For evolutionary psychiatrists, psychologists and others interested in sociophysiological Integration

ASCAP

Volume 11, No. 02 (Cumulative #123) February 1998

"Emotion is not simply a subjective internal experience; it is simultaneously a social act."

Peter Brown, M.D.[1]

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ASCAP Society Mission Statement:

The ASCAP Society represents a group of people who view forms of psychopathology in the context of evolutionary biology and who wish to mobilize the resources of various disciplines and individuals potentially involved so as to enhance the further investigation and study of the conceptual and research questions involved.

This scientific society is concerned with the basic plans of behavior that have evolved over millions of years and that have resulted in psychopathologi-cally related states. We are interested in the integration of various methods of study ranging from cellular processes to individuals in groups.

The ASCAP Newsletter Aims:

- A free exchange of letters, notes, articles, essays or ideas in brief format.
- Elaboration of others' ideas.
- Keeping up with productions, events, and other news.
- Proposals for new initiatives, joint research endeavors, etc.

The ASCAP Newsletter is a function

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Previous volumes are available. For details, contact Frank Carrel, the Managing Editor of *The ASCAP Newsletter,* at the address above.

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The ASCAP Newsletter* is the official newsletter of the *Psychotherapy Section* of the *World Psychiatric Association.

ADDRESSED TO & FROM

ASCAP Annual Meeting Notes

Suzie Gardner has been working hard on potential meeting arrangements. We are almost completely sure that the meeting will be held at Hall-mark/Ramada Inn, 110 F Street, Davis, California (corner of F and 1 st Streets). Phone is (530) 753-8406. Mention you are with ASCAP/HBES when making reservations as a lower rate will accordingly be available. The location is convenient to campus. HBES cites the distance as 15 minutes away by walking. The hotel has a spacious lobby and an outdoor pool.

The annual ASCAP meeting will be on Wednesday, July 8, 1998, from 8:00 a.m. to 4:00 p.m. with a business meeting to follow from 4:00 p.m. to 5:00 p.m. For members pre-registration costs will be $15.00 per person (all pre-registrations will include lunch). Deadlines for pre-registration is June 10, 1998. See form attached to the end of this issue.

Daniel Wilson and I are working on the program. More news on that next issue. The theme is 'Toward Empirical Research in the Clinical Application of the Human Evolutionary Sciences." Let us know if you have interest in presenting.

Registration on the morning of the meeting will be $25.00 for members and $55.00 for non-members; for non-members, this will include a membership and an *ASCAP Newslettersubscrip*-tion for 1998 issues. This also will include lunch, but to plan for this accurately, we urge everyone to pre-register.

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Editor's Note: On the last page of this newsletter, there is a meeting pre-registration form.

Human Behavior & Evolution Society - 10th Annual Meeting

University of California at Davis - July 8-12,1998

Web Site:

http://www.des.ucdavis.edu/events/event.htm

Submission and Registration Due Dates:

Paper, Poster, and Symposium* Abstracts: March 16,1998

New Investigators Competition: June 1,1998

Post-Doctoral Competition: June 1,1998

Registration: April 21,1998

*Symposia consist of 4 themati-cally linked paper abstracts demonstrating a synthetic and interdisciplinary focus.

Conference Begins:
Wed July 8,1998 -- 5:00 p.m.
(Reception in Dining Commons)

Davis is in California's sunny Central Valley, 20 minutes from Sacramento Metropolitan -International Airport. Davis is 90 miles east of San Francisco. Ir July temperatures can range from pleasantly warm (high 80°s F) to hot, (low 100°s) with cool nights (-60°). For visitors arriving before noon on Wednesday, we will plan trips to local attractions. Housing will be in UCD dorms, or in local hotels (HBES will provide a list of hotels).

XIV International Conference on Human Ethology at Simon Fraser University

Integrating proximate and ultimate explanations in the study of mind & behaviour

Burnaby, Canada 1998
Confirmed Dates:
Wednesday, August 19 to Sunday, August 23.1998

WebSite:
http://www.sfu.ca/cstudies/conf/humanwww

The 14th Bi-Annual Conference cf the International Society for Human Ethology will be held at Simon Fraser University in Burnaby, British Columbia, Canada August 19 - 23,1998. The conference focus is" Inte-

grating proximate and ultimate explanations in the study of mind and behaviour.

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Thoughts while Traveling

Traveling 2 hours by car four times a week, I listen to audio tapes including Mandelbaum's *Odyssey* and Fagles' *Aeneid*. Fagles' *Iliad* is yet to come and I know it will be a brutally heroic rendering. I had started it... "Agamemnon, most grasping of men ..." Strong language. I didn't feel up to it just then. But this oral literature makes much better listening than reading.

At the moment I am listening to a series of tapes on the Ring cycle of Wagner. You might call it faux-heroic. All muddled action. I don't understand why I am so drawn to it. (I hated Seigfried but loved the birds. I have always rooted for the Weltanschauung) Hearing commentary I learn how little I had understood in the past. I didn't understand that of the two giants, one really loved Freia. I had noticed that the Killer giant, the one who turned into a dragon, merely sitting on the all powerful ring, preferred the gold.) Still don't understand some things ... will listen again. It is really confusing, like real life. How do you use that ring of absolute power anyhow?

A. A. Berle wrote a book titled *Power.* Berle, a Roosevelt Brain Truster, wrote that people with power always considered themselves hemmed in by other, countervailing powers. Courts, labor unions, politicians, church, newspapers. Bottom line: No one feels particularly powerful. The whole thing is just an elaboration of usual cravings for stuff, status, sex, and security. (Imagine J. F. Kennedy's musing over the futility of constant copulation ... or worse, imagine he liked it!) It is a fantasy of having more! More!! And as we all know after a holiday season of too much eating and drinking, more is usually yuckie.

One of the enjoyable parts of mental status exams in my hands is asking for three wishes. It is usual to ask this of kids; I do it with adults too. This bit of fantasy land is always informative.

I have a videodisk collection. Movies, even great movies, are good only for one or two playings, but the opera I go back to again and again.

John K. Pearce
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Arguments

Not fond of, or good at arguments, I have dreaded being accused of wickedness as an evolutionary psychology guy. When attacked, one is hard pressed not to descend to black and white thinking (a fine predator avoidance response), so I have figured out in advance how to defend myself.

As Steve Pinker (and doubtless legion others) points out, mistaken ideas about human nature has led to millions of deaths at the hands of both the right and the left. The right kills for racial purity, the left kills to be rid of ideological impurity. The real enemy would seem to be mistaken ideas about human nature. Now a good question would be, is there a true understanding of human nature that can be shown to have tragic political consequences? It is true that the facts of EP suggest that it would be a stretch to get human beings to be good communists -- they would require constant re-indoctrination. Similarly Christians must constantly be reminded that all men and women are their brothers and sisters.

Arguments about adaptation hinge on how the word is used. It can be used for species universals like eyes or hearts, and it can be used for something as fragile as the mutation for sickle cell anemia-just a single alteration of a DNA site. (As you know, it causes the un-oxygenated form of the hemoglobin molecule to change shape, changing the shape of the red blood cell, rendering it inhospitable for the malarial trypano-some.)

Lots of things that we psychiatrists are interested in -- conduct disorders, depression, bipolar disorder, ADHD, etc. -- are strongly heritable and can be understood at stable polymorphisms. It is an idea that is difficult to test, so must be approached by heaping up evidence for and against the conjecture - consilience.

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Intro to The Unbeliever

I have been chided by my old comrade, Howard Bloom, for not explicitly mentioning him in returning to the topic of self-destruction. I am not entirely certain it was necessary, as we both agree that the published record clearly shows we independently came up with the notion that the propensities of humans and other species to self-destruct has a profound significance as yet unacknowledged by science. Where, of course, we differ is in my belief that the whole phenomenon can be explained purely in terms of selfish genes, whereas Howard believes far more all-embracing processes are at work.

Nonetheless I want to make amends, and this I now seek to do by taking up the cudgels on both our behalves and unleashing this poetic satire aimed at those benighted souls who can only see self-destructive behaviours in terms of some organic ill. To a less discerning audience it will go under the title of *"A Dairy Tale",* but for present purposes I am offering a limited edition under the title below:

Mike Waller
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The Unbeliever

There's some within my family believe a tale so dark It is perhaps the grimmest since the grounding of the Ark. They'll not hear of Mayerling, or that little spat at Troy, Instead they speak of Auntie Maude, and poor old Uncle Roy.

Now Aunt Maude was wed a virgin, as pure as driven snow, And though within a twelve-month, Roy, a soldiering had to go, Whilst he was out-foxing Rommel in places like Tobruk, She stood firm in London, telling Yanks to sling their hook.

It was under the wings of Victory that things began to sour. In a tired and grey old England, short of food and power. To eke out a harsh existence they decided to let a room, And accepted as a lodger, a dairyman called Croome.

To Royston it seemed like heaven, a veritable dream.
A steady weekly rental, plus butter, milk and cream.
But though Croome seemed a kindly man, he was in fact a fraud.
He had an appetite for flesh, the flesh of Auntie Maude.

Poor Roy, obsessed by all that food, saw not his wife suborned; And as he hit the eighteen stone, he earned the cuckold's horns. My family say that when, at last, he learned his wife, a tart, He quickly lost the will to live, and died of a broken heart.

But I'm a man of science; I won't buy old stuff like that.
I know what caused old Royston's death was all that butterfat.

Intro to Whippets

When the Scharnhorst, Gneisneau, and Prinz Eugen made their successful dash up the English Channel in 1941, ancient torpedo-carrying "Swordfish" biplanes were sent out against them, without fighter escort. They were slaughtered by German fighters; but to do it, because the Swordfish were so slow, the German planes had to put their undercarriages down to slow up sufficiently to bring their guns to bear. And that is the essence of one problem people have with me, operating at too rarefied a level! My relationship with my whippet is "across species" - pathetic ain't it!

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An Across-Species Comparison

[An exchange between father and son].

Canto 1 - Mother Love

I've just acquired a whippet, a thing of speed and grace, Yet small enough when cradled to caress against my face. At rest, she seems imperious, an animated sphinx. Unleashed, she's like an arrow, or a kind of canine lynx

Upon seeing my devotion, my wife demands to know Would I be much affected now were she to up and go. But I soon make it clear to her it simply isn't done To walk out on your husband when his whippet needs a mum.

Canto 2 - The Son Also Writes

So she's packed her bags and gone, and the whippet's all that's left, And hungry, lonely and unkempt, you find yourself bereft. 'Coz, though a whippet's just the thing for chasing and the rest, It finds it hard to turn its paw to cleaning up the mess.

And when no-one's left to talk to, and all the cleaning stops, Midst the mounting dust and squalor, the poor old penny drops. After all those years of housework and serving up your food, Why did it not occur to you to show some gratitude?

Resource Holding Potential

Bereft, I stumbled from the court, a sad and broken man.
She'd had the house, the car, the cash and half my pension plan.
I slunk into my local pub to drown the fairer sex,
But there I found, awaiting me, my second cousin's ex-.
She said that when she heard my news she'd cried 'n cried 'n cried
If she'd found a man like me, she'd have kept him 'til she died.
And though she thought my wife a friend, she really had to say
Her kind of crude materialism had surely had its day.
She'd learned in life that girls should give and never count the cost;
To measure love in days well spent and not in jobs they'd lost.

Her kindly words, the whisky mac, revitalised my heart; I wondered why, in times gone by, I took my cousin's part. I touched her knee, I raised my glass and said with little fuss: "Here's to the months and years ahead, and you and I as us".

With shining eyes and husky voice she spoke as glasses chinked: "Tell me love, the share of pension you've got left, is index-linked?"

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Please E-mail any contributions to ascap@utmb.edu, or mail hard copy and 3.5" HD diskette to: Russell Gardner, Jr., c/o Frank Carrel, Department of Psychiatry & Behavioral Sciences, University of Texas Medical Branch, Galveston, Texas 77555-0428, USA. WordPerfect, Microsoft Word or ASCII format preferred. Diskettes will be returned to you. Thank you.

ARTICLE:

by Tyge Schelde

A Coherent Hypothesis of Affective Disorder, Schizophrenia, and Schizo-Affective Disorder (an ethological - physiological perspective)

Abstract: A coherent glutamatergic-dopaminergic hypothesis is suggested as a genetic cause of both affective disorders and schizophrenia, including schizo-affective disorder. The genetic sites might be situated on the long arm of chromosome 11 (11q22-**q23).**

Results from behavioral studies of mentally ill subjects are of interest in creating hypotheses of the dynamics and the etiology of psychiatric disorders.[1]-[2] This paper illustrates what might be a relation of behavior to physiology in the mental area. Two tentative hypotheses are taken into consideration. Finally, they are regarded as one coherent hypothesis.

1. A SEROTONIN-DOPAMINE HYPOTHESIS:

In the course of time MAO-inhibitors and tricyclic antidepressants have proved to be reasonable agents for relieving depressive states; however, they are attended by a great number of side effects. The second generation of antidepressants - the SSRIs -seem to exert their primary mode of function within moderate and mild types of depression, and maybe with fewer side effects than those of the preceding agents.[3]

"The fact that there is so much focus on serotonin does not necessarily mean that the increased transmitter concentration in the serotonergic synap-tic clefts are primarily responsible for the anti-depressant effect. It might rather be a 'site' where it is possible to interfere with an unknown depression cause"(personal comment, Professor Vestergaard, Denmark). One can easily imagine that a serotonin activity which is increased by, for instance, fluoxetine, is efficient via other transmitter systems, e.g., acetylcholine[4] or dopamine.[5] It is also possible that an increased serotonin activity simply contributes to an increased blood flow in cortex, especially in the pre-frontal lobe. It is well-known that the antidepressant effect of both 1 st and 2nd generation agents is not obvious until after 3 weeks of medication, although the rise of the transmitter concentration manifests itself only a few hours after the administration of a dose. Researchers have been puzzled about this problem and have suggested some sort of time-consuming adaptation of various receptor systems.[6] To my opinion it might also mean that it takes three weeks -- at an increased blood flow -- for depleted cortical regions to regain their normal transmitter levels. If the circulation is not improved depression can last extremely long.

The question of a psycho-motor inhibition is an extremely difficult one to answer. The problem is whether certain parts of the psyche and certain parts of the motor apparatus are actively inhibited by hyperaroused systems in the brain, or whether certain psycho-motor parts are non-functional because of a transmitter depletion of various regions in the brain (cf. depletion of amines by reserpine causing depression). The essential fact might be a depletion of some regions. Consequently, such a partial depletion might cause a relative hyperarousal and an increased glucose metabolism in other parts of the brain, e.g., the cortico-limbic systems.[7]

It has been suggested that changes of the resting potential might cause nervous lability. Accordingly, a slight depolarization might lead to mania, and a greater depolarization to a considerable decrease of transmitter quanta, i.e., depression.[8]

A reasonable guess of serotonin's antidepressant effect might be its influence on the dopamine free-setting in striatum.[5] A reduced dopamine activity in major depression has been documented.[9]-[10]-[11] The seventies showed that the dopamine agonist

nomifensine was able to resolve depression, but the agent had many side-effects.

If you consider mania and depression behaviorally they clearly seem to be quite opposite in their manifestations. Therefore, one might argue that since mania can be reduced considerably by the dopaminergic antagonist haloperidol then it should be possible to resolve depression by dopaminergic agonists. Maybe the antidepressant effect of SSRIs is exerted via the dopamine system by an increased free-setting of dopamine in the striatum.[5]

According to Carlsson, dopamine is essential for the control of physical mobility.[12] It is also known that dopamine is a substance that is related to pleasure and reward.[13] The nervous circuits responsible for this probably proliferate from substantia nigra to nucleus accumbens and septum. On this background it seems possible to relate a reduction of the dopamine activity to a psycho-social-motor inhibition. Probably the motor inhibition is pronounced in severe depressions. (In this connexion it is interesting to notice that improvement from severe depression seems to start with a disinhibition of the motor tiredness: observations from Frederiksberg Hospital).

On the etiological-genetic level Egeland et al.'s investigation, refers to 19 subjects with major affective disorders from the Old Amish Order.[14] According to Egeland et al., psychoactive agents exert their effect on catecholamine transmitter systems like dopamine, norepinephrine, and epinephrine. From their lodscore on chromosome 11 they estimate that there might exist a mutation on the short arm of this chromosome encoding for the enzyme tyrosine hydroxylase which is the limiting enzyme of dopa, dopamine, norepinephrine, and epinephrine. This hypothesis has been controversial because of uncertain diagnoses in some of the patients.

However, it might be supported by Morrow's investigation, which maintains that tyrosine enhances behavioral and mesocortico-limbic dopaminergic responses to aversive conditioning.[15] Thus, if there is a deficit of tyrosine hydroxylase and dopamine in depression-vulnerable persons it is understandable that they have difficulties in coping with aversive situations.

Also in this connexion it is important to mention Drevets and Price's investigation, presented at the 6th World Congress of Biological Psychiatry in Nice, 1997.[16] They found that there was a decrease of blood flow and metabolism in the subgenual area, i.e., the anterior cingulate cortex ventral to the genu of corpus callosum. *"The finding appears at least partly accounted for by a left-lateralized, 40% reduction in local grey matter volume."* Normals have a well developed dopamine network in the subgenual region, so the decreased blood flow in this area in depressives may be interpreted as an insufficient dopaminergic nervous supply - or as a reduced number of dopamine receptors.

Clinical evidence includes alterations/aggravations in depressive symptoms with aging (concomitant with possible changes of dopamine metabolism)[11] This might indicate a decay of dopamine circuits by age. We know that Parkinson's disease is rather similar to major depression in its phenomenology. Parkinson-patients are characterized by depressions and body stiffness, and in addition shaking movements. The two first behavioral patterns they share with major depression patients. There is a decay of dopamine cells in Parkinson's disease. As dopamine is known to have an inhibitory effect on acetylcholine, there will exist a dopamine --acetylcholine dysbalance, which is probably responsible for Parkinson's disease.[3] Such a dysbalance might also -- perhaps in another version -- be responsible for manic-depressive illness. Parkinson's disease is treated by dopa and anticho-linergic agents.

Moreover, it should be noted that treatment with SSRIs can give rise to stereotyped movements like rocking with feet and underlegs, movements that are similar to the stereotypies of schizophrenics. As the stereotyped movements with schizophrenics are

thought to be related to an increased dopamine activity it is natural to relate the SSRI-stereotypies to an increased dopamine free-setting from striatum in depressives.

Finally, the behavioral investigations at Frederiksberg Hospital have shown the surprising finding that the physical mobility in schizophrenics is not only substantially higher than that of depressives, but also that it is significantly higher than that of normal controls. The finding indicates that schizophrenics and depressives are direct contrasts regarding physical mobility - a fact that may be due to a high dopaminergic activity in schizophrenics versus a low one in depressives.

Carlsson, mentions a low glutamatergic activity as the background of the schizophrenic hyperdopaminergic activity.[17] He also underlines that a high glutamatergic activity via acetylcholine activity is able to suppress monoamine transmitter free-settings (perhaps especially dopamine) which might probably correspond to a psycho-motor inhibition. This behavioral phenomenon is the most prominent symptom of major depression.

2. AN ACETYLCHOLINE-GLUTAMATE HYPOTHESIS:

The last mentioned information naturally leads us to a depression hypothesis which can be considered complementary to the serotonin-dopamine hypothesis. This is to be understood in the way that the serotonin-dopamine hypothesis mainly involves a low dopaminergic activity which leads to a DA/Ach dysbalance with dopamine at a low level.

On the contrary, the acetylcholine-glutamate hypothesis supposes a high acetylcholine activity in depression which also gives rise to a DA/Ach dysbalance.[18,19] In this respect the two hypotheses are related. This specific unbalance is considered important for psychiatric disorders.[3-Chapter 12] So --regarding major depression - a possible dysbalance may be caused either by a dysfunctioning dopamine system or by a dysfunctioning acetylcholine system.

Regarding an acetylcholine sensitivity, there is strong evidence that affective subjects respond much more significantly to cholinergic challenges, (e.g., physostigmine) than normal controls.[18,19] An increased cholinergic arousal level is associated with depressive feelings and thoughts and a considerable sense of tiredness (psycho-motor inhibition). According to this hypothesis the cholinergic system is probably very sensitive, i.e., it is depolarized to a higher degree than normal. This physiological state makes kindling very easy.[20] Or -- as expressed by Gardner - *"Manic and depressive episodes are triggered unusually easily and maintained unusually rigorously in spite of social reality."*[21] An upkindled high arousal leve might even approach tetanus-like states of the brain's acetylcholine system. Once the system has reached such a state the nervous processes will probably be self-increasing, and the system is very difficult to normalize; just think of depressives' eternal ruminations. According to the hyperarousal hypothesis, the increased acetylcholine level is supposed to exert an inhibitory effect on the monoaminergic receptors, thus causing a psycho-motor inhibition.[12] The reason of the increased degree of depolarization may be related to the acetylcholine system itself.

However, in the case of major depression, it is also possible that the increased cholinergic sensitivity is caused by an increased glutamatergic/ N-methyl-D-aspartate activity.[22] An increased activity of glutamate might exert an effect via acetylcholine. The increased excitatory effect of glutamate would then depolarize acetylcholine, and an increased cholinergic activity might be responsible for an inhibition of amine systems probably mainly the catecholamines dopamine and norepi-nephrine, because dopamine is related to the basal ganglia that are inhibited by a glutamatergic-cholinergictonus.[12]

Viewed from the above visual angle the two hypotheses are similar according to their DA/Ach dysbalance. But also in a specific way they seem to be related: The serotonin-dopamine and the glutamate-acetylcholine hypotheses might be

connected by a superior glutamatergic system. In *depression, a* high glutamatergic activity is assumed to enhance the cholinergic tonus which in turn is supposed to inhibit the monoamine activity.[12] In *schizophrenia, a* documented low level of glutamate,[23] probably contributes to an extraordinarily high free-setting of dopamine (corresponding to an increased motor activity) and an inhibition of acetylcholine (probably attended by specific cognitive and emotional dysfunctions).[24]

In fact the question of the physiological cause of depression is whether a cortical cholinergic superarousal state causes an inhibitory effect on subcortical amine systems or whether subcortical amine systems are dysfunctioning, for instance, showing a depletion state. It seems notable that depression can be relieved by MAO-inhibitors that cause a free-setting of all three amine systems, but also that depression can be treated by an increased free-setting of one of the amines separately; cf. SSRIs, e.g., fluoxetine). This indicates that major depression is probably not consistently related to one specific perturbing amine system.[25] In other words: " *The failure to evince consistent changes in serotonergic, dopaminergic, noradrenergic, GABAergic, andpeptidergic neurotransmitter systems across chronic antidepressant treatments cannot provide a coherent biochemical basis of depressive symptomatology"*[25] Finally, concerning major depression-it seems very important to quote Carlsson:[17] *"Our hypothesis predicts that the strong psycho-motor inhibition induced by removal of dopaminergic function through depletion of dopamine or inhibition of dopamine receptors can be relieved by reducing the glutamatergic corticostriatal tone."* Thus, it seems that a superior, mainly cortical depression cause might be responsible for major depression. Such a depression factor might be related to the glutamatergic/ N-methyl-D-aspartate system.

How does *mania* fit into the serotonin-dopamine or the acetylcholine-glutamate hypotheses? If we presume that mania is correlated to a high dopamine level (cf. the suppressing effect of the anti-manic agent haloperidol on dopamine) and that major depression is equivalent to a low dopaminergic activity we must conclude that the dopamine activity somehow is able to be up- and down-regulated in bipolar disorder. It is known that the serotonin level is increased during light periods, i.e., the summer (cf. Langer and Galzin's study of rabbit platelet membranes.)[26] The raised serotonin activity might contribute to a higher dopamine level in striatum[5] which in turn might correspond to a generally increased psycho-motor activity, but not necessarily lead to morbid mania (cf. increased summer activity and decreased winter activity: Seasonal Affective Disorder depression (SAD) can to a certain degree be ameliorated by light therapy).

But we know that mania does not only occur during summer, but also at other times of the year. Therefore, to my opinion, the acetylcholine -glutamate hypothesis offers a better explanatory model of mania. Affective patients have told me that according to the situation they could as easily gear up as down. Although manic-depressive illness is considered endogenously regulated, subjects are no doubt very sensitive to environmental stimuli, probably especially psycho-social encouragements or aversive stressors. Therefore, it seems likely to suggest that a very sensitive acetylcholine system is the mediator of both rewarding and depressing stimuli to the emotional limbic system.[19]

Aversive signals might be conducted in one direction to the limbic system, rewarding signals might be propagated in other directions, for instance to nucleus accumbens and other parts of the dopamine system or to the serotonin system (see discussion below).

Thus, the emotional result will depend on various action-specific energies (social releasers) which to normals will cause appropriate emotional reactions, but to manic-depressives will cause dramatic up-and down- regulations. As indicated above, El-Mallakh and Wyatt, have proposed that a slight depolarization of the nervous system(acetylcholine?) might be equivalent to a hyper-excitability which might correspond to mania.[8] A still greater

depolarization(caused by continuous kindling) would gradually lead to a depletion of transmitters from the vesicles. Thus -- in order to return to the problem of depression -- this mental deficiency might be a depletion state (cf. the effect of reserpine).

It might be a depletion in certain areas of the brain (the frontal lobe, the subgenual area). In other parts of the brain the acetylcholine activity might be relatively increased (cf. Andrew et al.'s paper about both hypo- and hyperaroused systems in the brain[7]). If, for instance, the cholinergic system is hyperaroused in certain regions of the brain it is possible to imagine that acetylcholine might mediate its effect via nervus vagus which is cholinergic and which exerts an inhibitory effect on the bronchia (breathing) and the heart rate and beat intensity. This seems to be in good accordance with the behavior of deeply depressed patients who would lie for at least half an hour in the morning in their beds quite immovable and with no signs of breathing at all (observational experience, Frederiksberg Hospital).

Regarding schizophrenia, the glutamate-acetylcho-line hypothesis supposes that the glutamate activity is lower than in normals.[23] The agent phencyclidine which is a glutamatergic antagonist is capable of mimicking schizophrenic symptomatology.[12] Accordingly -- as glutamate is the most important excitatory amino acid of the brain -- the acetylcholine system is probably only slightly excited in schizophrenia.

Presumably, this involves not only a weak physiological stimulation, but also a deficient influence and stimulation from the social environment which might lead to autism. In addition to impaired cognitive functions ~ among others delusions and hallucinations -- the reduced cholinergic activity might probably lead to a disinhibition of the amine systems.

Accordingly, the increased dopamine free-setting would correspond to an increased body mobility (mentioned above) including various types of stereotypies: rocking movements, leg swing .finger tapping, etc. An increased serotonin activity might correspond to the aggressive behaviors that are often seen with schizophrenics. Serotonin is known as the aggression/dominance hormone through the evolution in the Animal Kingdom and can be tracked back to the Crustaceans (crabs).

It is possible to point to four behavioral aspects which seem to distinguish depressives from schizophrenics **(Table 1).** Probably these aspects can be related to differences in the glutamatergic activity:

Table 1

	DEPRESSIVES	SCHIZOPHRENICS
1.	Motor inhibition (extreme tiredness)	Increased mobility (including stereotypies) (Man-Whitney, $p<0.05$)
2.	"Heavy" mind Depression Melancholy	"Easy" mind Smiles to self Laughs to self Talks to self
3.	Absence of self-assertion	Frequent hostility and aggression
4.	Thoughts relatively normal (realistic)	Thoughts abnormal (unrealistic)

Thus, it is obvious that a number of behavioral traits point to major depression and schizophrenia as opposite behavioral manifestations. This relation might be correlated to high, resp. low glutamatergic influences. That the glutamatergic system seems to be involved in major depression is seen by electro-stimulation studies in Rigshospitalet, Denmark.[27] In the rat repeated electroconvulsive seizures (ECS) produced significant expressions of neuropeptide Y in the cortex. NPY inhibits glutamate and kainate which may contribute to a kindling-like process causing both mania and severe depression.[20] Thus, a large free-setting of NPY

provoked by ECT may be responsible for the efficient antidepressant effect of ECT. But in spite of the fact that depression and schizophrenia behaviorally tend to be opposite manifestations we often see what might reveal a certain relationship between the disorders: patients may be diagnosed as schizo-affectives. In families with an affective tradition we sometimes meet such schizo-affective cases.[28] This indicates that there may be a sort of continuum between manic-depressive illness and schizophrenia.

The following table - **(Table** 2) elucidates behavioral similarities between mania and schizophrenia:

Table 2

MANIA	**SCHIZOPHRENIA**
1. Great physical activity	Increased physical activity
2. Lots of speaking (socially addressed)	Sometime lots of speaking (mostly autisticaily)
3. Megalomania	Megalomania
4. Unrealistic imaginations	Unrealistic thinking (Deficient logic and associations)
5. Treatment with Haloperidol efficient	Treatment with Haloperidol inhibits psychosis
6. Low levels of glutamic acid during brief periods of the manic phase.[23]	Low concentrations of glutamic acid in the plasma.[23]

It appears from the description above that there are arguments for both hypotheses. Results from behavioral investigations as well as from physiological and genetic studies have been included. The two hypotheses are:

1. The Serotonin-Dopamine hypothesis.

2. The Acetylcholine-Glutamate hypothesis.

In spite that the hypotheses have been presented on the background of scientific results they are still at a very preliminary and tentative stage. However, according to this description, it ought to be possible to test whether affective subjects, or some types of affective patients, are physiologically characterized by an increased glutamatergic activity or whether the main physiological cause might be a dopamine deficit.

Which of the two hypotheses is the more likely --especially for bipolar disorder- is difficult to say. The argumentation might support hypothesis 2.

The basic problem - according to the two described hypotheses - is:

1 A: Is schizophrenia caused by a weakly functioning glutamatergic system as a primary cause?

or:

1B: Is schizophrenia caused by an increased dopaminergic activity as a primary cause ?

<u>and</u>:

2A: Is major depression caused by a high glutamatergic -cholinergic activity with a probable suppression of monoamines (5HT,DA,NE) as a primary cause? (It should be possible to test whether the glutamatergic activity is increased in major depression).

or:

2B: Is it caused by a depleted dopamine system as a primary cause with an increased acetylcholine arousal as a secondary consequence?[27-29]

3: Mania might be correlated to high dopamine levels.

Ad1A,1B:

Based on Munkvad's[23] documentation of a decreased level of glutamic acid in the brain of schizophrenics and on Carlsson[12] assumption that schizophrenia will have to take into consideration not only a hyperdopaminergic but also a hypoglutamatergic dysfunction it seems sound to presume that the primary physiological cause of schizophrenia might be a hypoglutamatergic dysfunction or a decreased number of glutamate receptors.

This presumption involves that the corticostriatal tone is reduced in schizophrenia. A low glutamatergic activity causes a low excitation of the cholinergic system. Thus, the traditionally assumed inhibitory influence of the cerebral cortex on subcortical structures-mainly exerted via glutamatergic/aspatergic/cholinergic pathways --will be weakened in schizophrenia leading to a disinhibition of the dopamine system -- and probably also of the serotonin system (hence the stereotypies and the aggression seen in schizophrenics). An increased dopamine free-setting will in turn inhibit the cholinergic arousal, i.e., the cholinergic system is not only little stimulated by a dysfunctioning glutamatergic activity, but also inhibited by a hyper-dopaminergic arousal.

The possibility of such a state might account for the cognitive and emotional deficits characterizing schizophrenia.

In this connexion I might point to a specific behavioral reaction in the schizophrenic patients I observed in the psychiatric wards of Frederiksberg Hospital: very often when they started watching television or otherwise were occupied by social stimuli they would stop their stereotypies. However, when relaxing from television they would usually start the stereotyped movements again (rocking etc.). This might be an example illustrating the assumption that cortical stimulation inhibits lower nervous impulses, in this case dopaminergic ones.

Ad 2B,2A:

Randrup, et. al.[9] refers to three working groups that found significantly ($p < 0.01$-0.02) lower values of cerebrospinal homovanillic acid (HVA) in depressed patients than in control groups.[30]-[31,32] Brown and Gershon,[11] and Mann and Kapur,[10] also consider a dopamine hypothesis related to major depression.

Whether the low dopamine level is a primary physiological cause or a consequence of the above discussed corticostriatal inhibition is uncertain. But consequently -- on the basis of the literature just referred to - it seems reasonable to suggest that major depression might be caused by a decreased dopaminergic free-setting or a reduced number of dopamine receptors.

A reduced DA activity would lead to a DA/Ach dysbalance. As dopamine is known to exert an inhibitory effect on the cholinergic system[3] a low dopaminergic activity would cause a disinhibition of the acetylcholine system, most likely in the subgenual area.[16] Such a situation might involve a dysfunctioning modulation of cholinergic pathways from cortex to thalamus and the limbic system, in particular the amygdala which is known to play an important role in emotional reactions.[6] Based on particularly aversive social releasers and on intensive iterative/ persistent stimulation kindling) depression might be provoked(in this case the action-specific releasers/social releasers might determine the direction into which nervous impulses would be propagated).

Thus, the above model including a low dopaminergic activity may explain depression in the following way: a low dopaminergic activity disinhibits the cholinergic activity in the subgenual area which facilitates the propagation of aversive stimuli to the thalamo-limbic system.[16]

Ad 3:

Finally, it seems documented that mania is correlated to increased levels of dopamine. That bipolar disorder obviously switches between mania

(high dopaminergic activity) and depression (low dopaminergic activity) seems difficult to understand. A patient told me that after he had been in a hypomania for three months he woke up one morning in a deep depression. Such a "catastrophe"[33] might suggest a manic system's tendency-after a long-term stimulation- to switch its high arousal energy over to a complementary pathway system responsible for depression.[34]

(See GENETIC THEORY for a possible explanation of the up and down regulations).

CONCLUSION:

There seems to be evidence that:[12>23]

1. Schizophrenia is physiologically related to a reduced glutamatergic activity as a primary factor.

2. Schizo-affective disorder may have a slightly different physiological background **(see Genetic Theory).**

There seems to be evidence that:[9-16]

3. Major depression might be physiologically related to a relatively reduced dopaminergic activity as a primary factor or a relatively increased glutamatergic activity.

Finally, there seems to be evidence that:[23,30]

4. Mania may have a slightly other physiological constellation **(see Genetic Theory),** probably with a relatively increased dopaminergic arousal or a slightly(?) reduced glutamatergic activity.

GENETIC THEORY:

A possible genetic background.

Based on the above elucidation of the two tentative hypotheses it is of course tempting to speculate on a possible genetic background of the diseases in question. Genetic mapping studies have documented that the long arm of chromosome 11 contains two very closely situated sites, one coding for the glutamate receptor-4, the other coding for the dopamine D2 receptor (11q22-q23). -- **see Figure 1.** In the meiosis phase the homologous chromosomes 11 are placed parallel to each other, which facilitates translocations, deletions, deficiencies, and duplications.[35]

If -- as illustrated above - a coherent Glu/DA hypothesis is considered a plausible starting point it seems rather natural to relate it to the described specific chromosomal structure. One may imagine that a loss (deletion/deficiency) of the glutamate site in one of the chromosomes might lead to a zygotic situation in which the damaged chromosome meets an intact chromosome resulting in a zygote with a double dopamine site, but only with a single glutamate site (Glu/D2D2). Exactly this glutamate deficiency might be the genetic cause of schizophrenia.

Oppositely, a loss of a dopamine site in the meiosis phase might lead to a zygote containing two glutamate sites and only one dopamine site (GluGlu/D2) thus causing the genetic background for major depression. Probably, there is also the possibility that one chromosome may lose its glutamate site and part of its dopamine site as they lie very close to each other. In that case the zygote might contain one glutamate site, and say one and a half dopamine site (Glu/1 $^{1}/_{2}$ D2), probably corresponding to the genetic background of schizo-affective disorder.

Consequently, other combinations might be possible and thus constitute a background of the affective and the schizophrenic spectra. According to this model, the fact that schizo-affective disorder occurs as a well-established clinical diagnosis seems to be a crucial support for the proposed coherent hypothesis.

The physical cause of structural mutations in the Glu-D2 area might be an increased fragilibility of this chromosome region (cf. the 1 % prevalence of both manic-depressive disorder and schizophre-

nia). And the very fact that the two sites are placed closely to each other opens up for an array of deletion and duplication possibilities in that chromosome area. For instance, a glutamate receptor-4 site might be deleted ,but also a part of a D2 receptor site which might lead to schizo-affective disorder as mentioned above.

Such chromosomal deletions including partly Glu and DA sites would probably not occur or only occur with difficulty if the two sites were placed "far away" from each other, not even if they were located at some distance from each other on the same chromosome, In the case of very closely situated Glu and DA sites only two chromosome cracks are needed for a deletion of a Glu site and half a DA site; otherwise four cracks would be necessary, i.e., the clinically, commonly known incidents of schizo-affective disorder would not occur if the Glu and the DA sites were "far away" from each other (cf. the principle of parsimony).

Thus the fact that schizo-affective disorder *does* exist contributes to a coherent hypothesis, i.e., a hypothesis that includes the dynamics and the etiology of both manic-depressive disorder, schizophrenia and schizo-affective disorder. Schizophrenia is mainly treated by D2 receptor antagonists (e.g., chlorpromazine). From a heuristic point of view it is important to know that the D2 receptor is coded from a DNA site on the long arm of chromosome 11. Still more suggestive is the fact that this site is situated quite closely to the site that codes for the glutamate receptor-4. This indicates that relative glutamatergic and dopaminergic activities play a role in the etiology of schizophrenia ~ and probably also in affective disorders as suggested by the above discussed hypotheses.

These genetic speculations predict that:

1. Affective disorders would be appropriately treated by anti-glutamatergic agents(cf. ECT provoking NPYthat inhibits glutamate).

2. Schizophrenia would be appropriately treated by glutamatergic-enhancing agents.

As mentioned above there are problems about explaining the etiology of bipolar disorder. This is not surprising at all as it seems very peculiar that a brain's nervous activity can fluctuate so radically. But perhaps the difficulty can be accounted for by a close inspection of the two closely placed sites encoding for the Glu-4 and the D2 receptors.

The normal chromosomal constellation is two Glu sites and two D2 sites in each body cell: GluGlu/ D2D2, and a Glu/D2 constellation in each gamete. If a Glu-4 site is lost during meiosis the damaged chromosome may meet a normal chromosome from an opposite gamete resulting in a zygote with the constellation Glu/D2D2. This constellation might account for schizophrenia.

If a D2 site is deleted the zygotic constellation most likely would be GluGlu/D2, probably equivalent to the clinical diagnostic term of unipolar disorder(depression). The probable deficit of D2 receptors in the subgenual area[16] seems to be able to disinhibit the cholinergic cortico- thalamo-limbic pathways. Such an arrangement might be the cause of unipolar depression.

However, this specific constellation does not seem able to explain bipolar disorder, especially a manic episode characterized by a hyperdopaminergic state -- because an increased glutamatergic/ cholinergic tonus would inhibit dopamine in puta-men and other parts of the basal ganglia - and this inhibition is not coherent with the postulated characteristic hyperdopaminergic activity in manic patients. If manic-depressives have also only one DA site as suggested for unipolar patients it seems difficult to explain that a single DA site would be able to account for a hyper-dopaminergic state.

So in order to make a tentative account for bipolar disorder we might suggest the hypothesis that manic-depressive patients have the following genetic equipment: GluGluGlu/D2D2, arisen from a duplication of Glu in one chromosome. Such an arrangement would provide an increased glutamatergic/cholinergic sensitivity, but on another

background than the GluGlu/D2 constellation. But the GluGluGlu/D2D2 arrangement would still account for sensitive thalamo-limbic pathways involving the possibility of major depression.

How, then, to explain the rise of mania?:

1. As mentioned above it is difficult to understand that one D2 site -- as suggested for unipolar depression -- would be able to produce a hyper-dopaminergic activity as seen in mania. Therefore, it seems relevant to assume that a D2D2 constellation is one of the backgrounds of mania.

2. To account for the depressive episodes in bipolar disorder it is probably necessary to suggest an increased excitability/sensitivity of the glutamatergic/cholinergic pathways prolifer ating to the thalamo-limbic region like in unipolar depression. Hence the assumption of the constellation GluGluGlu that would be a relatively efficient ("strong") factor in an GluGluGlu/D2D2 arrangement.

3. Thus, the D2D2 constellation is a natural background for a rise of a hyperdopaminergic activity in mania. But still the rise of mania has not yet been accounted for!

   A possibility is to refer to the switch-over hypothesis that suggests that when a nervous system (in this case the "depression system") has been overloaded for a considerable time then it transports its high arousal energy to an opposite or rather a complementary "manic system" (cf. the catastrophe theory[33] and the switch-over hypothesis[34]). Compare the switch from depression to mania in certain patients treated with antidepressants, e.g., Fluoxetine.

   Also consider the sudden conversion from long-time hypomania to depression. An example from everyday life seems to confirm such conversions: think of intensive laughter converted to tears. (It is tempting to remind of sudden political revolutions, e.g., the fall of the Berlin wall in 1989, as an analogy to a depression-mania conversion[33]).

4. However, we cannot exclude another explanatory possibility, namely the "quality" of aversive and rewarding stimuli. Aversive influences might primarily excite the Glu/Ach arousal in the thalamo-limbic region leading to depression. Oppositely, rewarding stimuli might diminish the arousal level of the Glu/Ach system.[23] thus causing an increase of the dopaminergic activity involving a basis of mania. In this connexion it should be emphasized that it has been documented that environmental stimuli have a considerable influence on serotonin, dopamine, and norepi-nephrine.[6,16,36]

A specific tentative explanation of bipolar disorder:

The above indicated idea about "quality" may be substantiated in the following way as for manic-depressive disorder.

1. The hypothesis assumes a chromosomal GluGluGlu/ D2D2 constellation.

2. This arrangement involves an increased glutamatergic/cholinergic sensitivity (excitability).

3. A high Glu/Ach sensitivity is probably respon sible for depression, and a reduced sensitivity might be responsible for mania. The releasing factors of depression might be external aversive stimuli in cooperation with kindling. The releasing factors of mania would probably be rewarding stimuli in connexion with kindling.

4. Neurochemical mediators of external stimuli might be numerous, but the cholinergic system and the serotonin system might be empha sized.[36]

5. The 5 HT system is known to be influenced by light intensity[26] and by social stimuli originating from the dominance hierarchy.[36]

6. If -- during winter -- the light intensity is low the serotonin level falls. This means that serotonin's stimulation of the dopamine free-setting in striatum is reduced. This in turn includes that the dopaminergic activity is too weak to sufficiently inhibit and balance the cholinergic/glutamatergic activity. Conse quently the high acetylcholine level causes a psycho-motor inhibition (major depres sion).[18,19]

7. If -- during summer -- the light intensity is high the serotonin level increases. This involves that serotonin's stimulation of the dopamine free-setting in striatum is also increased. This includes a better inhibition by dopamine of the acetylcholine arousal. However, the point probably is that the cholinergic activity is not quite reduced to normal values, but to levels a little above normal. Such a slight transmitter dysbalance probably opens up for an in creased psycho-motor activity.[8] In combina tion with still increased light intensities (intensive, iterative, and persistent stimulation or kindling) such a state might turn into mania.

   If there were an overweight of mania during summer this might be ascribed to an affect of a high light intensity. But this does not seem to be the case. Mania and depression in bipolar disorder might be better explained by social releasers (although very weak) that originate from the dominance hierarchy.

8. Aversive social stimuli decrease the serotonin level.[36]

9. The consequence is a weak stimulation of the dopaminergic system followed by a deficient inhibition of the cholinergic system causing a psycho-motor inhibition. Kindling in the form of ruminations may contribute to the mainte nance of the depression for a long period.

10. A rewarding stimulus -- or a number of rewarding stimuli ~ increase the serotonin level.

11. The consequence is a stronger stimulation of the dopaminergic activity followed by an increased inhibition of acetylcholine, i.e., a better DA/Ach balance. However, as the Ach level is probably not quite brought to normal (because of the overweight of Glu in manic-depressives compared to normals) there is a risk that rewarding kindling factors may bring the situation to a hypomania or a severe mania. The kindling process may take some time (days), but intensive rewarding stimuli might also very soon cause a manic episode.

As noted above an increased glutamatergic/ cholinergic tonus probably inhibits the dopaminergic activity to a certain degree. If a decreased serotonin level - be it for some kind of stressing, aversive social stimuli -- is added to this tonus it is possible to imagine a still greater impairment of the dopaminergic activity, which in turn accounts for a still greater cholinergic tonus involving depressions. Thus a vicious circle seems to be responsible for sort of a self-increasing effect in depression --probably equivalent to the behavioral aspect of ruminations. And the basic cause -- according to the presented hypothesis ~ of maintaining such a state is the generally increased glutamatergic activity.

To summarize this specific model of mania:

The basically operating system is the increased glutamatergic/cholinergictone (GluGLuGlu) which is considered to be responsible for a tendency to dysthymia or depressions. The accompanying regulating factor is the serotonin system. External aversive stimuli cause a considerable decrease of the serotonin level leading to an aggravation of depression. External rewarding stimuli increase the serotonergic activity considerably, leading to hypomania or mania. Thus, bipolar disorder might be caused by an interplay between glutamate, acetylcholine, serotonin, and dopamine.

The presented model of bipolar disorder has pointed to some difficulties in explaining its pathogenesis, but also suggested a contingency between the

serotonin fluctuations and the dopamine/acetyl-choline balance that may have gone awry. Although the model is tentative it may be of a potential epistemological value.

Finally, the chromosomal constellations involve an attempt to explain schizo-affective disorder. If a structural mutation involves a loss of the Glu-4 site plus part of the closely placed D2 site the following zygotic situation might be Glu/1^{1}/2D2, i.e., a D2 overweight.

When taking an overview of the coherent hypothesis, the mentioned mental disorders seem to be rather closely related in as much as the hypothesis concentrate on the glutamate receptor-4 site and the D2 receptor site on the long arm of chromosome 11. However, this does not rule out the Egeland et. al[14] hypothesis of a possible dysfunction of tyrosine hydroxylase on the short arm of chromosome 11. Also, the statement of a possible role of chromosome 18 invites to an assumption of a *heterogenous* genetic background of these diseases.

Prediction for an optimal treatment:

1. Major depression might be treated by DA agonists including Glu antagonists.

2. Mania might be best treated by DA antago nists (momentary treatment) and Glu antago nist(prophylactic treatment).

3. Schizophrenia might be optimally treated by Glu-enhancing agents and DA antagonists. Specifically, as for schizophrenia it seems as if 20-30 years of the disease will leave irreversible brain damages such as enlarged ventricles, damaged association pathways, etc. Therefore, early intervention seems to be imperative.

4. Schizo-affective disorder might be treated by Glu-enhancing agents, probably supple mented by a "little" antidopaminergic medi cine.

CONCLUSION REGARDING POSSIBLE GENETIC CAUSES:

Based on the above arguments as for the chromosomal constellation of the Glu receptor-4 site and the D2 receptor site and their interplay in affective disorders and schizophrenia it is relevant to suggest the following genetic hypothesis:

1. Schizophrenia is caused by a Glu4/D2D2 constellation.

2. Schizo-affective disorder is caused by a Glu4/ 1^{1}/2D2 constellation.

3. Major depression is caused either:

   a. By a Glu4Glu4/D2 constellation or

   b. By a Glu4Glu4Glu4/D2D2 constellation.

4. Mania is caused by a Glu4Glu4Glu4/D2D2 constellation.

   a. A low serotonin level plays a down-regulating role in psycho-motor activity (depression).

   b. A high serotonin level plays an up-regulating role in psycho-motor activity (mania).

Acknowledgment:

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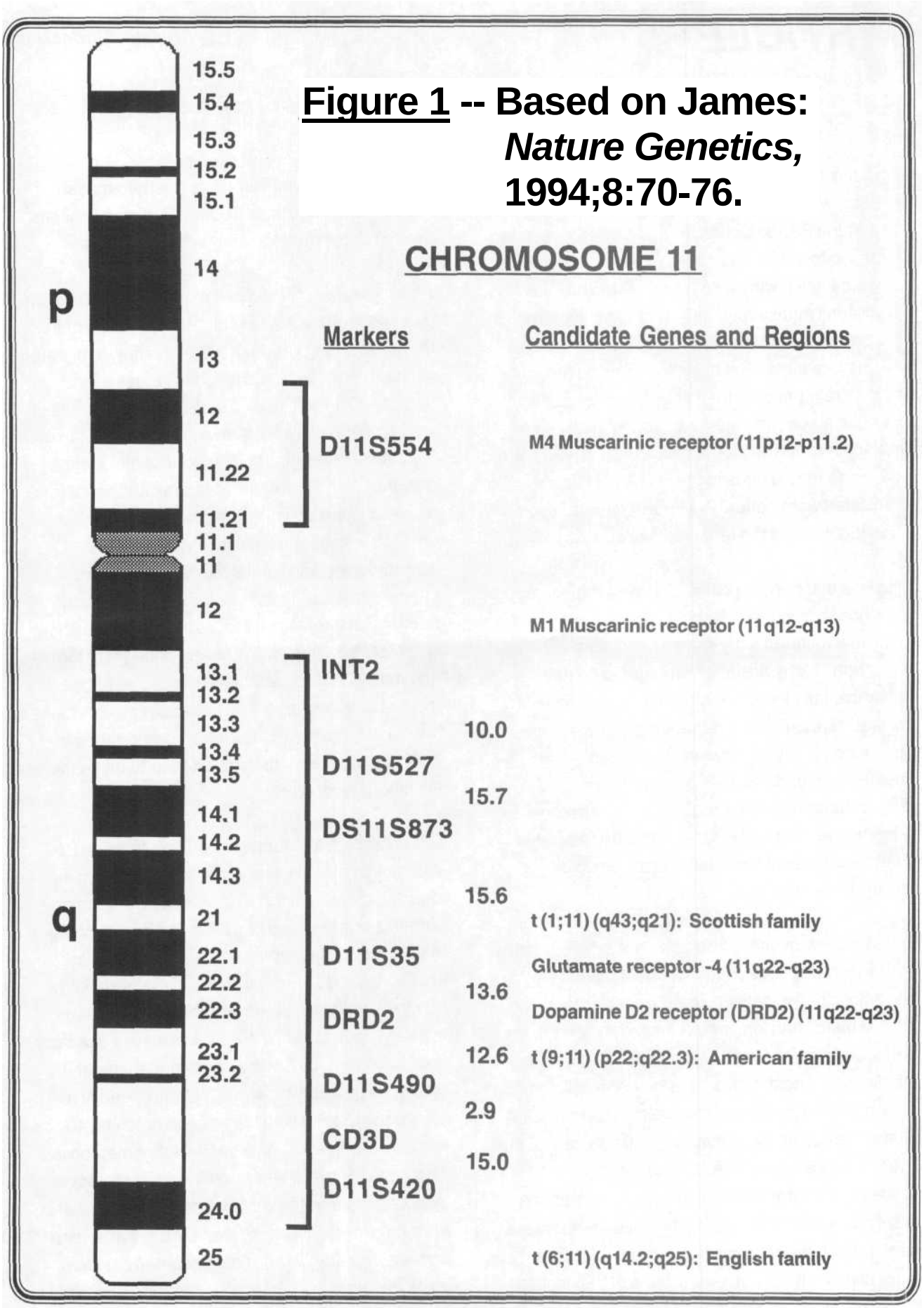
Figure 1 -- Based on James: Nature Genetics, 1994;8:70-76.
CHROMOSOME 11
Markers
Candidate Genes and Regions
p
q
15.5
15.4
15.3
15.2
15.1
14
13
12
11.22
11.21
11.1
11
12
13.1
13.2
13.3
13.4
13.5
14.1
14.2
14.3
21
22.1
22.2
22.3
23.1
23.2
24.0
25
D11S554
M4 Muscarinic receptor (11p12-p11.2)
M1 Muscarinic receptor (11q12-q13)
INT2
10.0
D11S527
15.7
DS11S873
15.6
t (1;11) (q43;q21): Scottish family
D11S35
Glutamate receptor -4 (11q22-q23)
13.6
DRD2
Dopamine D2 receptor (DRD2) (11q22-q23)
12.6
t (9;11) (p22;q22.3): American family
D11S490
2.9
CD3D
15.0
D11S420
t (6;11) (q14.2;q25): English family

ARTICLE:

by Russell Gardner, Jr.

Language and Stories: Thinking of Dinosaurs in Mexico

On a family-oriented vacation in Puerto Vallarta, Mexico, we look up over the Bahia de Banderas, a bay off the Pacific Ocean, and see three, five, often more, up to a dozen and a half large birds with forward angled wings, soaring over the city like prehistoric monsters. Their long, often separated, twin tail feathers signal their name here: tijeretas — scissors-birds. Relatives living in this area tell us they're named for their storyline — since they look like a scissors, they are named such. The metaphor tells a slight but distinctive story. They're known as frigate birds in the U.S. but I like the translated word better. I've known more scissors than frigates and the resemblance speaks to me.

I believe that the distinctively human evolutionary advance involved generation of the neuron-connections that fostered story-making and story-consumption. Many assume language to be that advance, but I think that story-telling did the trick instead. Language — rather languages as I am reminded visiting a land with different one — are means to an end. Stories probably happened before human languages. Of course, speech and language refined and extended the telling of tales. They're wonderful tools, but I hold them to be means to narrative ends nevertheless.

Some stories involve dinosaurs. Not to be outdone by the tijeretas, lines of even more impressively prehistoric brown pelicans (pelicanos) hint with their angled heads and long beaks something of how the aerial world may have looked long long ago, when the dinosaurs held forth before the earth collided 65 million years ago with an immense meteorite in the Gulf of Mexico on the Yucatan Peninsula horn of the country we visit. A consensus now easily describes this environmental event to have darkened skies and killed these creatures that dominated the earth for 165 million years. They held reign for a mere blip of time on the entire scale of things, but the feat remains impressive to the mammalian successor writing this. Subsequent mammalians haven't dominated for near half the time.

I am reminded of *Raptor Red* by Robert T. Bakker, paleontologist, a novel whose title names a half-ton, 20-foot long Utahraptor heroine newly migrated to North America from Mongolia across a land bridge 120 million years ago.[1] The early pages of the book present a line drawing of a world map of the time. Following are a number of other line drawings of the individual creatures additionally featured in the book. A summarizing endsheet gives size comparisons of twelve dinosaurs contemporary with Raptor Red. Their bit-part stories also occupy the book. Turtles make the book to illustrate very effective adaptations without large brains but weren't sizeable enough for the endsheet *dramatis personae;* minuscule furball mammals at one ounce each certainly didn't make the cut despite their considerable importance in Bakker's story and their importance to us as their eventual descendents.

Bakker known as "Jurassic Bob" in Medicine Bow, Wyoming, gained his considerable fame from the idea that dinosaurs must have been more like our current warm-blooded birds than their more phlegmatic present day reptile counterparts such as lizards or turtles. From present animals we know that leg length plus stride length gives a measure of an animal's speed. Both measures are available from fossil records and he calculated that early dinosaurs probably moved about the speed of a coyote pack today with top speeds reaching 40 miles per hour, entailing a much higher metabolism than previous hypotheses had allowed. Moreover, *"Neck bones and torsos have deep cavities that... must have been filled with air chambers arranged just like those of birds. This pneumatic system gives the birds the highest lung efficiency possible*

in any living species, far better than that of lizards or crocs or even us humans. When [these] dinosaurs breathed, the air passed through a high-tech ductwork system, built to an avian blueprint, that supplied oxygen to all... tissues at a tremendous rate."

Did birds descend from dinosaurs? The question fuels hot debates. For instance, several recent studies dispute that birds descended directly from dinosaurs. Diaphragms of crocodiles and people resemble pistons drawing air in, but John Ruben and colleagues showed that birds have a different system that uses oxygen exchange in the abdomens more directly. Other experts noted, however, that the soft tissue remnants were from a squashed specimen and that crocodiles differ in other ways.[2] Meanwhile (to use a story-telling term — all science involves stories after all), Kevin Padian and Luis Chiappe devote a recent *Scientific American* article to the dinosaur-bird transition.[3]

They note Thomas Huxley first saw a resemblance (a suite of 35 characters that both dinosaurs and birds possess but do not characterize other animals). They disclose that John Ostrom from Yale (one of Bakker's teachers) revived and modernized the Huxley idea. Padian and Chiappe[3] mention in passing the opposing idea that the *"complex lungs of birds could not have evolved from theropod lungs."* They rebut, *'This assertion cannot be supported or falsified at the moment, because no fossil lungs are preserved in the paleontological record."* We have yet to see how Padian and Chiappe will deal with the piston *vs.* abdominal theories. We wait like good story-audiences for the next chapter, for what will happen around the next bend of the road, probably in *Scientific American,* as their editors know what the public likes.

The very first dinosaur discovery was made about 1822 by a surgeon, Gideon Mantell, near Lewes in Sussex near the South Downs, about ten miles from where The ASCAP Society was founded at John Price's Odintune home about 170 years later. Mantell labored against the conventional wisdom of the time and suffered accordingly. Mantell's latter day neighbor, John Price, has also encountered skepticism and lack so far of professional or public acceptance (or even much debate) of his idea that depression might stem from genes influencing social rank behaviors. He asserted these likely persist in each of our genomes yet and stemmed from long before Raptor Red's time. That this is still hardly known or thought about can be seen in Andrew Solomon's just published impressive description in the *New Yorkeroi* his personal depressive illness.[4] John's theory of depression as a basic plan is simply not mentioned.

Two ASCAPians were quoted, however. One, Randy Nesse, basically cited mismatch theory *('The investment to achieve modern life goals, the number of opportunities we have, is probably beyond the range our mind was designed to handle').* The other, George Brown, said, *"Social systems can play a powerful role in generating both psychiatric and physical disorders. ...the rate of major depression among single mothers is double that of women raising children with a partner."* Still the major contribution of Price didn't surface, although it bears on Brown's formulation and it might have helped the author, Andrew Solomon. He had introduced the section by saying,"/ *wonder constantly whether these experiences have served any purpose."* He apparently never learned that social rank signals may be extremely ancient and extremely powerful, more a product of brain parts arising before the time of the dinosaurs rather than in the hunter-gatherer phase of human evolution touted by Randy and other evolutionary psychologists.

I have seen patients helped by comparisons and contrasts of people to other animals. I often deploy the shiver metaphor originated also by John. Shivering is a thermogenic response to cold just as depression, or anger, or panic, or other reactions are automatic responses to communicational stimuli from other people. Other animals shiver too, probably from the same inherited genome and neuronal codings, and they also have many of the stereotyped automatic reactions. I then juxtapose this formulation of the problem with the ATP method of obtaining help. The initials indicate the particu-

larly helpful features of the enlarged bulbous human brain, three times bigger in mass than are gorilla or chimpanzee brains. A = allies (the most important of the three initials as people are unusually gregarious; allies are warm friendly people willing to help), T - thinking which happens better if done with allies, and P = planning which happens more adequately if one's situation is better thought through with comfortable allies. ATP is not easily deployed sometimes, and can be impossible if one has gone over a slippery slope and lower brain has taken over. But even then, the patient can importantly use it later to conceptualize and then prepare for future constellations of stressors.

Often in this time of effective medications, the plan will include drugs. Andrew Solomon did have allies (notably his father and doctors) and he used Prozac and other medications. In the article he described serotonin and dopamine as important, but did not mention the social correlations of serotonin levels. These include that whole blood serotonin is twice higher in alpha monkeys and subordinate monkeys become alpha if fed Prozac known to elevate serotonin. These correlates did make 1998's first *Newsweek* issue though and two discoverers of this phenomenon, Michael Raleigh and Michael McGuire, were interviewed. We learn that McGuire's blood serotonin is higher than Raleigh's (matching their relative ranks). Still, the relationship of depression, drugs for it and the relationship of both to social rank remains stubbornly out of public awareness, not emerging in *Newsweek* either.

I was pleased with the *Newsweek* piece, however, and I will show it to my patients. I often tell them that their goal is to be in charge of themselves: euthymia (being neither depressed nor manic) is the state of being in charge of yourself and your components rather than being under the thumb of another whose exact role is maddeningly hard to pin down, when depressed. If depressed, the state itself seems to push towards misleading others about one's capabilities, "See how badly off I am. I am no threat whatever."

And Prozac works in opposite ways for monkeys vs. people: The lower ranker shifts to being in charge of other monkeys. In humans, however, the object of leadership may not necessarily be other people, but in the story-telling animal, the person him or herself. For the artists each of us are, self-components become metaphoric subjects, such as how one deploys time, moves household items, sets territorial boundaries, or chooses with zest what to eat and with what seasoning (a meaningful issue in Mexico). One may choose deliberately to be subordinate rather than resentfully submit (Leon Sloman's "giving way" *vs* "giving in").

So what will happen to the social rank theory in this sphere of clinical science? Partly we need to publicize the theory more so that creative people like Andrew Solomon and other patients will have something to use in planning their lives more practical than what they currently possess. He accurately depicts the rather unattractive bleak formulations out there now. Through this example of an accurately presented intellectual desert, he illustrates David Evans' point that we need artists to help convey experiences accurately. They are the ones who will come up most inventively with juncture points between system levels, such as group, individual, brain, cell, molecule. This makes Jurassic Bob's literary experiment an exciting one.

Also important for overcoming outmoded paradigms of thinking, we need scientific data from lower system levels, such as that on the skeleton of the genome, of the dinosaurs within. We need to delineate the fossilized DNA sequences that code for the ancient behaviors even as they are indispensable for current function. At the moment this may seem as outlandish as Mantell's discovery in Lewes was for 1822. But consider the lowly yeast if we think dinosaurs were primitive. Consider that thirty-one percent of the yeast genome is homologous with genes of humans.[5] We can presume them to be operative still, still making differences in how we live (or *that we* live given many of these genes are "housekeeping genes" for cell integrity). I predict that not too long from now, certainly before

another 100 years more have passed, ancient behavior-producing genes will be documented in humans. What fun to be part of that developing scientific story, on the cutting edge of a data base yet to be gathered. I'm proud to have been there at Odintune when history got made once more in the South Downs in the forming of the ASCAP Society. Speaking of ancient behavioral programs such as conflict between conspecifics (members of a same species), dinosaur bone discoveries fostered major human drama. Fifty years after Dr. Mantell's discoveries near the South Downs, O.C. Marsh from Yale and Edward Cope from Philadelphia conducted dinosaur-wars in the western U.S., excavating many tons of massive bones but treating each others' crews as outgroup members, finally assassinating each others' reputations in the press.[6] They behaved, in short, like territorial animals of Raptor Red's time. Tiger and Fox pointed this kind of thing out in 1971. [7]

Some Bakkers other than Robert, ASCAPians Cornelis and Marianne, suggested two years later that humans use other means of combat for parallel territorial aims.[8] Cope himself exemplified this, "When a wrong is to be righted, the press is the best and most Christian medium of doing it. It replaces the old time shot gun & bludgeon & is a great improvement." And of course the bludgeon was gentler by far than the terrible claw of Raptor Red. However they got there, the bones that furnished the museums of the world also fueled the self-story lines of future scientists, among them Robert Bakker (unrelated to Cor and Marianne). Jurassic Bob's mother, he tells us in a dedication, took him many times across the George Washington bridge to the New York Natural History Museum where he related vigorously to the bones. We gather that his personal storyline had its inception around then, fostered by his mother's encouraging audienceship of then Jersey Bob. When mothers and other parents hear and appreciate the storylines of their sons and daughters, they have profound impact on their offspring, persisting throughout their lives.[9] Bakker appreciates his mother's role. He says, "Mom, this book's for you!"

In the 1960's as a student, he helped excavate a pod of smaller versions of Raptor Red and tells in the introduction about the size of the animal's brain: *"anatomists probed... raptor braincase bones and found to their surprise that the raptor's brain was as large for its body weight as it is in many modern groundrunning birds."* From a reputation commencing then, Bakker was asked to be consultant for the artists of the movie *Jurassic Park.*

In the introduction he tells how Steven Spielberg complained that the movie's plot required a killing machine beast many times larger than the human-sized raptor described to that date by Bakker and colleagues. This requirement by the master storyteller put in despair the artists who hoped for verisimilitude, but who also knew research data for a bigger monster were wanting. So Bakker reacted upon hearing colleague James Kirkland tell of a monster fossil claw newly discovered by the talented amateur, Bob Gaston. Bakker tells the following on himself, *"Jim, Jim — Jim!,"* I yelled, *"You have found Spielberg's raptor!"... "Jim thought I was daft."* Daft perhaps, but Bakker obviously also had Kirkland's respect as he named the creature "Utahraptor" just as Bakker suggested.

The movie conveyed less respect, using the more generic velociraptor instead. This term has now entered the general parlance because *Jurassic Park has* become part of our cultural myth (or general storyline) for all its stereotyped plot and wooden acting on the part of humans; the dinosaurs, however, were portrayed convincingly. Bakker notes that a few moviegoers knew that utahraptors were in fact the featured beasts. Now with this new and apparently popular book, more will be clued in (at least I was).

Late breaking news has even the Utahraptor claw outdone. A still larger dinosaur claw has been discovered in Patagonia. A notice in *Science* tells of a Christmas present last year for Houston dinosaur buffs in the form of a cast presented to the Houston Museum of Natural History by its discoverer, Fernando Novas, of the Argentine Museum of

Natural Sciences in Buenos Aires.[10] The Megaraptor comes from Northwest Patagonia, not too far, I suppose, from where ASCAPian Valentina Farias lives in Bariloche, Argentina. This monster had a claw 54% longer than that of Utahraptor. The *Science* note begins, *"In case Steven Spielberg is casting about for villains for another Jurassic Park movie, here's one suggestion.* "Dr. Novas suggested that the Megaraptor stemmed from a more primitive branch of dinosaurs than those found in Utah, with a less broad and steady foot from which to launch its assaults.

Bakker's novel about the more evolved more broadly based heroine felt like a *tour de force.* Even after *Jurassic Park,* who would expect a dinosaur heroine to gain meaning for human readers? Maybe especially after *Jurassic Park*! I read the book from the special interest of human-nonhuman contrast-comparisons. But obviously these fictional dinosaurs must have sufficient congruence with people to have made it a good seller. Paperback publication followed hardcover by 11 months.

I found it by chance at an airport bookstall along with Tom Clancy, Dean Koontz and the like. *Raptor Red's* cover possesses a holographic picture of a many toothed dinosaur head seen from the side at two angles or coming at me head-on, depending on how I held the book. One cover blurb from the *San Jose Mercury News* talked of the *"compassion-even sweetness— with which Bakker chronicles his predators".* But meat-eating violence come s through in comic book portrayals of sound: "THNKTHNK!," and "SQWAKKKKKKKKK!"

Strategies of going for the soft underbelly of even armored beasts and descriptions of devouring delicious raw bloody liver are hardly neglected nor is the fact of female dominance in predator species exemplified by golden eagles in our modern day. For all the book's aim at a younger set who might be impressed with noisy, comic-like components, the book is in fact a sophisticated primer on evolutionary biology. Looking it over reminded me of a Max Planck sentiment with which I began some of the early issues of *The ASCAP Newsletter* many years ago, something to the effect of: *"One never overcomes the biases of the old believers during an intellectual revolution. They never give in, but it doesn't matter as the next generation assumes the previously heretical stance to be obvious truth."* Bakker helps assure that for evolutionary biology. No education is as powerful as that disguised as an entertaining good story.

The reason that Bakker makes an interesting and convincing novel about a monster is that his heroine suffers from lost love, she intensely bonds to her sister and sister's children, she needs to cope with major life changes in family and circumstance, and she has many narrow escapes from danger. Raptor Red and her family as new emigrants from Mongolia thereby make their living somewhat more easily because their prey haven't yet adapted to them, although they also experience a down side of vicious American predators in the form of ticks. Fortunately, sinorns, tick-loving birds, have followed them so a cross-species mutualism persists, augmenting the survival of both birds and raptors: food and protection from macropredators for the birds; protection from micropredators for the utahraptors, like domesticated animals and humans. In a similar kind of mutualism, some say, for example, that the dogs and other animals chose to be domesticated.[11]

Bakker makes raptor-human contrasts. Dinosaurs like birds had faces with little mobility and expression. Birds communicate body state with movements of the entire body, such as twists, shakes, leans in stereotyped sequences elicitable with appropriate stimuli without explicit learning. With less energy expended, the human's mobile face requires less energy, yet transmission of more extensive and flexible meanings. Subtleties, shadings and combined meanings make available more compromise than Raptor Red probably had in her somewhat rigid repertoire.

There are a features of Bakker's fictionalized dinosaur that do not jibe with my previous knowledge: for instance, he postulates that she had

dream time (meaning rapid eye movement or REM sleep) whereas in fact there is no evidence of REM sleep in reptiles or birds. Jonathan Winson has made much of the difference between early and later mammalians.[12] An early one, the echidna, has no REM sleep but does have a disproportionately large frontal lobe; REM sleep, Winson postulates, allows other mammalians to process the past day's activities and experiences "off line" as it were, whereas the echidna has to do all that computing more immediately. So I believe that Bakker overly anthropomorphizes, or this case, "mammalomorphizes." But again we readily forgive him. After all, it takes courage to write a novel about a dinosaur heroine, and if he makes her more human than she had truly been, so be it. We need not hold authors of airport novels to scientific standards.

Bakker illustrates how the dinosaur chicks may have learned from their parents that the birds are helpers not prey; he also provides his heroine an incipient story-making capacity by giving her a sensori-emotional memory of the location where the relief took place: *"In Raptor Red's mind, this meadow will always be associated with healing ministrations from the sinorns. 'Tick-bird Meadow" is a good translation of how her memory labels the locale."* But let's think about this. Did the dinosaurs likely have symbol-making, story-making capacities? It's certainly human to think of such a meadow that way. But do birds, lizards, even large mammals think of it that way too? There's room for skepticism but even more great new questions. What kind of essential brain mechanisms *are* needed? If the dinosaurs did have symbol-making capacities, was it convergent evolution like streamlining of the body for watergoing vertebrates?

The whale and sharks invented their smooth shapes independently, the whales after their ancestors left land for the ocean but the sharks never left the ocean for land in the first place. Of course both creatures have skin, as did their common ancestor. Skin may have been modified but never got discarded (was always useful) so that re-invention was hardly needed. As we learn more, how will we see the parallels in ancient brain to have unfolded ~ like the shape convergence or like the skin (homology)? Will we learn of sensori-emotional memory mechanisms in common like skin or will these components be shown to have evolved separately in the widely separate creatures? If they were new at some point, at what point was it and with which common ancestor? And if sensori-emotional memories are key to stories, when did they cross over the line to the distinctive story forms that humans seem able to generate and enjoy but that other related creatures, such as the bonobos studied by Sue Savage-Rumbaugh, can do only primitively?[13]

Bakker also tells of other human-utahraptor similarities such as how she and her kind together or apart predate more efficiently when not alone. He tells early of sibling rivalries which differed according to lifestage and how the individual mature animal works out competing strivings toward mates *vs* alliances with kin who share genes. He knows the selfish gene theory of Hamilton, Dawkins and Trivers, illustrating their theories and findings. Some of the dramatic twists of the book's plot feature Red Raptor's confusions about loyalties towards kin *vs* sexual-mating urges. Will helping her sister's chicks (strivings toward inclusive fitness) win out over less certain but more direct investment in her own offspring via a mate? For me an even more interesting conjecture is that the ancient genomic sequences pushing them for mating and other conspecific relating probably exist presently in humans as well, but deployed differently according to our different attributes.

Moreover, relevant for John Price and another ASCAPian, Michael Waller, Bakker describes dinosaur depression in the psychology and physiology of defeat. He describes lekking gastonia bulls in combat (were they too found by Bob Gaston, the gifted amateur?). These thickly armored creatures like alligator-sized armadillos with very small brains engaged in sexual selection, competing for the attention of mating females. One bull who does not succeed becomes a food item despite his impressive armor. *"Raptor Red senses that this bull is*

special. He's not severely injured. He's not limping. But something is missing. "His light has gone out. "His eyes have a dull constant stare. He looks but doesn't focus on anything.... Inside his small gaston brain, this male has given up.... this is the third year he's left the mating grounds without a female consort, and his biological clock has wound down — he's genetically superfluous. The genes that run his behavior don't provide specific instructions for an elderly loser. Why bother? Even if he tries his best, his chances of fathering offspring next year are too low."

The relatively intelligent raptors were then able to find and butcher the defeated tired bull in a mudbath, relaxing his guard from defeat and tiredness. Using their stabilizing tails (and, as we know from megaraptor better than did the author when he wrote, broadly based feet), they aimed their extraordinary claws and agile bodies at his soft underbelly. So how does this fictional version of the ancient gaston relate to depression, to a state that John Price suggested is identical in low ranking birds and depressed people and that Leon Sloman calls involuntary subordinate strategy or ISS? If imbued with the ISS, one unconsciously takes on the demeanor of a defeated person who constitutes no threat nor rivalrous intent and one is all the more convincing because one doesn't consciously deceive.

Mike Waller suggests in his anthropomorphic depictions of natural selection that animals prune themselves from the tree of life. He believes that "comparator genes" *do* provide instructions for a loser; the instructions read, "You've lost. Go die." Rather, Bakker describes that the gaston bull relaxed his guard from weariness but did not actively suicide. As I read it, Bakker illustrated neither the ISS nor an actualization of Waller's comparator genes. Rather he told us of a third alternative, a commonsensical one: defeat, is an exhaustion theory for the gaston's state. It was no more motivated than a plant dying from lack of water. Winning energizes. Losing doesn't. Stress on a system reduces immune and other functions, but this does not mean it purposefully self-destructs. When John Price and Leon Sloman talk of ISS, they refer to a state that mimics defeat, not defeat itself, though the physiologies of the two states may overlap in a manner deleterious to the individual.

Raptor Red encounters many other dinosaurs not mentioned here and we are introduced as well to early flowering plants and the abounding insects that coevolved with them. But of course most interesting for us involved in genealogy on this family-oriented visit to Mexico are Bakker's aegi, one of a hundred species of tiny, furred and bewhiskered insect-eating furball creatures, who mouselike lived underground and fearfully survived the tramplings of multi-ton creatures locked in mortal combat above ground. Still, despite our coming from that mammalian line, we can identify with Raptor Red's vertebrate story which ends with her finding a mate, having little ones and living happily ever after—well, for one or two million years more for her species. Her era was, after all, 45 million years before that Yucatan collision.

Our trip to Mexico on this vacation involved more than tijeretas-watching and our genealogy from 120 million years ago. A human family get-together happened too. Some of those assembled met for the first time, marriages had happened, busy lives evolved in farflung places. Reunion of seldom seen cousins were replete with videotape reviews; respected elders identified ancestral photographs. We feel better in Puerto Vallarta for having a family member who lives and has married in this otherwise foreign city; in my imagination at least, there is somehow less danger, I feel less alien, less outgroup. I have a personal storyline for the time being that has me safer than my status as a tourist alone gives me.

Moreover, on the last day of the Festival for Our Lady of Guadalupe when we arrived, we experienced the warmth and family spirit of Mexicans in the streets, completely occupying the cobbled pavement. Thousands of people joined in a common spirit, experiencing each other with mutual tolerance quite different from that of Raptor

Red and her non-mating, non-family utahraptor peers. They celebrated their common identity echoing a long-standing group storyline. The Virgin of Guadalupe is brown-faced and uniquely Mexican. Babies are all over, dandled and cosseted by mothers and fathers, grandmothers and grandfathers, other family members.

Love for one's offspring and related young was true of Raptor Red as well of course; one doesn't need a human sized brain for that nor for grouping. Even the small brained and armored gastons found protection in groups (many eyes despite the greater number of mouths) and we all know birds flock and also space from each other within flocks. How do such groupings and the human version differ? Human groupings involve storylines. Our family gathered to flesh in and to further its own story. The twelve day celebration of Our Lady of Guadalupe involved thousands of people on the cobbled streets of Puerto Vallarta all responding to a widely shared storyline. And those of us not sharing it directly nevertheless found ourselves respecting those who do.

And help is generously given to non-relatives, even those without the same language. One of our number was wheelchair bound and the cobbled streets of downtown Puerto Vallarta stimulated assistance from complete strangers, help quickly proffered, tips not an issue. Of course, payment as a means of reciprocal exchange is another storyline feature widely shared amongst humans. It helped perhaps, that some of our number were native born or fluently spoke the language, but fundamentally we were also tourists and contributed as a group to the welfare of the tourist town. So we felt treated well because the present day occupants of western Mexico calculate that tourist dollars help all of them and they build that into their cultural storylines. Plus they're nice people. We would have been treated less well 120 million years ago. Then we would have been food items only, dispatched quickly by those enormous claws. *c8*

ABSTRACTS & EXTRACTS...

Volodymyr IP, DeBiasi M, Williams JT, Dani JA: Nicotine activates and desensitizes midbrain dopamine neurons. *Nature,* 1997;390:401-404.

Abstract: Tobacco use in developed countries is estimated to be the single largest cause of premature death. Nicotine is the primary component of tobacco that drives use, and like other addictive drugs, nicotine reinforces self-administration and place preference in animal studies. Midbrain dopamine neurons normally help to shape behaviour by reinforcing biologically rewarding events, but addictive drugs such as Cocaine can inappropriately exert a reinforcing influence by acting upon the mesolimbic dopamine system. Here we show that the same concentration of nicotine achieved by smokers activates and desensitizes multiple nicotinic receptors thereby regulating the activity of mesolimbic dopamine neurons. Initial application of nicotine can increase the activity of the dopamine neurons, which could mediate the rewarding aspects of tobacco use. Prolonged exposure to even these low concentrations of nicotine, however, can cause desensitization of the nicotinic receptors, which helps to explain acute tolerance to nicotine's effects. The effects suggest a cellular basis for reports that the first cigarette of the day is the most pleasurable, whereas the effect of subsequent cigarettes may depend on the interplay between activation and desensitization of multiple nicotonic receptors.

Luck SJ, Vogel EK: The capacity of visual working memory for features and conjunctions. *Nature,* 1997;390:279-281.

Abstract: Short-term memory storage can be divided into separate subsystems for verbal information and visual information, and recent studies have begun to delineate the neural substrates of these working-memory systems. Although the verbal storage system has been well-characterized, the storage capacity of visual working memory has not yet been established for simple, supra-threshold features or for conjunctions of features. Here we demonstrate that it is possible to retain information about only four colours or orientations in visual working memory at one time. However, it is also possible to retain both the colour and the orientation of four objects, indicating that visual working memory stores integrated objects rather than individual features. Indeed, objects defined by a conjunction of 4 features can be retained in working memory just as well as single-feature objects, allowing 16 individual features to be retained when distributed across 4 objects. Thus, the capacity of visual working memory must be understood in terms of integrated objects rather than individual features, which places significant constraints on cognitive and neurobiological models of the temporary storage of visual information.

Kamil AC, Jones JE: The seed-storing corvid Clark's nutcracker learns geometric relationship among landmarks. *Nature,* 1997;390:276-279.

Abstract: Many animals regularly return to particular locations such as hives, nests, wintering grounds, or cache sites. This ability clearly implies that animals possess information that allows them to find a route from their current location to their goal. However, the nature of this information is, in many cases, unknown. One particularly important issue is whether this information encodes at least some of the geometric relationships among real-world objects, which would meet a strict definition of a cognitive map. Are animals sensitive to such geometric relationships? Although there is clear evidence that animals can learn vectors that represent a goal location in terms of absolute distance and direction to a landmark, there is little evidence of any ability to extract abstract geometric rules. Here we report data demonstrating that the corvid Clark's nutcracker *(Nucifraga columbiana)* can learn to find the point halfway between two

landmarks that vary in the distance that separates them. This learning is based on a general principle, as the birds correctly find the halfway point when the landmarks are presented with new distances between them. This demonstrates the ability to find the halfway point when the landmarks are presented with new distances between them, this demonstrates the ability to find a point defined not by the relationship between a goal and a landmark, but by the relationship between landmarks. Further experiments demonstrate that there were 2 distinct processes involved in locating the halfway point, the use of directional bearings to find the (hypothetical) line connecting the landmarks and finding the correct place along that line.

Brambilia R, Gnesutta **N, Minichiello L, White G, Roylance, AJ, Herron CE, Ramsey M, Herron CE, Ramsey M, Wolfer DP, Cestari V, Rossi-Arnaud C, Grant SGN, Chapman PF,** Lipp **H-P, Sturani E, Klein R: A role for the RAS signalling pathway in synaptic transmission and long-term memory. *Nature,* 1997;390:281-285.**

Abstract: Members of the Ras subfamily of small guanine-nucleotide-binding proteins are essential for controlling normal and malignant cell proliferation as cell differentiation. The neuronal-specificguanine-nucleotide-exchange factor, Ras-GRF/CDC25Mm, induces Ras signalling in response to Ca^{2+} influx and activation of G-protein-coupled receptors *in vitro,* suggesting that it plays a role in neurotransmission and plasticity *in vivo.* Here we report that mice lacking Ras-GRF are impaired in the process of memory consolidation, as revealed by emotional condition-ing tasks that require the function of the amygdala; learning and short-term memory are intact. Elec-trophysiological measurements in the basolateral amygdala reveal that long-term plasticity is abnormal in mutant mice. In contrast, Ras-GRF mutants do not reveal major deficits in spatial learning tasks such as the Morris water maze, a test that requires hippocampal function. Consistent with apparently normal hippocampal functions, Ras-GRF mutants show normal NMDA (AAmethyl-D-aspartate) receptor-dependent long-term potentiation in this structure. These results implicate Ras-GRF signalling via the Ras/MAP kinase pathway in synaptic events leading to formation of long-term memories.

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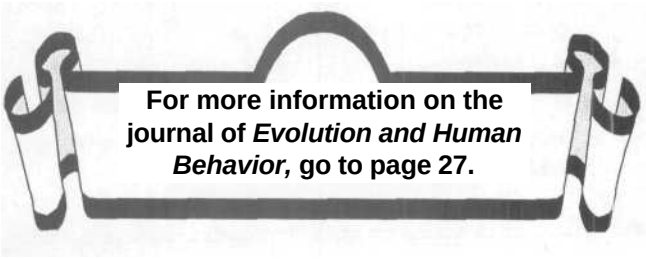
de Waal FBM: The chimpanzee's service economy: Food for grooming. *Evolution and Human Behavior,* 1997; 18(6):375-386.

Abstract: Evidence is presented that the reciprocal exchange of social services among chimpanzees *(Pan troglodytes)* rests on cognitive abilities that allow current behavior to be contingent upon a history of interaction. Food sharing within a captive colony of chimpanzees was studied by means of 200 food trials, conducted on separate days over a 3-year period, in which 6,972 approaches occurred among the 9 adults in the colony. The success rate of each adult, A, to obtain food from another adult, B, was compared with grooming interactions between A and B in the 2 hours prior to each good trial. The tendency of B to share with A was higher if A had groomed B than if A had not done so. The exchange was partner-specific, i.e., the effect of previous grooming on the behavior of food possess-ors was limited to the grooming partner. Grooming did not affect subsequent sharing by the groomer, only by the groomee. The effect of grooming was greatest for pairs of adults who rarely groomed. Nevertheless, the effect was general: 31 dyadic directions showed an increase in sharing following grooming, and only 11 had a decrease. Food possessors actively resisted approaches by individuals who had not groomed them. After food trials, there was a significant reduction of grooming by previous possessors towards those individuals with whom they had shared.



For more information on the journal of *Evolution and Human Behavior,* go to page 27.

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***A Coherent Hypothesis of Affective Disorder, Schizophrenia, & Schizo-Affective Disorder* - page 6**

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