MICROBE @ MANKIND

SOCIAL TRANSMISSION OF MICROBES

INFECTIOUS KISS

INFECTION @ MORALE

MORALE

- **Strong moral control on intimacy**
- **Strong moral aversion against sexual trauma**

INFECTION

- **Is there a biological cause of this morale: Infection?**
- **Does loosening of sexual contacts lead to biological “punishment” with herpes?**
- **Is schizophrenia therefore on the rise since 1600?**

TRANSMISSION OF INFECTION

- **Herpes**
  - Jumps from neuron to neuron into brain
  - Sometimes jumps back
  - Creates epigenome in human cell nucleus
- **HIV**
  - Resides in immune cell that trafficks to the brain
  - Incorporated retroviruses (30%) in human DNA
- **Treponema/ Borrelia**
  - Corckscrew into brain
  - Erythrocyte “latency”, and invasion in tissues

TRANSMISSION IN GERMLINE

- **Sexual replication**
  - After Meiosis (2x) Fusion of male and female DNA

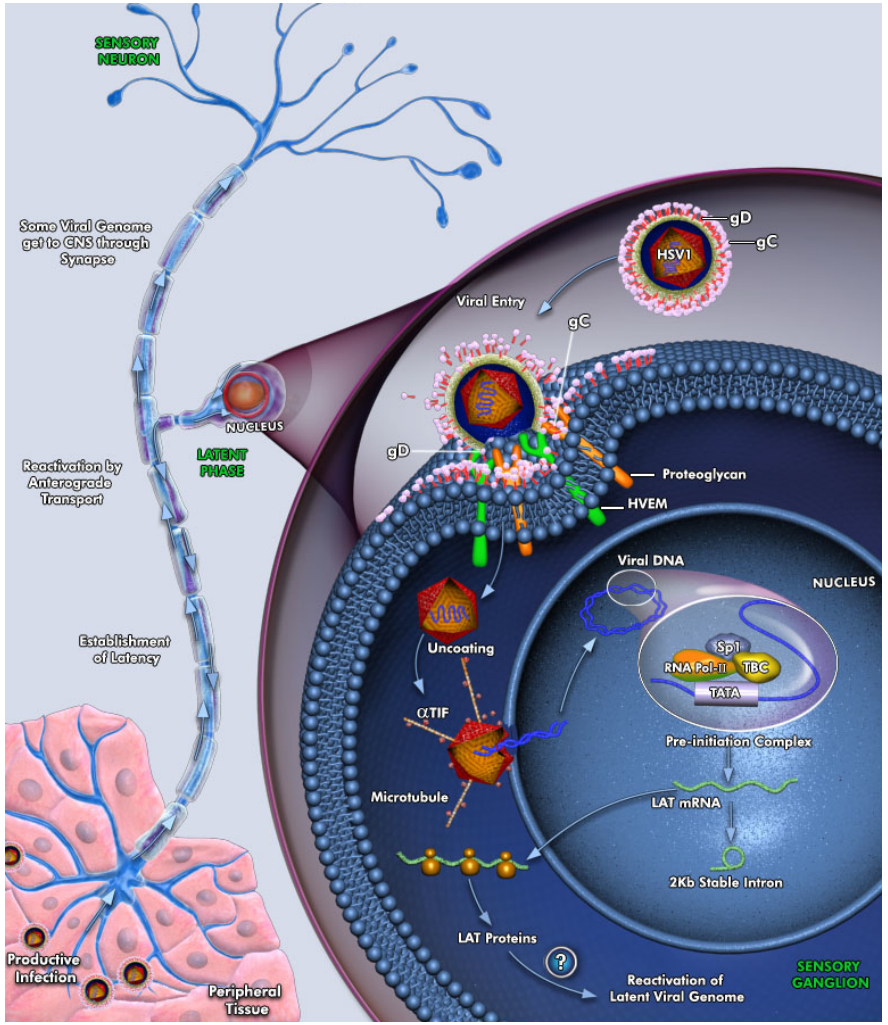
- **Vertical transfer of infectious elements**
  - Proteins: Prions
  - DNA (virus)
  - RNA (retrovirus)
  - Symbiotic partners: Mitochondria
  - Parasites (Toxoplasma
  - Bacteria (listeriosis, spirochetes)

TRANSMISSION OF SCHIZOPHRENIA

1. **STD mother en sexual activity during pregnancy (OR=2.6)** *[Buka 2008, Biol Psychiatry]*
2. **Sexual trauma (OR=2.9)** *[Bubington 2004, Br J Psychiatry]*
3. **Brain infections youth (OR=4.8)** *[Rantakallio 1997 Int J Epidemiol]*
4. **Loosening of social structures**
    1. GB: Wel bij Carribean **(IRR=7.7)**, niet bij Indiers **(IRR=1.0)** *[Morgan 2008, Psychol Medicine] [Kirkbride 2008 Br J Psychiatry]*
    2. NL: Wel bij Marokkanen **(IRR=3.69)**, niet zo bij Turken **(IRR=1.75)** *[Veling 2008 Am J Psychiatry]*
5. **Cannabis?**
6. **Emigration?**

HSV = CHAMPION

- Presence in about 80% of the human population
- Establishes latency in the trigeminal ganglion
  - Reactivation by UV-light, stress, hormonal changes
- Herpes encephalitis
  - Symptoms: fever, headache, **psychosis**
  - Temporal lobe specific



HSV = HIDDEN

HERPES SIMPLEX VIRUS TYPE 1 DNA IS PRESENT IN SPECIFIC REGIONS OF BRAIN FROM AGED PEOPLE WITH AND WITHOUT SENILE DEMENTIA OF THE ALZHEIMER TYPE

Jamieson et al., J Pathol, 1992

Age distribution of latent herpes simplex virus 1 and varicella-zoster virus genome in human nervous tissue

Liedtke et al., J Neurol Sci, 1993

Herpes Simplex Virus Genomes in Human Nervous System Tissue Analyzed by Polymerase Chain Reaction

Baringer et al., Ann Neurol, 1994

Detection of Herpesviridae in postmortem multiple sclerosis brain tissue and controls by polymerase chain reaction

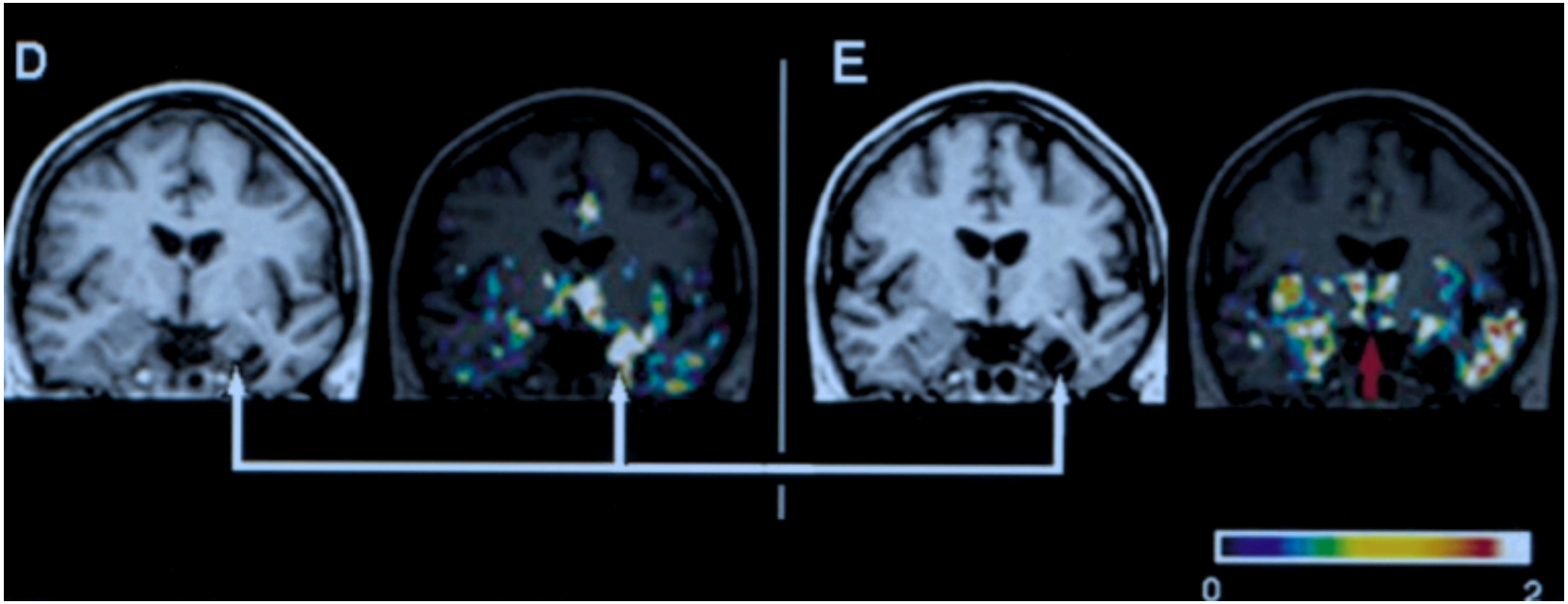
Sanders et al., J Neurovirol, 1996

Detection of herpes simplex virus (types 1 and 2) and human herpesvirus 6 DNA in human brain tissue by polymerase chain reaction.

Gordon et al., Clin Diagn Virol, 1996

PSYCHOSIS = HERPES COMING OUT?

- Manic behavior
- Paranoid Delusions
- Persecutory hallucinations
- Decline in cognition (dementia)
- Decrease of hippocampal volume



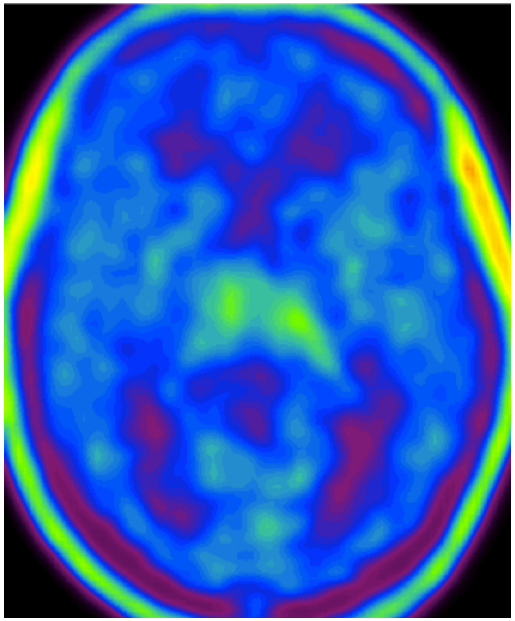
[Cagnin 2001, Brain]

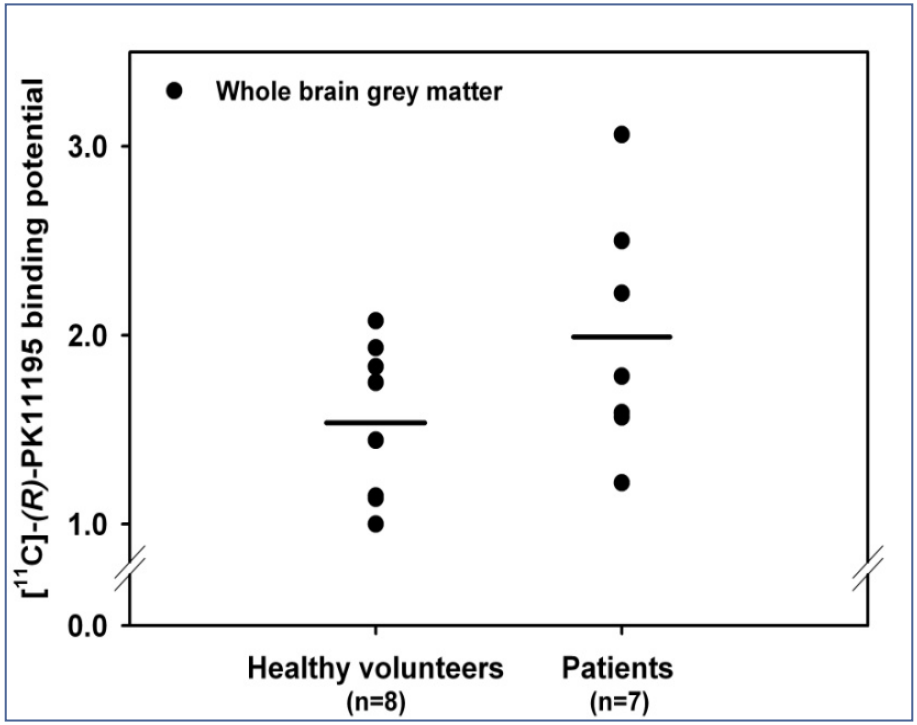
PSYCHOSIS = HERPES ACTIVATION?

- HIPPOCAMPAL INFLAMMATION?
- HIPPOCAMPAL INFECTION?



PSYCHOSIS = INFLAMMATION?





[11C]PK11195 *[Doorduin 2009 J Nucl Med]*

PSYCHOSIS = INFLAMMATION

	Gezonde vrijwilligers	Patienten	p-waarde
Frontale lobe	1.76 ± 0.75	2.08 ± 0.76	0.459
Occipitale lobe	1.83 ± 1.20	1.93 ± 0.74	0.892
Temporael lobe	1.28 ± 0.34	1.64 ± 0.56	0.079
Parietale lobe	1.77 ± 0.93	2.28 ± 1.22	0.720
Basal Ganglia	1.39 ± 0.28	1.82 ± 0.59	0.017
Thalamus	1.61 ± 1.44	1.49 ± 0.35	0.742
Hippocampus	1.37 ± 0.30	2.07 ± 0.42	0.004*
Mid-brain	1.68 ± 0.60	2.63 ± 0.40	0.014
Cerebellum	1.11 ± 0.22	1.45 ± 0.48	0.040
Pons	1.54 ± 0.32	2.85 ± 1.42	0.027

[11C]PK11195 *[Doorduin 2009 J Nucl Med]*

PSYCHOSIS = INFECTION

	Mild Aangedaan(n=4)	Ernstig Aangedaan(n=4)
Frontale lob	6.9E-04 ± 2.3E-04	6.6E-04 ± 3.4E-04
Parietale lob	4.9E-04 ± 1.2E-04	3.6E-04 ± 1.7E-04
Occiptale lob	3.7E-04 ± 1.7E-04	5.4E-04 ± 6.0E-05
Temporale lob	3.8E-04 ± 1.0E-04	5.9E-04 ± 1.1E-04*
Thalamus	3.7E-04 ± 1.8E-04	3.8E-04 ± 1.4E-04
Basale ganglia	4.2E-04 ± 1.9E-04	4.7E-04 ± 1.1E-04
Cerebellum	5.2E-04 ± 2.9E-04	3.0E-04 ± 1.7E-04

[18F]FHBG *[Doorduin 2010, Thesis RuG*

INFECTION = DEMENTIA

Patient 2,4,6 severely affected

Patient 1,3,5,7 and 8 mildly affected

	PANSS			15 WT				CPT	
Pat#	Positive	Negative	Global	Imm. recall	Del. recall	Recognition	Total score	RT (ms)	d'
1	14	25	33	34	2	30	66	636	2.1
2	23	28	42	23	2	22	47	648	1.7
3	16	24	51	27	6	29	62	744	2.5
4	20	30	53	12	2	28	42	377	0.6
5	16	11	41	43	8	30	81	692	2.1
6	24	23	52	15	2	22	39	833	0.6
7	12	19	32	27	7	29	63	639	2.7
8	19	15	39	33	1	24	58	622	4.2

RESCUE COGNITION WITH ANTIVIRAL

- Valaciclovir treatment trial 4 times 2 gram daily
- PK11195 before and after treatment
- Cognitive tests before and after treatment
- Target n=24
- Current n=12
- Clinicaltrials.gov Schizophrenia and Valaciclovir and Groningen

CONCLUSION

- **Social MORALE might reflect the rule for protection of our germline.**
- **HERPES might be a one of the NEMESES of our human species.**
- **We must CRACK the barriers of the brain BY MOLECULAR IMAGING of infection**

NEMESES OF HUMAN SPECIES!

- **Herpes**
- **Spirochetes: Borrelia, Treponema**
- **Malaria**
- **HIV**
- **Tuberculosis**
- **Flu**

Entrance in brain may be very easy!!!

[Kristensson 2011, Nat Rev Neuroscience]

INFECTION = ORIGIN OF SPECIES