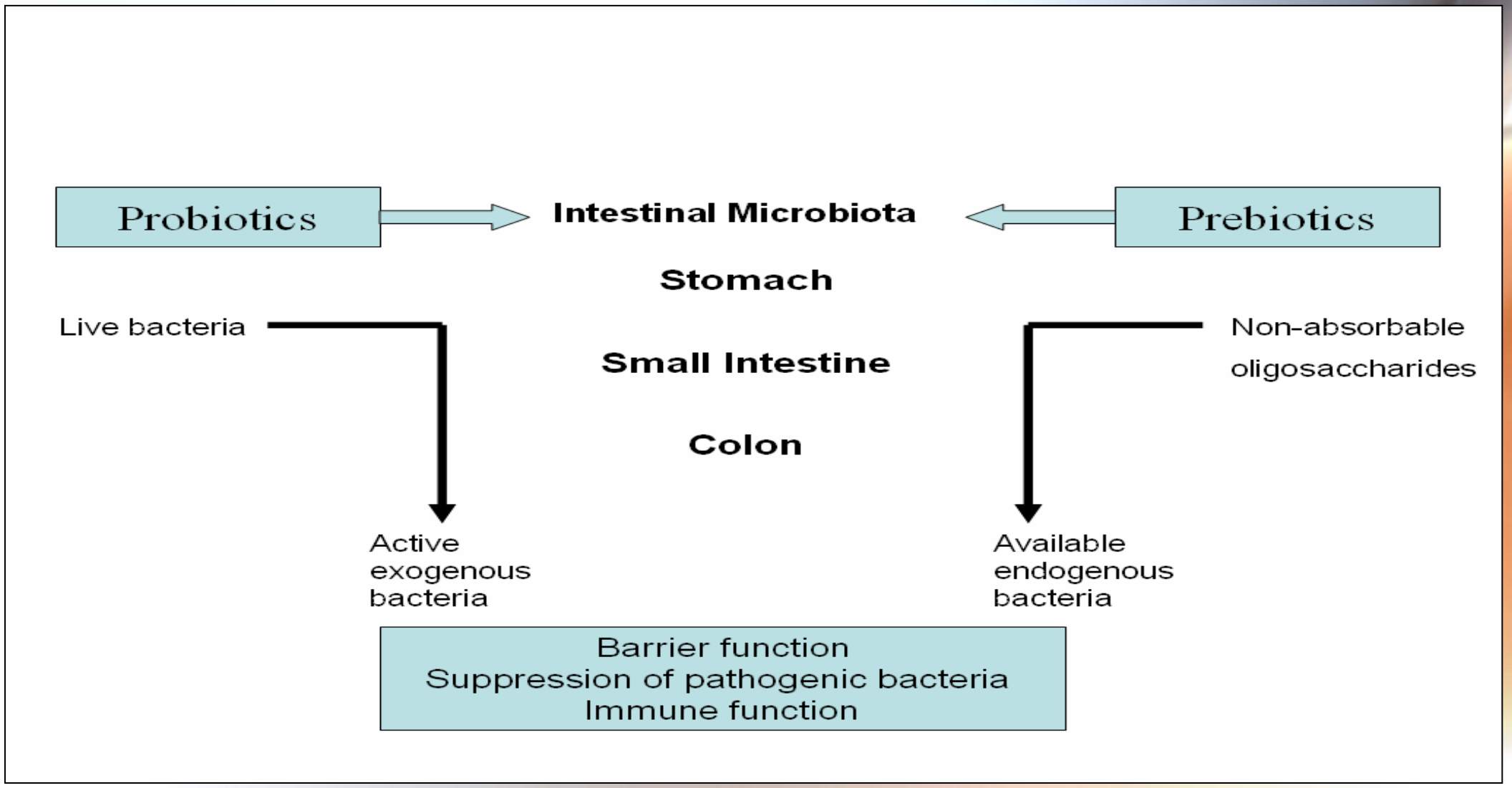
- Definition:

  "a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon"

- Example: Inulin, FOS
- Source: banana, onion, wheat, garlic, leeks, wild yam

Gibson & Roberfroid, 1995; Van Loo J et al, 1995; Roberfroid et al, 1998

Concept of Probiotics and Prebiotics



Harish and Varghese, 2006

Synbiotics

- **Synbiotic = Probiotic + Prebiotic**

➢ The concept of synbiotics has been proposed to characterize health-enhancing foods and supplements used as functional food ingredients in humans (Gibson, 2004).

➢ Potential synergy between pro- & prebiotics

➢ Improve survival in upper GIT

➢ More efficient implantation

➢ Stimulating effect of Probiotics

Some of the major health benefits of synbiotics

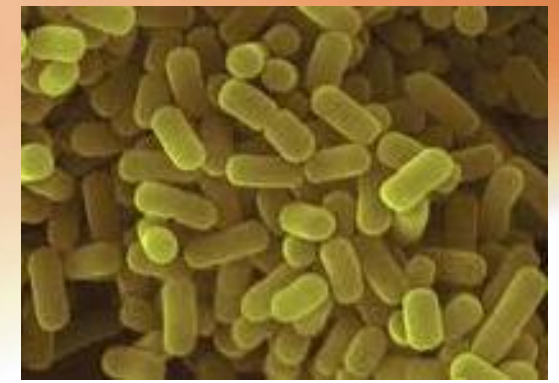
- ✓ Improved survival of live bacteria in food products, prolonged shelf life,
- ✓Increased number of ingested bacteria reaching the colon in a viable form
- ✓Activation of metabolism of beneficial bacteria, antagonistic toward pathogenic bacteria
- ✓Production of antimicrobial substances (bacteriocins , hydrogen peroxide, organic acids etc)
- ✓Immunostimulation
- ✓Anti-inflammatory, Anti-mutagenic, Anti-carcinogenic, and production of bioactive compounds (enzymes, vaccines, peptides etc)

(Nagpal et al, 2007)

Probiotic Foods

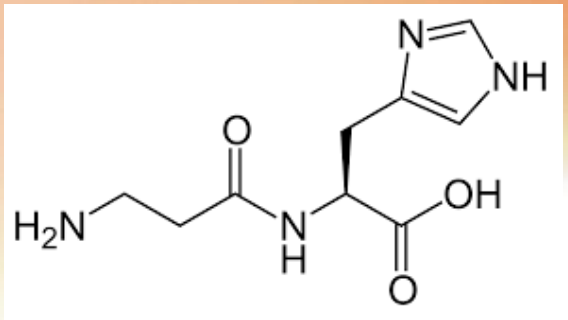
Probiotics for Autism: Clinical Research

- ✓Probiotics for Autism: Clinical Research
- ✓Probably the most well-known study into probiotic for autism was that run in 2006 by Professor Glenn Gibson at the University of Reading
- ✓40 autistic children all between 4 and 13 years old were randomly separated into a trial group, and a control group. The trial group were given a probiotic supplement with the species *Lactobacillus plantarum* whilst children in the other group were given placebos.
- ✓Comments from parents of participants in the probiotic group included not only reports on digestive health improvements, such as, 'better formed stools' but also potentially mental & behavioural improvements, such as, 'more calm, relaxed, not stressed' and 'improved ability to listen and concentrate'.



L-carnosine supplementation in autism

In the Chez et al study, researchers treated 31 autistic children, ranging from 3 to 12 years in age, with either 400 mg of L-Carnosine, twice a day, or a placebo, for 8 weeks. At the end of the study the children treated with L-Carnosine showed significant improvements in behavior, socialization, and communication, as well as increases in language comprehension based on CARS (Childhood Autism Rating Scale), vocabulary tests (E/ROWPVT) and biweekly parent reports. In the conclusion to their report the researchers state, “Oral supplementation with L-Carnosine resulted in demonstrable improvements in autistic behaviors, as well as increases in language comprehension that reached statistical significance.”



L-carnitine trial in autism

- SRCTN54273114
- A Clinical Trial of Levocarnitine to Treat Autism Spectrum Disorders
- A Prospective Double-Blind, Randomized Clinical Trial of Levocarnitine to Treat Autism Spectrum Disorders
- The hypothesis tested in the present study was that blood carnitine levels in patients diagnosed with an ASD have a significant impact on behaviour, cognition, socialization, and health/physical traits associated with an ASD diagnosis. The present prospective, double-blind, placebo controlled trial evaluated whether a standardized treatment regimen of liquid L-carnitine administered to patients diagnosed with an autism spectrum disorder (ASD) on a daily basis for 3-months would result in improved behaviour, cognition, socialization, and health/physical traits associated with an ASD diagnosis.
- Autism Research Institute (USA)

Thank You!