NEUROENDOCRINOLOGY OF PROLACTIN REGULATION IN BIRDS

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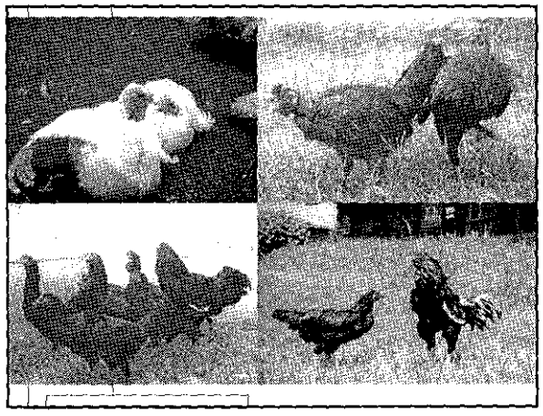
Prolactin (PRL) has long been associated with avian reproduction. PRL secretion, which is under tonic control in avian species, is stimulated by vasoactive intestinal peptide (VIP), which meets the classical criteria required for releasing factors. VIP mediates PRL gene expression via a 35-bp VIP response element located between position –70 and -40 on the turkey PRL promoter gene. The group of VIP neurons regulating PRL secretion is located in the infundibular nuclear complex (INF) of the caudal hypothalamus. While neurotransmitters regulating the VIP/PRL system remain uncertain, groups of dopamine (DA) cells are prominent in the avian hypothalamus. Both D_1 and D_2 DA receptors display abundant mRNA in the hypothalamus and pituitary, and have been shown to mediate, respectively, the stimulatory and inhibitory influences on PRL release and gene expression. The stimulatory effect is mediated via preoptic area (POA) dopaminergic stimulation of hypothalamic VIP release and gene expression. The inhibitory effect occurs at the pituitary level where DA from the dorsolateral INF DA neurons overrides the stimulating effect of VIP on PRL secretion. It has been demonstrated that the changes in the expression of VIP receptors at the pituitary level were in part, regulated the variations in prolactin secretion as well. The interaction between VIP and DA at the pituitary level is mediated by intracellular Ca^{2+} with VIP increasing intracellular Ca^{2+}, and DA closing Ca^{2+} channels.

Key words: *Birds, Dopamine, Prolactin, Vasoactive intestinal peptide*



Neuroendocrinology of Prolactin Regulation in Birds

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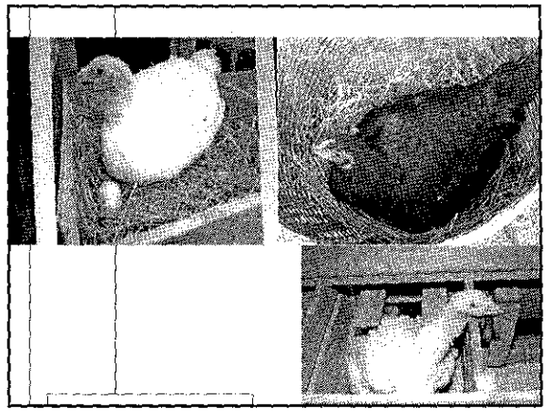
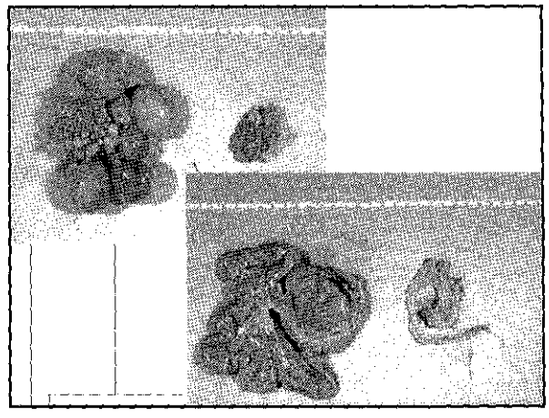
Avian Reproduction

- The reproductive efficiency of turkey is low in comparison with chicken
- Poor egg production due to:
  - -The onset of incubation behavior
  - -The cessation of egg laying
- Expression of incubation behavior (broodiness) is a costly problem

The Onset of Incubation Behavior

-6- to 10-fold increase in PRL
-FSH and LH decrease
-Ovarian steroid decrease
-Cessation of ovulation
-Ovarian regression
-Brood patch
-Eat and drink less
-Nesting activity increase





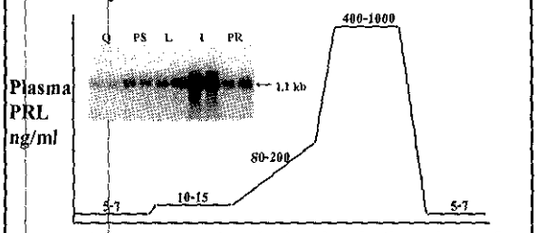
Prolactin

* Riddle and co-workers, 1932
* An anterior pituitary hormone
* 198 amino acids
* More than 300 different physiological functions
  - Reproduction
  - The immune response
  - Osmoregulation
  - Promotion of growth and behaviors

Prolactin

* Associated with the reproductive cycle in several avian species
* Cessation of ovulation, ovarian regression, and induction of incubation behavior
* The onset and maintenance of broodiness in birds

Profile of Circulating Prolactin in the Turkey Hen



Wong et al., 1992

Neuroendocrine Regulation of PRL Secretion

- Avian PRL secretion is under stimulatory control
- Vasoactive intestinal peptide is the avian PRL-releasing factor (PRF)
  - -28 amino acid
  - -Said and Mutt, 1970
  - -VIP as the PRF in mammals

Neuroendocrine Regulation of PRL Secretion

- Avian PRL secretion is under stimulatory and inhibitory control
- Dopamine, Serotonin (5-HT), dynorphin

Neuronal Regulation of Prolactin

- Vasoactive intestinal peptide (VIP), the avian prolactin releasing factor (PRF).
- Dopamine (DA), a prominent neurotransmitter in the avian hypothalamus.
- Regulation of prolactin by VIP, DA, 5-HT.
- Hypothalamic 5-HT-DA-VIP pathway

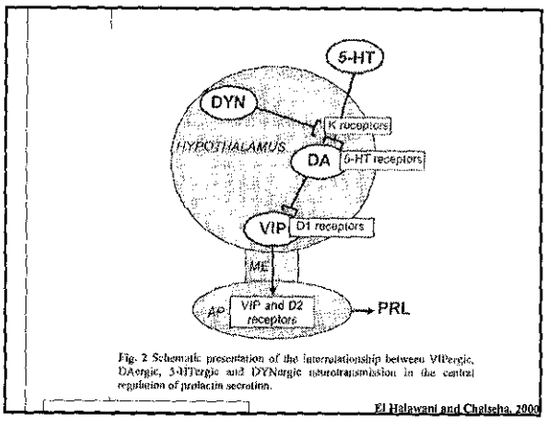


Fig. 2 Schematic presentation of the interrelationship between VIPergic, DAergic, 5-HTergic and DYNergic neurotransmission in the central regulation of prolactin secretion.

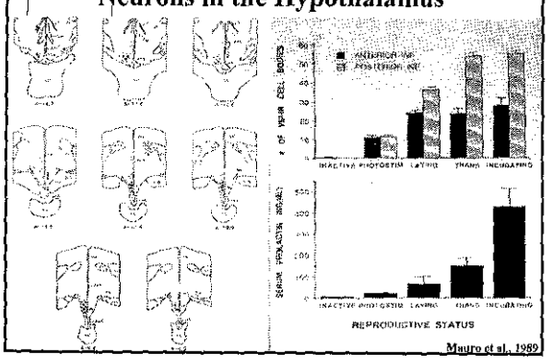
El Halawani and Chalsena, 2000

VIP: The Avian PRF

VIP meets the classical criteria for defining as the hypophysiotropic PRF in birds:

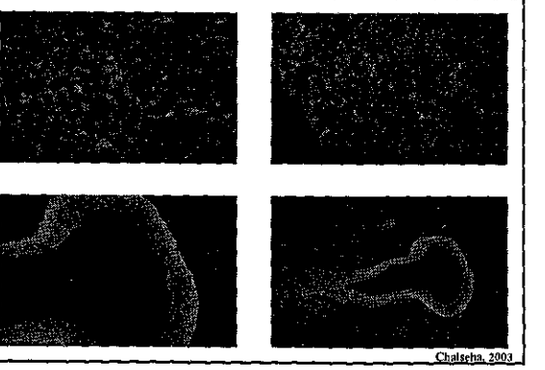
1. The presence of VIP-immunoreactive neurons in the hypothalamus
2. The secretion of VIP into portal blood
3. The modulation of VIP secretion into portal blood
4. The presence of VIP-specific receptor on anterior pituitary cells
5. The ability of VIP to regulate anterior pituitary lactotrophs
6. The alteration of pituitary function, due to antagonism of VIP

The Presence of VIP-immunoreactive Neurons in the Hypothalamus



Mauro et al., 1989

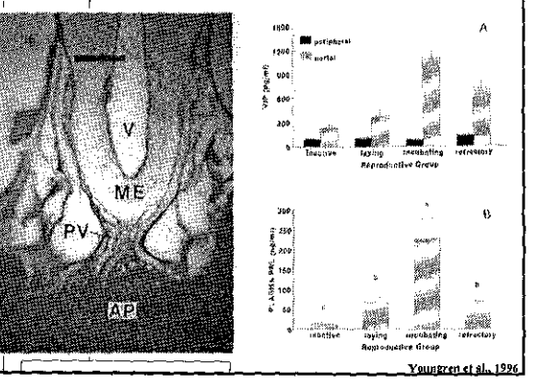
Presence of Hypothalamic VIP-like Neurons



Chalsena, 2003

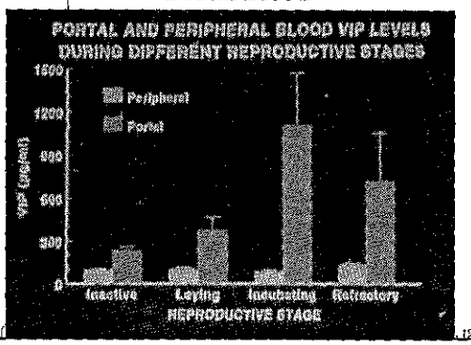
The Secretion of VIP into Portal Blood

Youngren et al., 1996



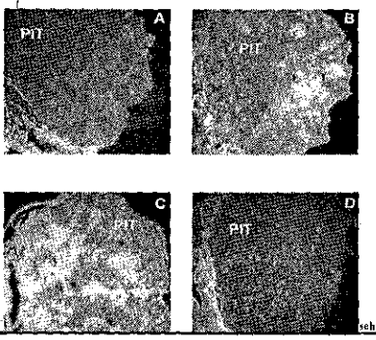
Youngren et al., 1996

The Modulation of VIP Secretion into Portal Blood



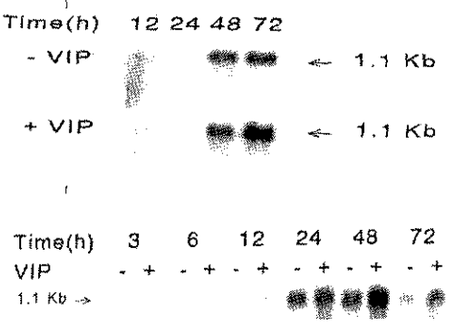
1996

The Presence of VIP-Specific Receptor on Anterior Pituitary Cells



Ischa et al., 2004

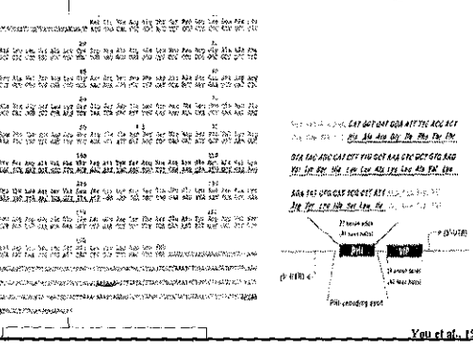
The Ability of VIP to Regulate Anterior Pituitary Lactotrophs



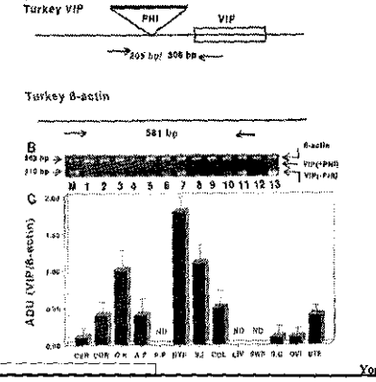
Xu et al., 1996

VIPergic Control of Prolactin Secretion in Birds

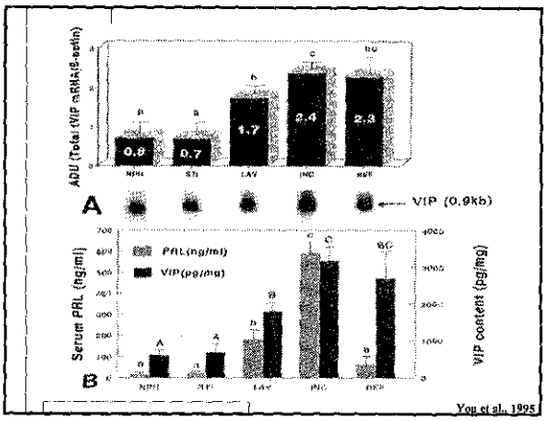
Vasoactive Intestinal Peptide

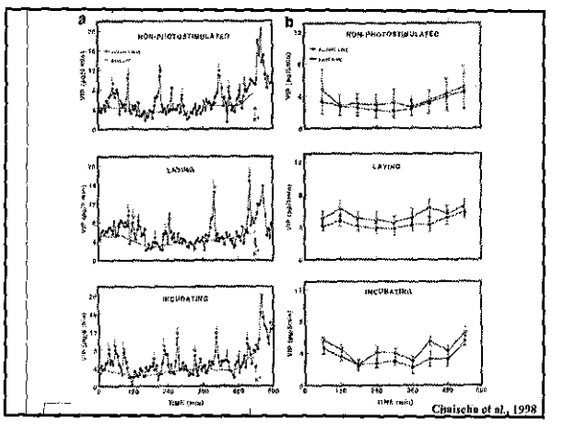


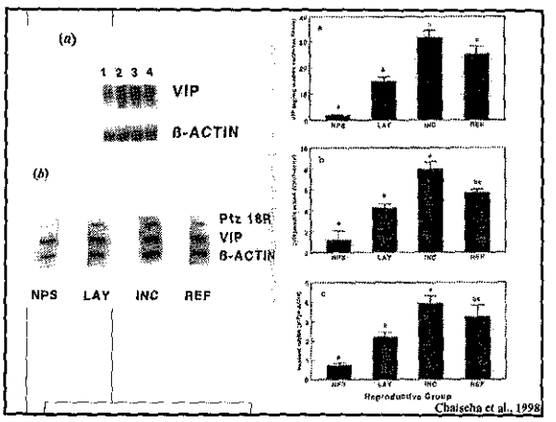
You et al., 1995

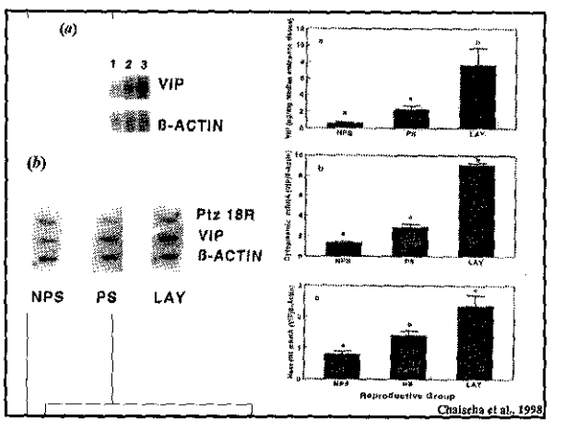


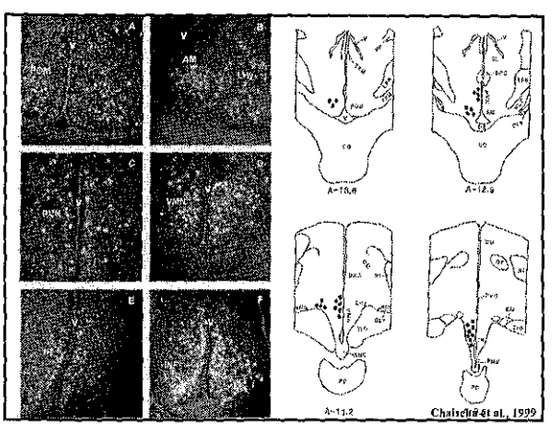
You et al., 1995

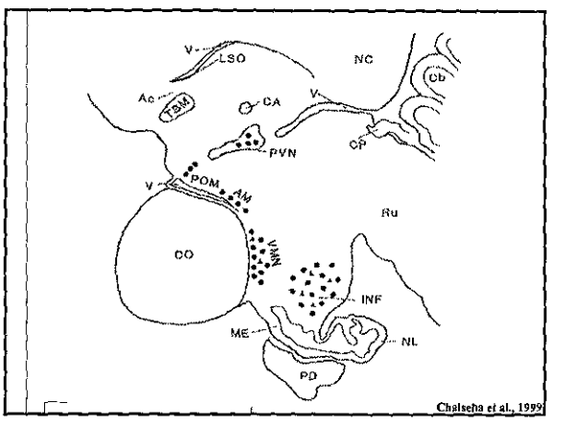

ADU (Total VIP mRNA/B-actin)
0.8
0.7
1.7
2.4
2.3
NPH
STI
LAY
INC
REF
A
VIP (0.9kb)
PRL(ng/ml)
VIP(pg/mg)
Serum PRL (ng/ml)
VIP content (pg/mg)
B
Yoo et al., 1995

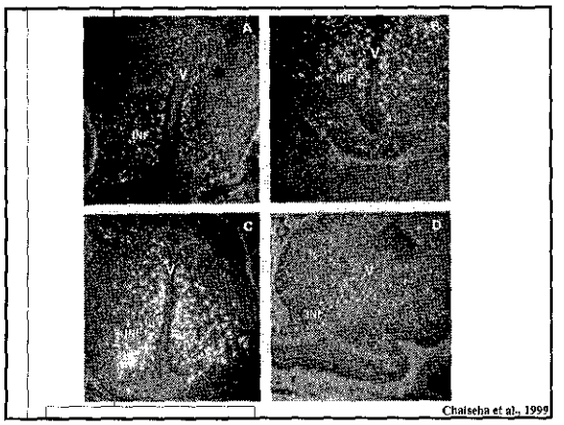

a
b
NON-PHOTOSTIMULATED
LAYING
INCUBATING
Chaiseha et al., 1998

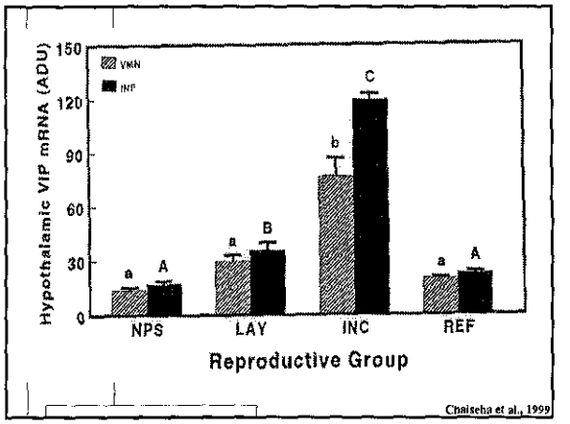

(a)
1 2 3 4
VIP
B-ACTIN
(b)
Ptz 18R
VIP
B-ACTIN
NPS
LAY
INC
REF
Reproductive Group
Chaiseha et al., 1998

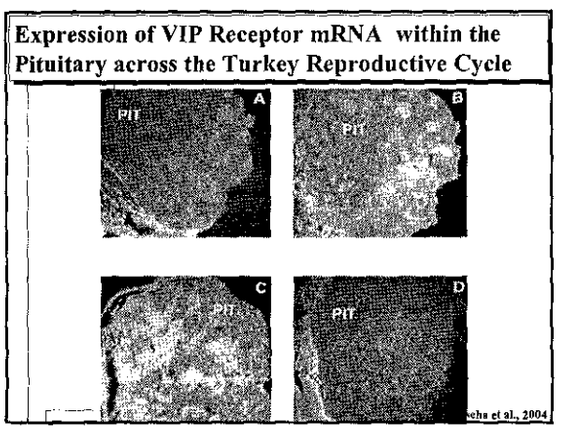

(a)
1 2 3
VIP
B-ACTIN
(b)
Ptz 18R
VIP
B-ACTIN
NPS
PS
LAY
Reproductive Group
Chaiseha et al., 1998


A
B
C
D
E
F
V
AM
POM
VMN
PVN
CO
A-10.8
A-12.6
A-11.2
Chaiseha et al., 1999

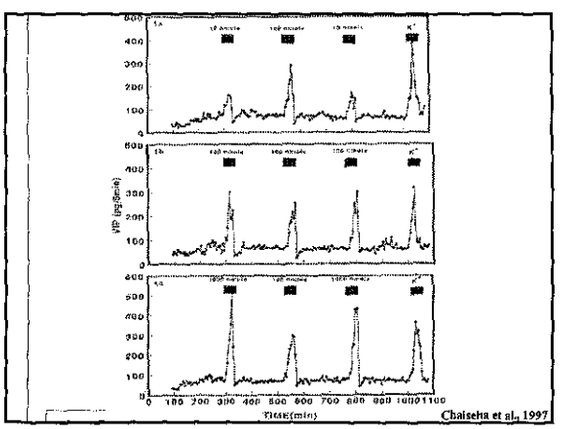

V
LSO
NC
Cb
Ac
TBM
CA
PVN
CP
POM
AM
Ru
CO
VMN
INF
ME
NL
PD
Chaiseha et al., 1999

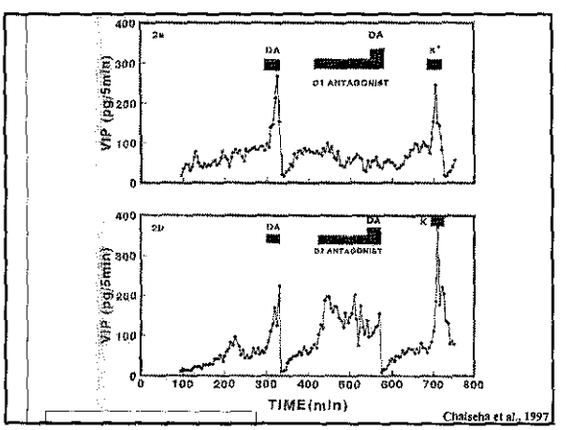


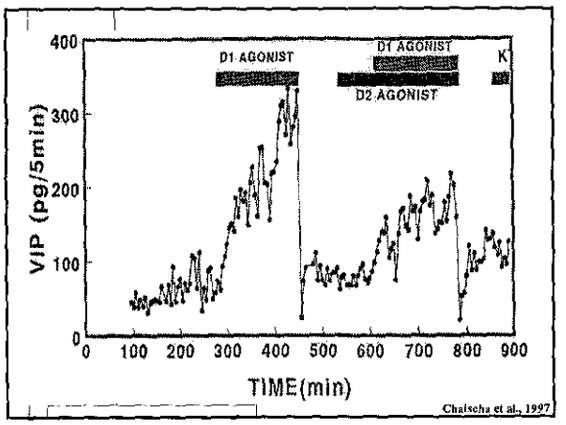


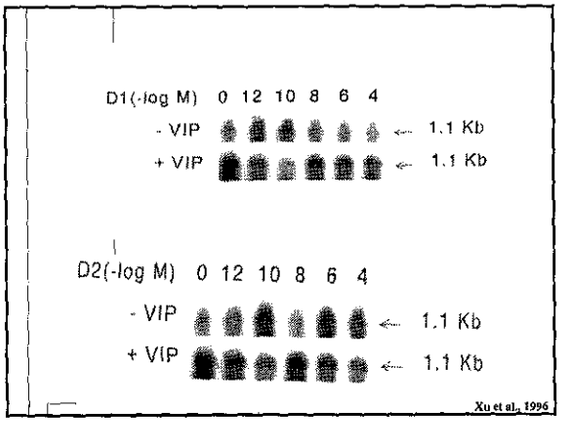


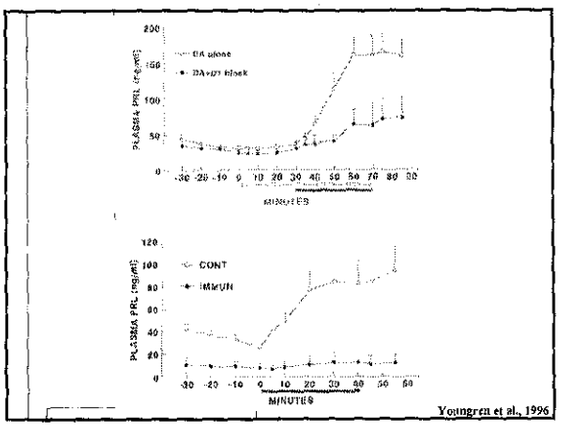
Dopaminergic Control of Prolactin Secretion in Birds

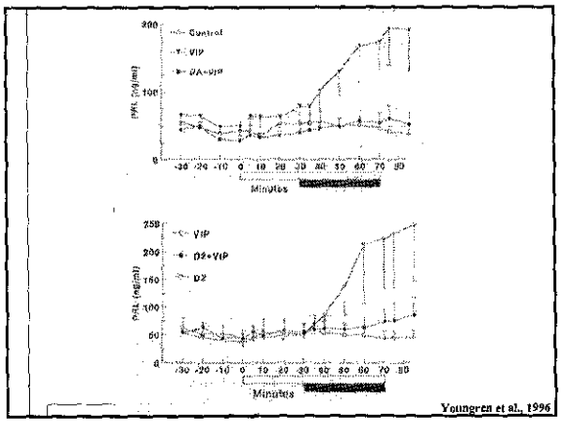


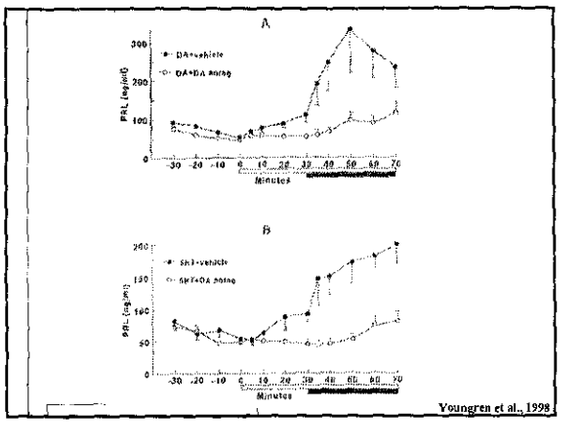


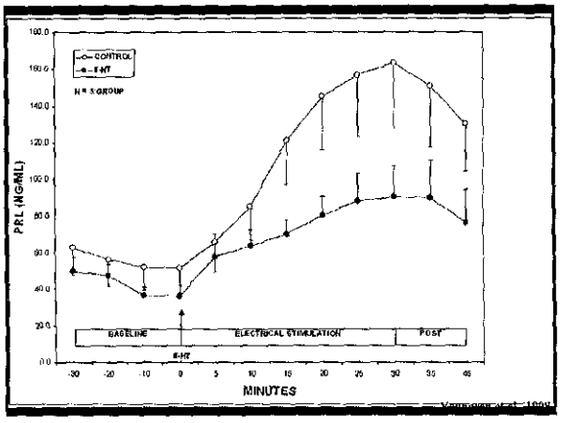

D1 AGONIST
D1 AGONIST
K
D2 AGONIST
VIP (pg/5min)
TIME(min)
Chaiseha et al., 1997

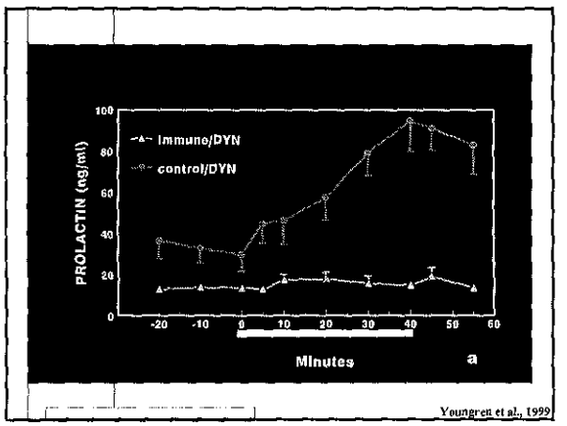

D1(-log M) 0 12 10 8 6 4
- VIP
+ VIP
1.1 Kb
1.1 Kb
D2(-log M) 0 12 10 8 6 4
- VIP
+ VIP
1.1 Kb
1.1 Kb
Xu et al., 1996


DA alone
DA+D1 block
CONT
IMMUN
MINUTES
Youngren et al., 1996

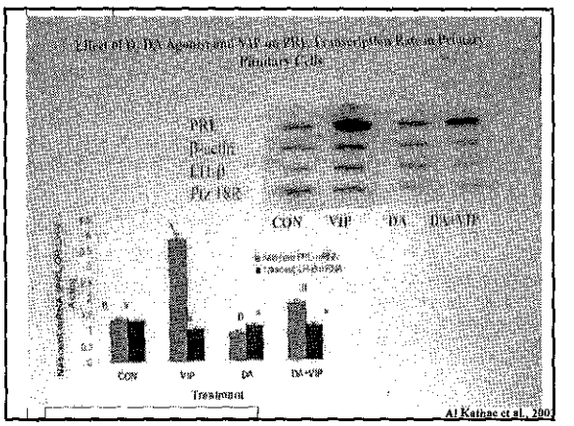

Control
VIP
DA+VIP
Minutes
VIP
D2+VIP
D2
Minutes
Youngren et al., 1996


A
DA+vehicle
DA+DA antag
Minutes
B
Minutes
Youngren et al., 1998


CONTROL
5-HT
N = 5/GROUP
PRL (NG/ML)
BASELINE
ELECTRICAL STIMULATION
POST
5-HT
MINUTES



Youngren et al., 1999



Al Katnae et al., 200

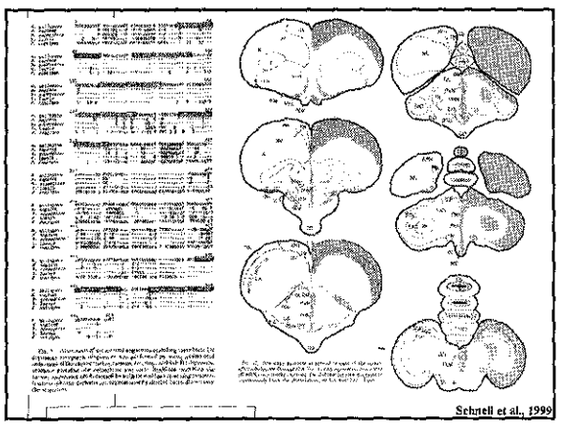
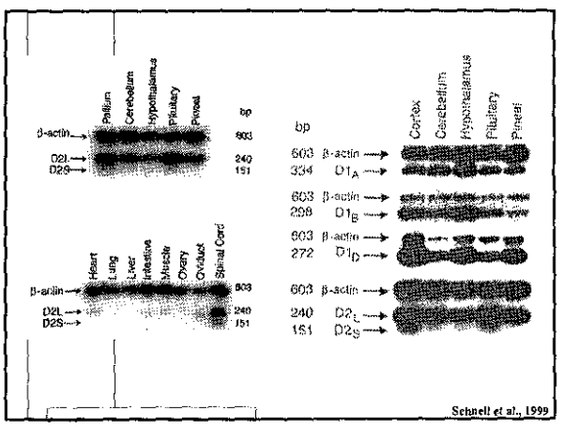

Schnell et al., 1999

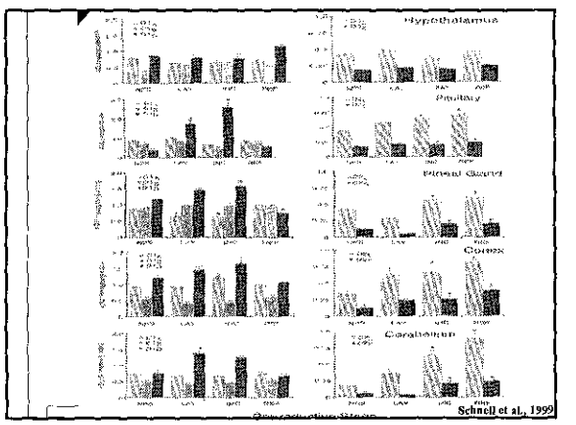
TABLE 1. Primers and PCR products used for RT-PCR analysis.

PCR product	Primers 5′ → 3′	No. of cycles	Product size (bp)
$D1_A$		26	334
$D1_B$		26	298
$D1_D$		30	272
D2		32	240 ($D2_L$) 151 ($D2_S$)
β-Actin		26	603

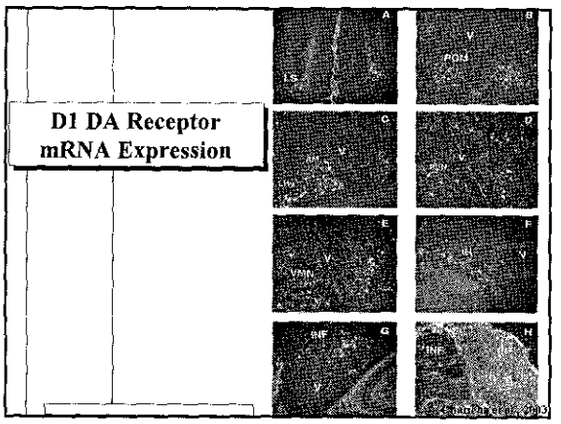
Schnell et al., 1999

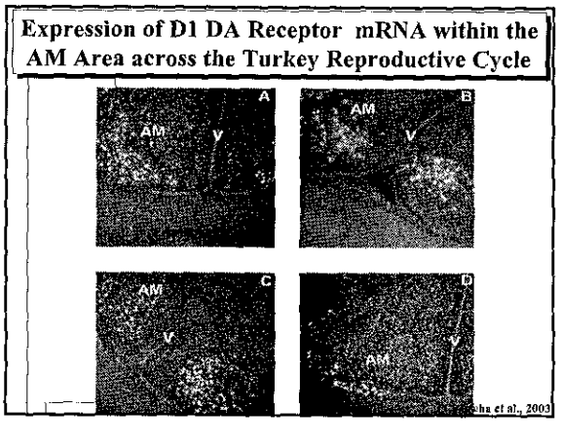


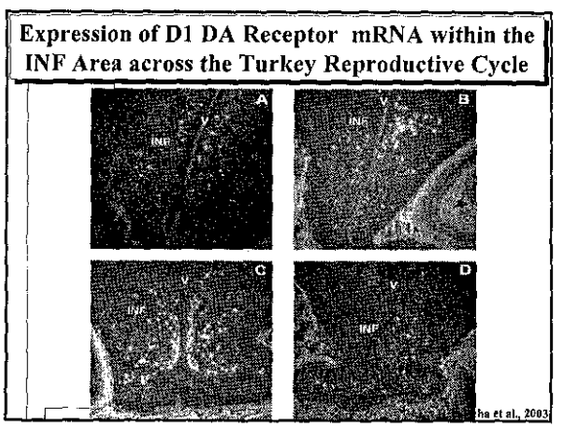
Schnell et al., 1999

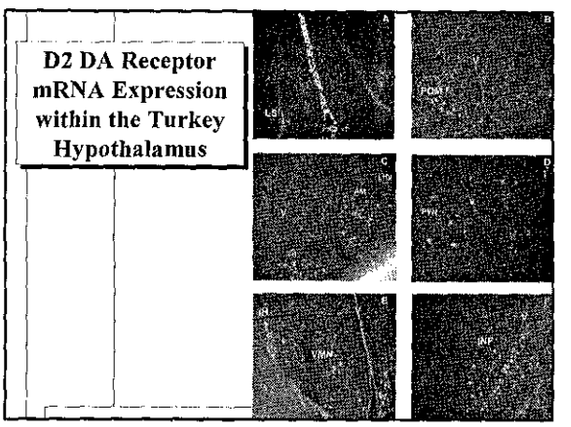


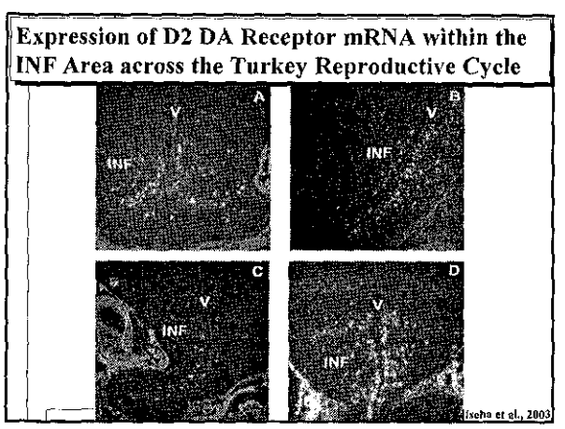
Schnell et al., 1999

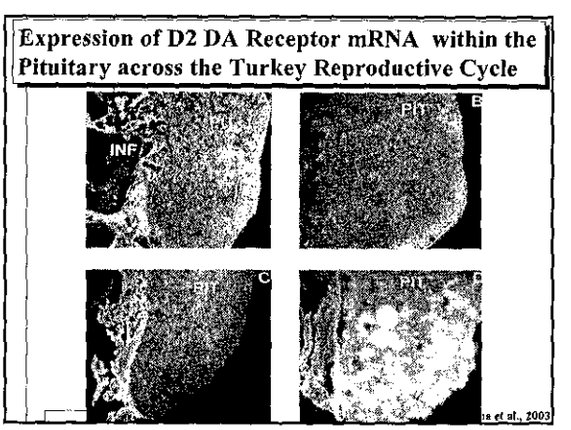

D1 DA Receptor
mRNA Expression

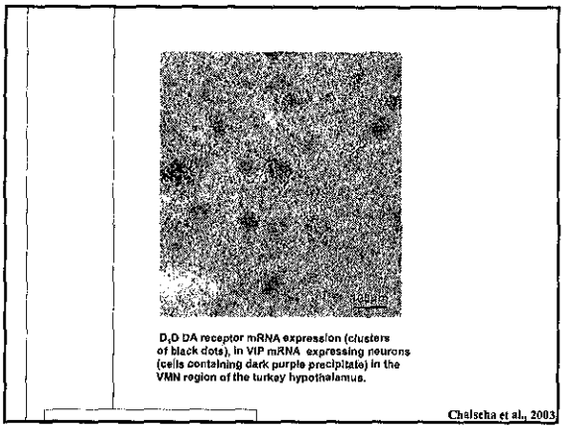

Expression of D1 DA Receptor mRNA within the
AM Area across the Turkey Reproductive Cycle


Expression of D1 DA Receptor mRNA within the
INF Area across the Turkey Reproductive Cycle


D2 DA Receptor
mRNA Expression
within the Turkey
Hypothalamus


Expression of D2 DA Receptor mRNA within the
INF Area across the Turkey Reproductive Cycle

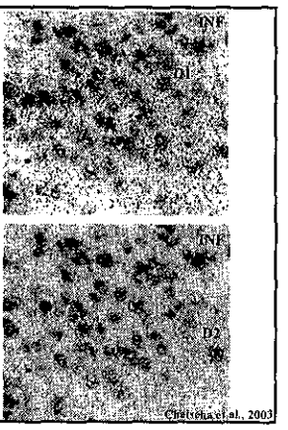

Expression of D2 DA Receptor mRNA within the
Pituitary across the Turkey Reproductive Cycle



D_1D DA receptor mRNA expression (clusters of black dots), in VIP mRNA expressing neurons (cells containing dark purple precipitate) in the VMN region of the turkey hypothalamus.

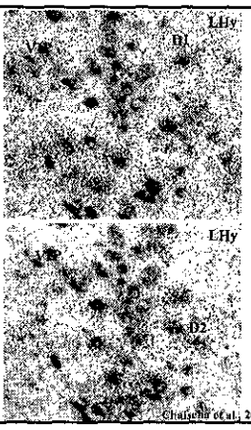
Chalcsha et al., 2003

VIP / DA Receptors Coexpression



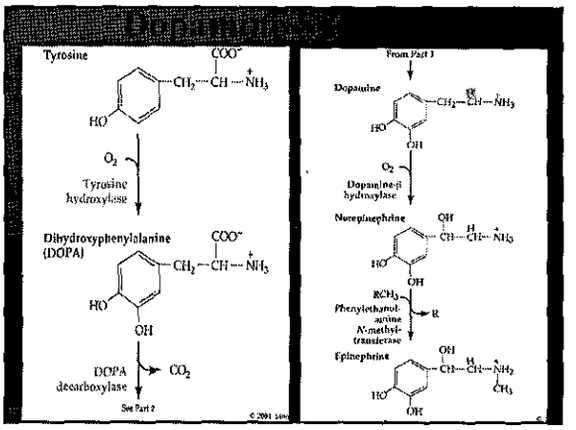
Chalcsha et al., 2003

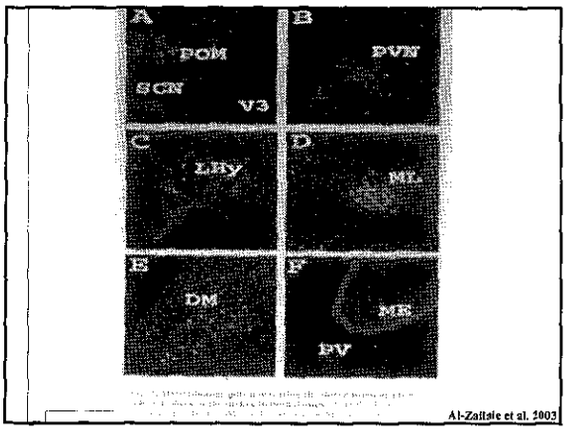
VIP / DA Receptors Coexpression



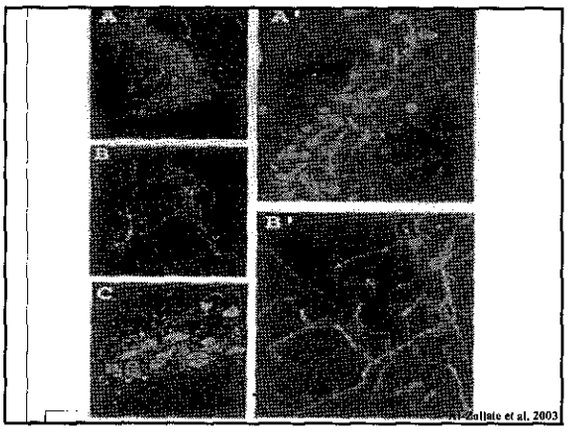
Chalcsha et al., 2003

Dopamine

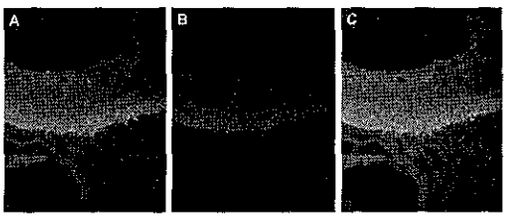




Al-Zoffale et al. 2003

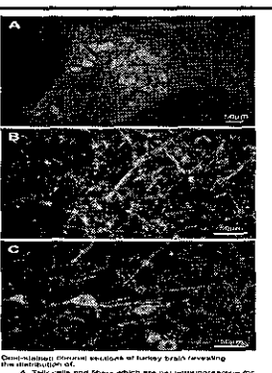


Al-Zoffale et al. 2003

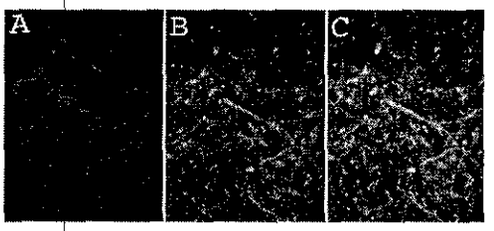


The distribution of tyrosine hydroxylase (TH; A), vasoactive intestinal peptide (VIP; B) and both TH and VIP (C) immunoreactive fibers in the median eminence of the female turkey.

Al-Zailaie et al. 2003

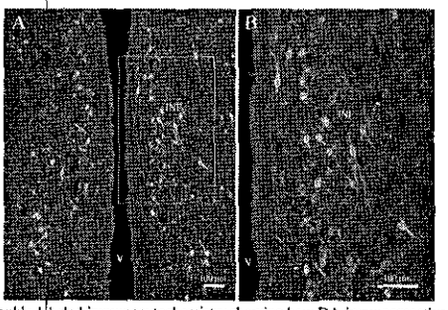


Al-Zailaie et al. 2003



Double-staining of coronal sections in the lateral septum within the turkey hypothalamus revealing the distribution of:
A) Fibers immunoreactive to TH (red).
B) Fibers immunoreactive to DBH (green).
C) Fibers immunoreactive to both TH and DBH (yellow). Orig. Magni. X 20

Al-Zailaie et al. 2003

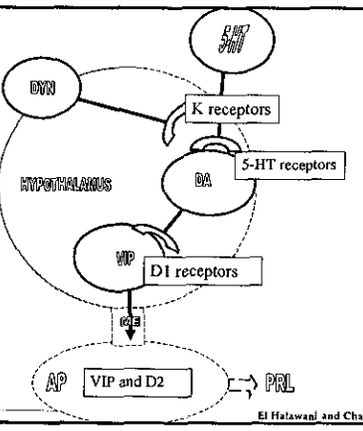


Double-labeled immunocytochemistry showing how DA-immunoreactive terminals (red) are intermingled with VIP-immunoreactive neurons(green) in the INF of the hypothalamus.

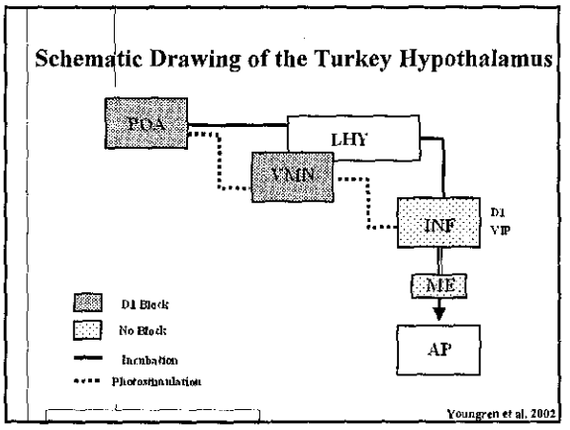
Al-Zailaie et al. 2003

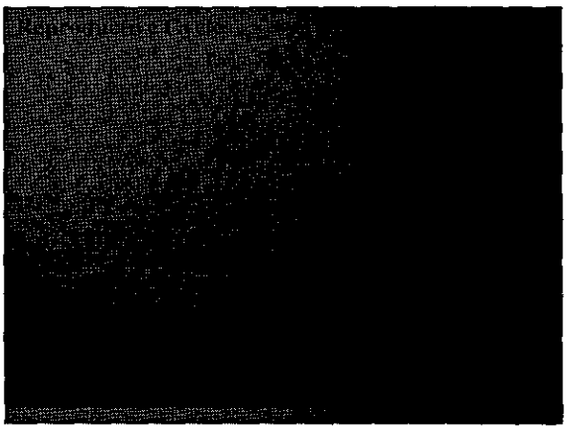
Summary

- **The regulation of avian prolactin (PRL) secretion and PRL gene expression is influenced by hypothalamic vasoactive intestinal peptide (VIP), the PRL-releasing factor in avian species.**
- **Dynorphin, serotonin, dopamine (DA), and VIP stimulate PRL secretion via a serial pathway, with VIP as the final mediator.**

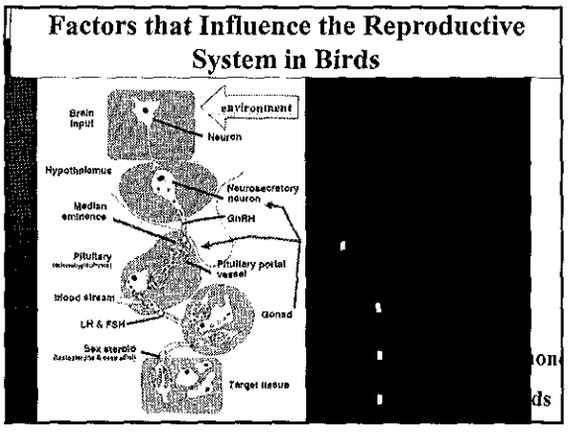


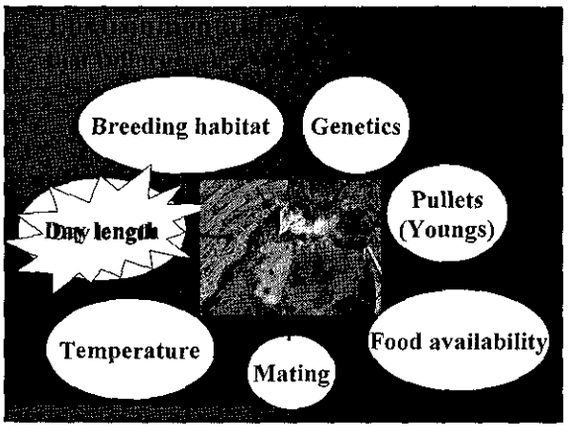
El Halawani and Chaiseha, 2000

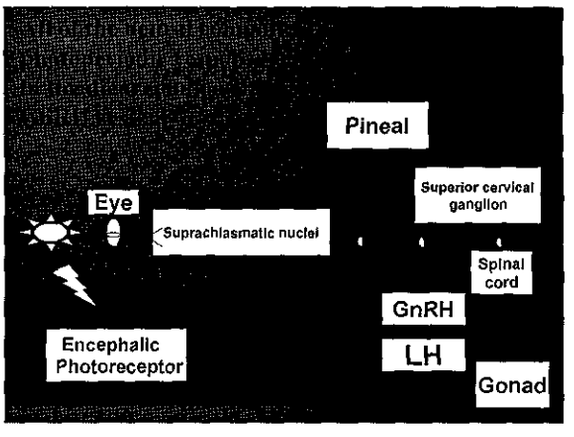

Schematic Drawing of the Turkey Hypothalamus
POA
LHY
VMN
INF
D1
VIP
ME
AP
D1 Block
No Block
Incubation
Photostimulation
Youngren et al. 2002




Thank you


Factors that Influence the Reproductive System in Birds
Brain Input
environment
Neuron
Hypothalamus
Neurosecretory neuron
GnRH
Median eminence
Pituitary
Pituitary portal vessel
blood stream
Gonad
LH & FSH
Sex steroids
Target tissue


Breeding habitat
Genetics
Day length
Pullets (Youngs)
Temperature
Mating
Food availability


Pineal
Eye
Suprachiasmatic nuclei
Superior cervical ganglion
Spinal cord
GnRH
LH
Encephalic Photoreceptor
Gonad