Early-Life Stress Induces Long-term Morphologic Changes in Primate Brain

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Presented by Zain, Isabella, and Patricia

INTRODUCTION

The study focuses on how early-life stress can affect primates' chances on developing neuropsychiatric disorders

Stress is a known risk factor in developing psychiatric disorders

Study induces stress by separating Rhesus Monkeys from their mothers/parental figures for 6 months in early childhood

Peer Raising (Separating participants from parental figures) has been used in past studies as well to cause stress

Trauma in one's early life has been shown to affect regions in the brain as well, such as an increased cortisol and norepinephrine response to subsequent stressors.

INTRODUCTION (cont.)

Rearing Condition: Mother reared & peer reared

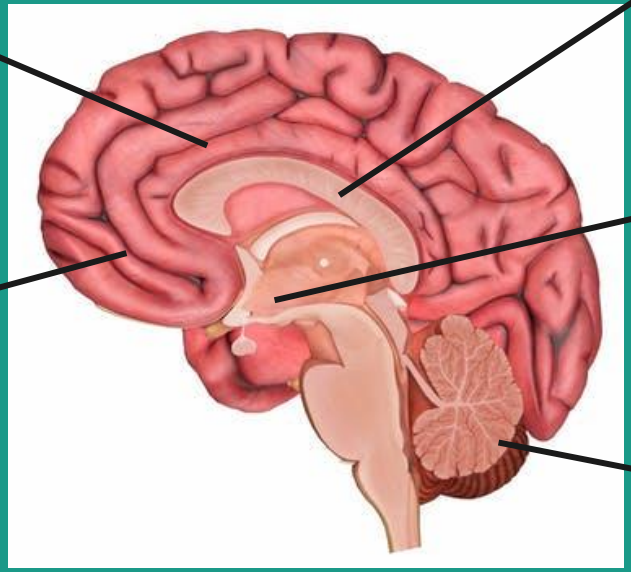
Study took place at the National Institute of Health Animal Center

Objective: To study how early stressors in one's life may affect the risk of neuropsychiatric disorders in Rhesus Monkeys

Regions of Interest

Anterior Cingulate Cortex (ACC)

Medial Prefrontal Cortex (mPFC)



Corpus Callosum (CC)

Hippocampus (HC)

Cerebellar Vermis (CBV)

Frequently Used Terms

CSF Sample: a way of looking for conditions that affect your brain and spine. It's a series of laboratory tests performed on a sample of CSF which is the clear fluid that cushions and delivers nutrients to your central nervous system (CNS).

Cortisol Levels: the level of a steroid hormone made by your adrenal glands. It helps your body respond to stress, regulate blood sugar, and fight infections.

Rater: when a human evaluator subjectively judges the response of a patient to a medical treatment

Volumetric Differences: changes in image features that are solely related to the progression or regression of a particular disease or to a pathomorphological condition

Hypothesis: Stress-sensitive brain regions which are the region of interest would be smaller in juvenile PR monkeys as compared with MR monkeys

Design of study

28 rhesus monkeys

Aged 23-32 months

13 males and 15 females

Peer rearing vs. Mother rearing

Mother Rearing (MR)

15 monkeys

Reared with mothers and fathers in social groups

Benefit: social interaction and support

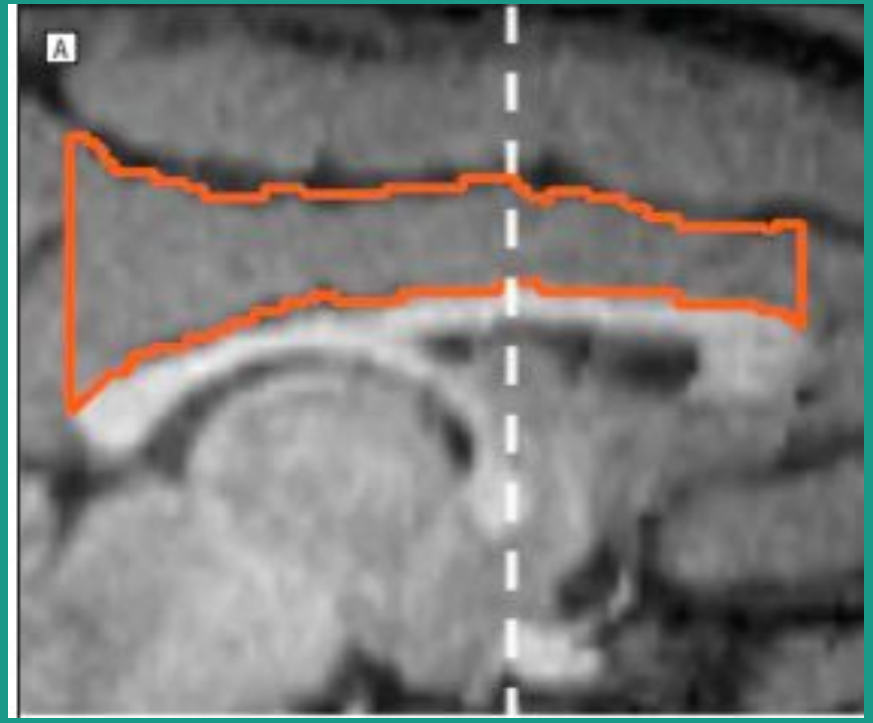
Peer Rearing (PR)

Neurochemical sampling & Analyses

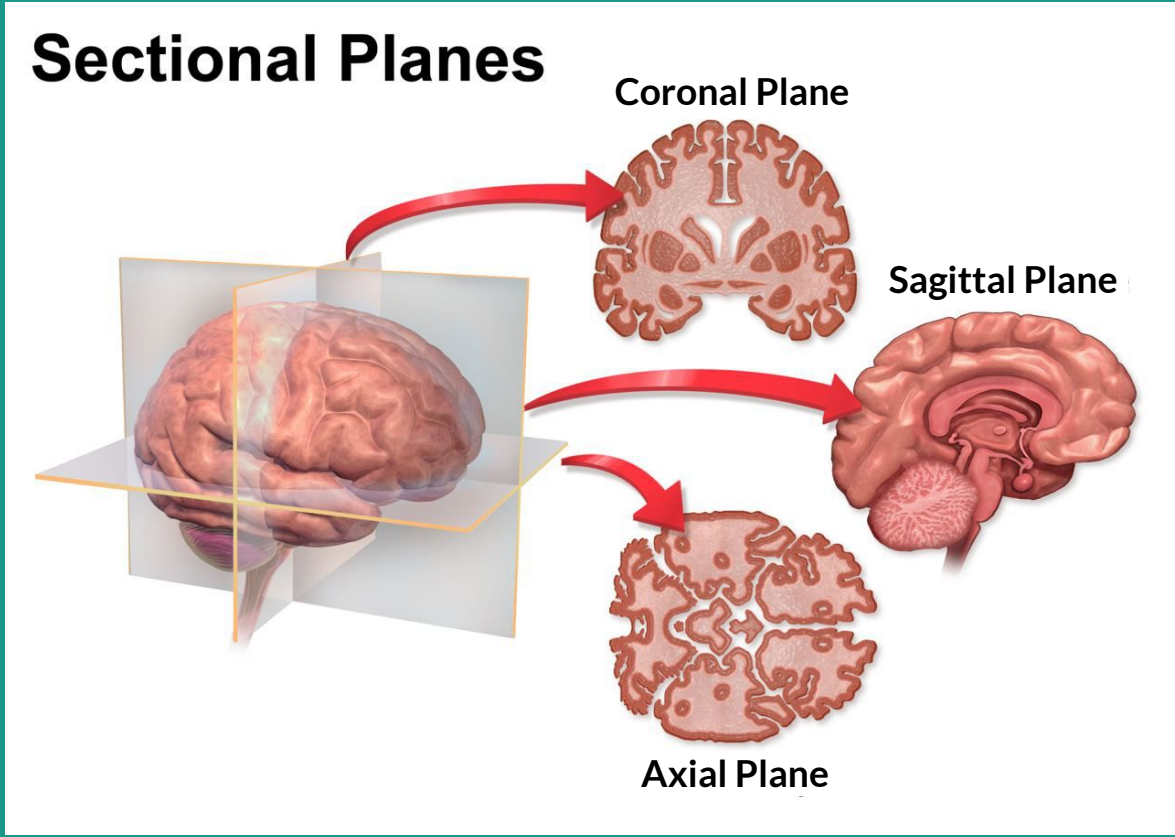
CSF and blood samples were collected

Activity of HPA axis and serotonin system may be related to regional structural changes.

Brain Image Acquisition and Analyses



Anatomical Subdivisions



Predictors of the Volumetric Differences

PEER REARED VS MOTHER REARED
SEX: FEMALE VS MALE
5-HIAA: CSF SEROTONIN
PLASMA & CSF CORTISOL

DATA ANALYSES

StatView 5.0.1 software

Kolmogorov-Smirnov normality test
Pearson Correlation (R)

P-values for each statistical analysis

RESULTS: Physiologic data in MR & PR

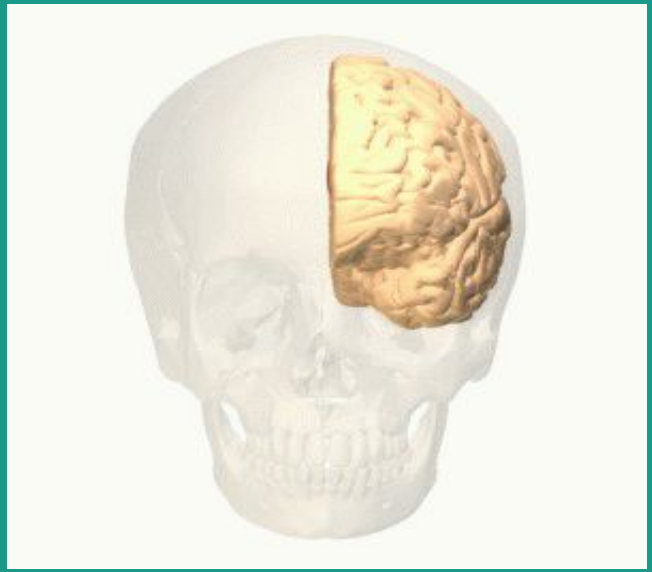
Table 1. Physiologic Data in MR and PR Monkeys

Variable	Mean (SEM)		
	MR Monkeys	PR Monkeys	Statistical Analysis
Age, mo	27.40 (0.90)	26.39 (0.33)	$F_{1,24}=0.89$; $P>.35$
Weight, kg	3.61 (0.13)	3.44 (0.09)	$F_{1,24}=0.96$; $P>.33$
Cortisol, µg/dL	33.02 (1.22)	34.62 (1.80)	$F_{1,24}=0.43$; $P>.23$
5-HIAA, pmol/mL	268.18 (16.18)	241.28 (13.85)	$F_{1,24}=1.51$; $P>.51$

BRAIN ANATOMICAL MEASURES

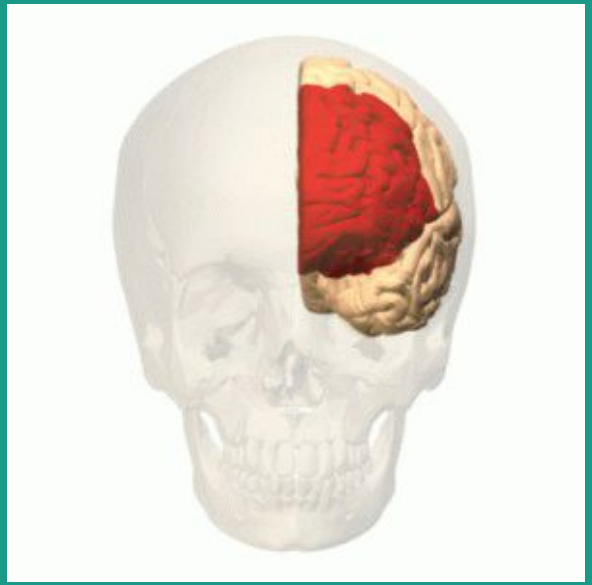
RESULTS:

CINGULATE CORTEX



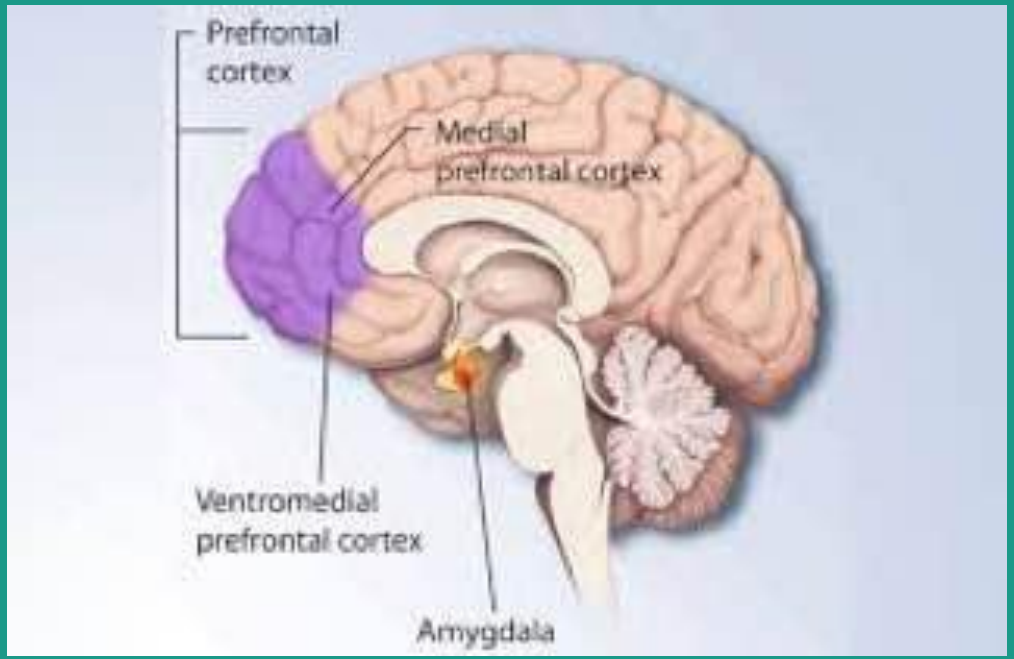
RESULTS:

PRE-FRONTAL CORTEX



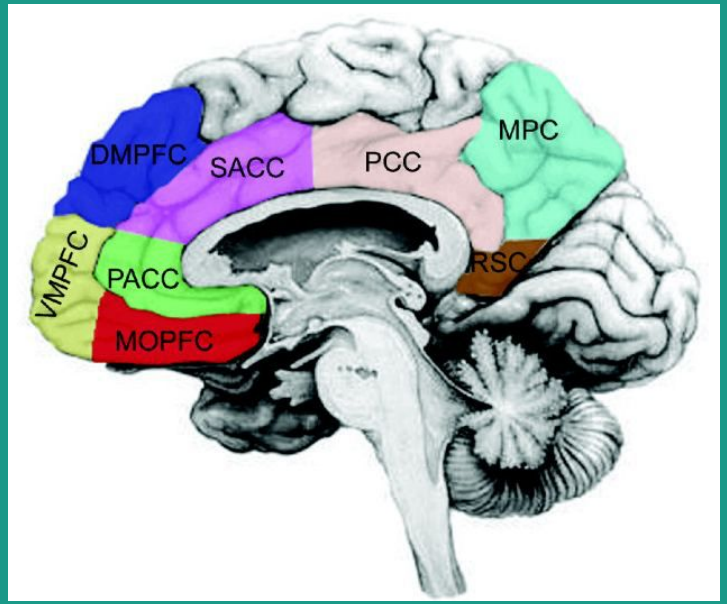
RESULTS:

MEDIAL PREFRONTAL CORTEX



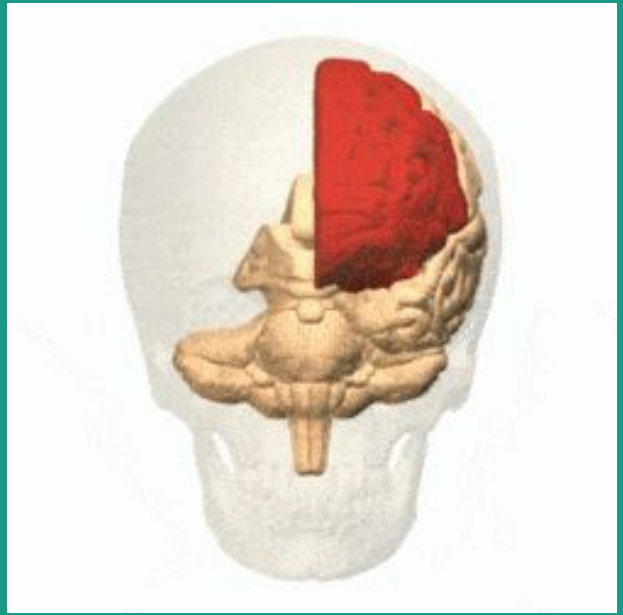
RESULTS:

DORSOMEDIAL PREFRONTAL CORTEX



RESULTS:

PREFRONTAL LOBE

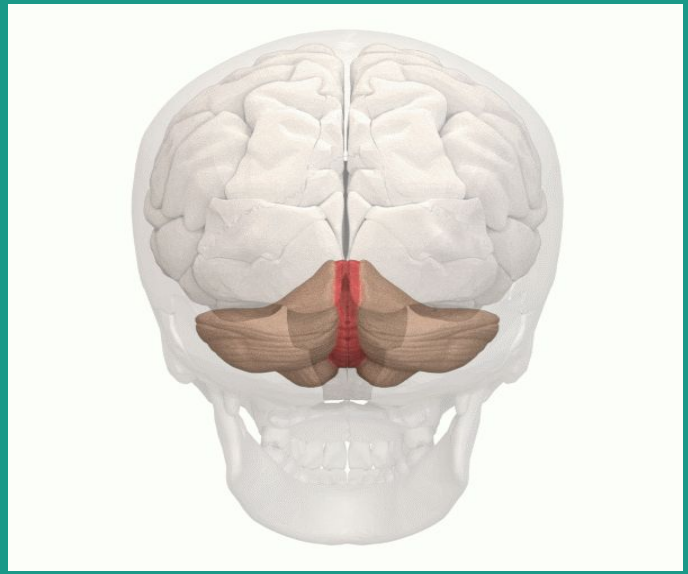


RESULTS:

HIPPOCAMPUS

RESULTS:

CEREBELLAR VERMIS



RESULTS:

CORPUS CALLOSUM

NORMALISED AND ABSOLUTE VOLUMES OF BRAIN AREAS MEASURED IN MR & PR GROUPS

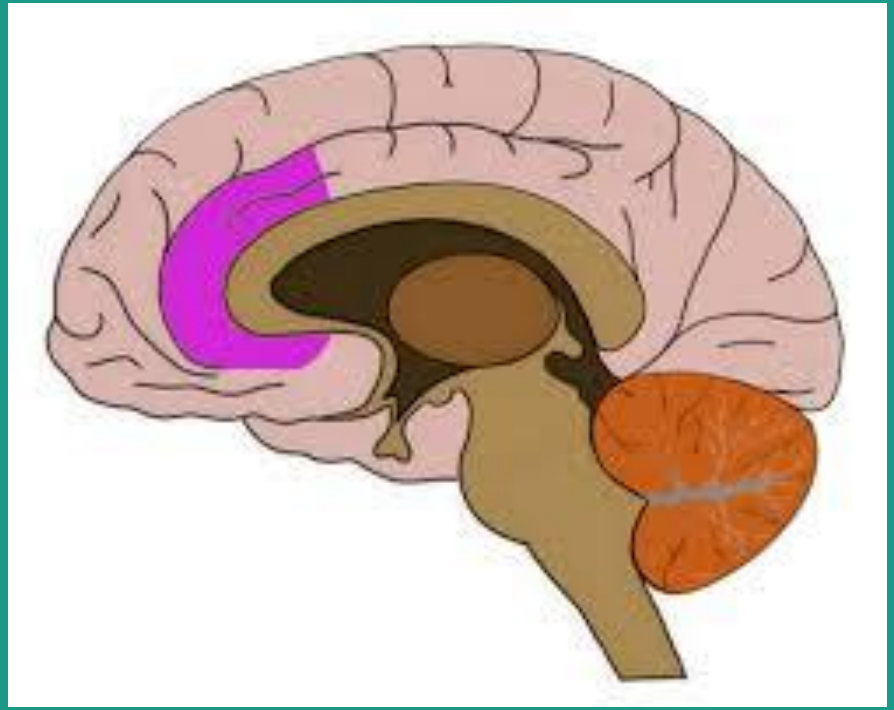
Table 2. Normalized and Absolute Volumes of Brain Areas Measured in MR and PR Groups

Brain Area	Mean (SEM)				Absolute Volume Difference, %	Statistical Analyses for Normalized Values
	Normalized Volume[a]		Absolute Volume, mm^3			
	MR Monkeys	PR Monkeys	MR Monkeys	PR Monkeys		
ICV	. . .	. . .	91 121.10 (1904.22)	92 561.94 (2413.57)	1.61	. . .
dACC	5.29 (0.13)	5.74 (0.17)	481.98 (15.84)	531.71 (21.87)	10.32	$F_{1,24}=4.46$; $P<.05$
PCC	10.81 (0.27)	10.93 (0.22)	984.99 (32.91)	1011.61 (34.23)	2.70	$F_{1,24}=0.07$; $P>.79$
Right mPFC	7.59 (0.14)	7.99 (0.23)	692.13 (19.16)	741.37 (23.37)	7.11	$F_{1,23}=2.20$; $P>.15$
Left mPFC	7.53 (0.14)	7.90 (0.23)	685.99 (18.90)	734.04 (23.87)	7.00	$F_{1,23}=1.87$; $P>.19$
Right dmPFC	6.12 (0.13)	6.64 (0.18)	557.97 (16.43)	616.35 (16.78)	10.46	$F_{1,23}=6.37$; $P<.02$
Left dmPFC	6.15 (0.12)	6.67 (0.16)	560.57 (15.4)	618.74 (16.93)	10.38	$F_{1,23}=6.88$; $P<.02$
Right PFL	35.31 (0.50)	36.13 (0.91)	3218.09 (80.31)	3336.38 (100.03)	3.68	$F_{1,24}=0.52$; $P>.47$
Left PFL	36.42 (0.50)	36.68 (0.81)	3317.83 (79.04)	3393.01 (109.48)	2.27	$F_{1,24}=0.08$; $P>.77$
Right HC	5.31 (0.11)	5.18 (0.12)	481.66 (8.45)	479.28 (16.06)	−0.49	$F_{1,24}=0.48$; $P>.49$
Left HC	5.16 (0.10)	5.04 (0.12)	467.77 (6.90)	465.82 (13.44)	−0.42	$F_{1,24}=0.52$; $P>.47$
CC	125.21 (1.20)	125.28 (1.81)	31.79 (0.82)	32.21 (1.15)	1.32	$F_{1,24}=0.03$; $P>.87$
CBV	254.66 (2.09)	264.43 (1.56)	131.99 (2.31)	142.93 (2.66)	8.29	$F_{1,24}=14.33$; $P<.01$

CORRELATION WITH BASELINE PLASMA CORTISOL & CSF 5-HIAA CONCENTRATIONS

Brain Area	Cortisol, µg/dL	5-HIAA, pmol/mL
dACC	$R=0.18$; $P>.35$	$R=0.16$; $P>.44$
Right dmPFC	$R=0.01$; $P>.97$	$R=0.40$; $P<.05$
Left dmPFC	$R=0.12$; $P>.54$	$R=0.37$; $P>.06$
CBV	$R=0.25$; $P>.19$	$R=0.01$; $P>.97$

Anterior Cingulate Cortex



Cellular Changes

Abnormal ACC development could be mediated by several cellular processes

Conclusion

Peer rearing during infancy induces enlargement in stress sensitive brain regions

Questions?