For evolutionary psychiatrists, psychologists and others interested in sociophysiological Integration

ASCAP

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"The embryo ... is to me the most beautiful thing in the world, quite exquisitely beautiful, and the idea that one could eventually describe how it is formed and grows just in terms of molecules and genes and pathways doesnt detract from the beauty at all, makes it more awesome, in fact." Brigid Hogan[1]

Contents

[1] Wade N: In the ethics storm on human embryo research. *New York Times* D1-D7, Sept. 28 1999

The Across-Species Comparisons and Psychopathology (ASCAP) Newsletter is a function of The ASCAP Society & of The Psychotherapy Section of the World Psychiatric Association

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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 members and resources of various disciplines 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 behaviorthat have evolved over millions of years and that have resulted in psychopathologically 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, other news.

♦Proposals for new initiatives, joint research endeav ors, etc.

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The World Psychiatric Association is an organization of psychiatric societies aimed at advancing psychiatric and mental health education, research, clinical care and public policy.

The basic members of the WPA are 110 national psychiatric societies, representing more than 140,000 psychiatrists worldwide.

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ADDRESSED TO & FROM ...

Resubscription **2000**

We have had the 1999 subscription forms in the last page of each issue through the September issue (we have gathered new recruits throughout the year), so that some of you — happily — have resubscribed already, probably by accident. But thank you — we express strong reinforcement for such quick help and you have paid for the next year, regardless of the increased fee described below; your promptness means you have saved $5.

As you all know we (Suzie and I and the headquarters for *The ASCAP Newsletter)* have moved to Madison, Wisconsin, far from the fiscal headquarters at UTMB in Galveston, Texas, our former abode. Ourtime there will be up this coming year and we have to steel our nerves to the facts that producing and sending the newsletter independently of institution will be more expensive. For that reason we are raising the annual cost to $55 of which $15 will continue to be dues for the World Psychiatric Association (WPA) Psychotherapy Section. Now $40 ($5 more than the former $35) will go to the expenses of the newsletter.

We are working out the details of the nonprofit organization that will in the future handle the organization. It has been incorporated in the state of Wisconsin but we are in the midst of requesting a tax-free status for the Neuropsychiatry and Social Brain Institute (NASBI).

In another new development, I have been in dicussion with John Price who graciously offered to share his European Editorship with others. I suggested instead that he become the Associate Editor in charge of regional editors and coordinators for the ASCAP Society on the one hand and for the Psychotherapy Section of the WPA on the other hand. We have a number of people now from abroad who are part of our group. In future issues an Associate Editor's column will reflect his work.

Russell Gardner, Jr.
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ASCAP in Hamburg

August 6 was by far the best and most rewarding day of that mammoth congress. Thank you ever so much for having me informed about this event. I thought I was a member of ASCAP but I couldn't find any proof for membership and therefore have decided to become a member of ASCAP now. The subscription and membership sheet I have is probably out of date since you have moved to Madison. Please inform me by e-mail where to send my contribution.

It was a pleasure meeting you and other ASCAP members.

Detlev Ploog
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Did Tiger and Fox meet in the zoo?

Did I mention that debate in *Harper's Magazine* in a recent issue between Lionel Tiger and Barbara Eisenreich? It's on gender, mostly, and there are sparks from beginning to end. A friend of mine in Nebraska recently pointed out that you don't see girls playing pick-up basketball in the playgrounds like you see guys. A few maybe. But Eisenreich would have us believe that gender is strictly a cultural matter. There's plenty of biology in it, seems to me, and yet of course culture is part of it too. But so many these days are ignoring the deep history of the species. Anyway, it's an interesting debate in HARPER'S. I've been a fan of Tiger's ever since I read *The Imperial Animal* maybe 3 decades ago. Also heard somewhere that he met Robin Fox at a zoo, but that can't be right.

David Evans
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Missed ASCAP at HBES

I missed having the ASCAP meeting at HBES this year. I really have enjoyed a meeting that is focused on helping people, something that HBES doesn't offertoo much of. I wont have been able to make it to the other ASCAP events this year; I hope they go well. I'm sure we'll get the usual detailed report in the newsletter.

Anyway, I just wanted thank you for having the ASCAP meetings at HBES in years past. It's always nice to start off a conference with good conversation and good karma.

Ed Hagen
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Living mechanics of evolution

H. Allen Orr suggests that, faced with environmental change, organisms can evolve through a mix of many minute genetic tweaks, a lesser number of moderate changes, and a few major mutations. The new idea runs counter to standard theory on evolutionary genetics, which holds that only the tiniest of genetic changes contribute to adaptation.

This is NOT such a big deal; after all, Chuck was a saltationist until late in his career.

We are confused by our assumption that a big change is random, in which case the analogy with TV sets or jet planes holds. However, BIG changes may consist of the recall of prior experiments. Some of that junk" in our DNA may be sequences that were useful in earlier times and may be activated or inactivated in large sequences. (Weiner refers to some of these possibilities in *Time, Love Memory,* which ought to be required reading along with Nancy Segal's *Entwined Lives* and Dave Cohen's *Stranger in the Nest.* These are cited in September *ASCAP Newsletter)*

The jet plane is not randomly changed but an earlier, vacuum tube transponder is switched back into service if an atomic blast or a sun spot (another atomic blast!) makes the semiconductor edition worthless. Or, as in the case of growing functional eyes on a fly's wing, the transponder is moved from the cockpit to the lavatory without disrupting connections to ground control.

Finally, our "reworking an engine from scratch" is a poor analogy because living units are coded in ways that allow mutual recognition. In the analogy, regardless of where we put the fuel pump, it would seek its own connections to the gas tank and fuel injectors.

In regard to rapid changes, I'm thinking especially of heat shock proteins that ordinarily work against deformation of other proteins but, once distortion passes a certain point and the stress passes, will protect the mutated form. Heat, radiation, and starvation — I believe these are some of the stressors and all of them appear to be evolutionarily relevant.

The importance also lies in the nature of the deformations—they are not apt to be random but, as a function of electrochemical bonding, will change in an orderly fashion. If so, then a male and a female subject to the same disruptions may express the same mutated phenotypes. It has already been shown that such things breed true if, with human intervention so far, they are kept alive and mated.

Of course, another route for BIG changes is with viral free riders (retroviruses?) that would infect both males and females and have some effect on the older genome for each sex—another "Story."

Jim Brody
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Contained Replicator Selection Problem.

I have a question that I would love you to publish, if possible:- Genes, cells, organisms, organism groups and meta groupings are all contained WITHIN each other like a set of Russian Dolls, within nature, and they can all reproduce themselves.

This produces what I have termed "The Contained Replicator Selection Problem."

If A is a subset of B and both A and B can reproduce, then A has three different strategies to reproduce itself:
1. Reproduction of A only within B.
2. Reproduction of A only when B reproduces.
3. Reproduction of A within AND with B (both 1&2).

If any unit A or B is to be selected, it must have more representations of itself in a population than its competitors A' and B'. This must push the reproduction of any one unit to a maximum level in any population for it ever to be selected.

Question:-
If A is to be selected what solution does it opt for 1,2, or 3?

John Edser
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WPA PSYCHOTHERAPY SECTION

Notes from Psychotherapy Section Chairman, Russell Gardner, Jr.

We have an active section. Piero De Giacomo quickly started the ball rolling with his noting that the Paris Conference would be a good one for us to attend. John Price agreed to lead the endeavor, although as he notes below, we are too late for a formal symposium. Please respond to his request if you can go to that meeting.

I immediately thought of the annual American Psychiatric Association meeting that will occur next year in Chicago (not far from Madison), but alas, we are too late there too for symposium or course requests (deadlines are in early June) **But let us plan ahead and begin now thinking of the the 2001 meeting as the deadlines for that will be in early June of 2000.**

Please tell us of other meetings that we should consider. Some of our European colleagues, for instance, noted several at which we might have a presence. But I noted them inadequately and need your reminder of what they are. Write in and tell us.

Some other groups that we might consider stem from my gathering meeting announcements in Hamburg. These are not meetings that I at this moment intend to attend, but feel I must let us think about them. They include:

The Mexican Psychiatric Association meeting in its 17th National Congress at Melia Cancun Hotel, Quintana Roo, Mexico, November 16-20,2001. This meeting is in collaboration with the Regional Symposium of the WPA and the Regional Mexico-Centroamerican Meeting of the Latin-American Psychiatric Association. MPA President is Dr. Enrique Camarena Robles. MPA address is Periferico Sur 4191, Ier Piso, Jardines del Pedregal, C.P.01900, Mexico, D.F.

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In thinking about why I mentioned the next one, we must remember that there is nothing unbiological about psychotherapy.

The Seventh World Congress of Biological Psychiatry will occur 1 -6 July 2001 in Berlin, Germany. Host Organizers will be the 'world Federation of Societies of Biological Psychiatry and the German Society of Biological Psychiatry. Submission deadlines for Symposia, Teaching Courses, and Pro-and Con-Debates is November 15, 1999 if on paper and November 30, 1999 if electronic via the internet. Deadlines for Papers and Posters are October 20,2000 (paper) or October 31 if electronic.

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John Price calls for papers for the Paris WPA Conference: Rethinking Psychiatry

I have now got the "Second announcement" of the Paris conference on "Rethinking Psychiatry" (June 26-30,2000). We are too late to arrange a symposium, but individual papers are accepted until December 15. Also then the registration fee goes up. Abstracts have to be submitted in both French and English. On the whole, Antonia and I are inclined to go, so we would be glad to hear from any other Ascapians who are also going. We have to put our papers into one of their headings, and since they do not offer a heading of "evolutionary psychiatry", I suggest we all choose the heading 3f. 3 is "interdisciplinary issues in research" and the subheading f is "psychopathology, cognition, emotion and behaviour". If we choose that, we might find ourselves speaking on the same day, and, hopefully, in the same session.

Piero De Giacomo gives more Paris information

I send data about the conference in Paris we spoke about in Hamburg. In case the section decides to participate I would like to present some material:
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http://psydoc-fr.broca.inserm.fr.
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ARTICLE:

by Tyge Schelde

A Perspective on Manic-Depressive Disorder: Behaviorai, Physiological, and Genetic Implications

On the whole I agree with what Russell Gardner wrote in his 1982 paper,[1] especially with the paragraph of "The Inherited Weak Link in Those Vulnerable to Bipolar Illness." However, I am not sure whether manic-depressives are characterized by fixed action patterns or stereotypies. At any rate they do not show motor stereotypies like the schizophrenics.

I admit that there may exist ruminations, particularly in depressed patients, but such stereotypies are difficult to determine by systematic observations. I would rather say that their social and motor behaviors are so inhibited that there are no visible stereotypies.

I will take the starting point in your abstract: Bipolar states are *triggered* unusually easily and *maintained* unusually rigorously in spite of social reality. They are *genetically* transmitted via mechanisms that enhance this ease of onset and rigidity of maintenance.

I will formulate my ideas in the following paper:

Hypothesis: An increased glutamatergic activity plays an important role in manic-depressive disorder. This activity causes easy depolarization of cortico-limbic pathways, for their high arousal level, and fora long-term potentiation of the relevant circuits. The depolarization state corresponds to an increased sensitivity of the entire nervous system. The extended degree of depolarization probably results in manic and depressive seizures being *"triggered unusually easily," and* the long-term potentiation likely explains why these attacks are *"maintained unusually rigorously in spite of* social reality."[1]

Having studied the behavior of depressives, schizophrenics, and controls on the wards of Frederiksberg Hospital for 12 years, it struck me that it might be possible to build a bridge from behavior to physiology.

Behavioral Patterns of Schizophrenia and Major Depression

1. *Schizophrenics* are characterized by:[2]
nonblinking staring
a high motor activity (p<-05) a flat facial expression a flat social interaction autistic talking to themselves autistic smiling to themselves autistic laughing to themselves body stereotypies bizarre behavior physical aggression now and then.

2. Endogenously depressed patients never showed such behaviors.[3, 4, 5]
in some cases depressives breathed heavily (sigh, groan), a behaviorthat was not observed in schizophrenics.

Possible relevant physiology of the two groups.

The just mentioned behaviors not only seem to be simple differences, but also diametrical contrasts between schizophrenics and major depressives (presence, not presence). Since behavior is supposed to reflect brain physiology.and since schizophrenia and depression seem to exhibit a number of antagonistic behaviors in couples, it may be hypothesized that the two diagnostic groups may be opposite in a particular physiological parameter. Several investigations have pointed to a reduced glutamate release or a reduced glutamatergic activity as a characteristic trait of schizophrenia.[6, 7, 8, 9, 10] From this follows that

major depression might be characteristic of an increased glutamatergic activity. This hypothesis probably not only includes major depression, but also mania, as demonstrated below. Thus, *alow-glutamatergic activity hypothesis* is suggested for **schizophrenia,** and a *high-glutamatergic activity hypothesis* for **manic-depressive disorder.**

Physiological Dynamics of Schizophrenia.

1. Reduced glutamatergic activity.

According to the hypothesis, the release of glutamate from the vesicles of the glutamate cells is reduced *or* the density of various glutamate receptors is diminished, e.g. the density of ionic NMDA receptors, metabotropic NMDA receptors, AMPA receptors, or kainate receptors.[11] This arrangement results in less than optimal stimulation of cortical pathways.

2. Development of atrophy.

The consequence during the development of the disease is atrophy among cortical cells leading to enlarged ventricles and possibly also hypo-frontality.[17] At the same time this atrophy is probably responsible for the schizophrenics' well-known reduced sociability and their dysfunctional way of thinking, e.g. paranoia, delusions, and hallucinations.

3. Increased body mobility, including stereotypies.

The low glutamatergic activity is also thought to contribute to the increased body mobility of schizophrenics (their body mobility is significantly higherthan that of depressives and that of controls).[2] The weak glutamatergic activity stimulates the puta-men in the basal ganglia. The stimulus is propagated through the basal ganglia via two GABA pathways, one glutamate pathway, and one GABA pathway ending up in thalamus. As the GABA inhibition here is weak, the glutamate output from thalamus to the motor cortex is extraordinarily great. This may explain the increased body mobility, including stereotypies.[8,12,13]

4. Increased dopaminergic activity.

Finally, an increased dopaminergic activity should be mentioned as an important physiological parameter in schizophrenia. "According to the low-glutamate hypothesis, the high activity of dopamine is not surprising. In putamen, dopamine (DA) and glutamate (Glu) pathways compete so as to establish a DA/Glu balance. When Glu is low - as in the case of schizophrenics - the balance will be abolished, and the DA activity will dominate.

Physiological Dynamics of Manic-Depressive Disorder

1. Elevated glutamatergic activity.

According to the suggested hypothesis, manic-depressive illness is physiologically caused by either an increased release of glutamate or by a higher glutamate receptor density than with controls.[15, 16, 17] The receptors in question may be ionic NMDA receptors, matabotropic glutamate receptors, AMPA receptors, or kainate receptors.[18, 19, 20, 21]

2. Triggering and maintenance of depression and mania.

In this paragraph I deal with Russell Gardner's two statements: Depression or mania are *a) "triggered unusually easily",* and are *b) "maintained unsusually rigorously in spite of social reality."*

As far as I can see these specific qualities (dysfunctions) depend on an **elevated glutamatergic activity** and on the ability of such an activity to cause an increased **depolarization** (compared to the resting potential) and finally on a **high arousal level** maintained as what is called **long-term potentiation (LTP)** of specific nervous circuits considered to be responsible for either depression or mania.

The immediate effect of the increased glutamatergic activity is a more or less constant excitation of probably cortical, mesocortical, and limbic circuits. This causes a more or less pronounced depolarization

of the nervous cells in question. This depolarization corresponds to an increased cell sensitivity which means that action potentials are more easily provoked than in controls *(triggering mechanism).* Repeated glutamatergic stimulation of the nerve cell brings its arousal level up to a tetanus-like state. After that follows a very long period of post-tetanic potentiation or long-term potentiation (LTP).

This state of long-term potentiation is probably the basis of the *"rigorous maintenance"* of both major depression and mania; to express it by a metaphor, *The joint construction of a depolarized nervous system and its long-term potentiation is the sounding board on which manic-depressive illness plays its euphoric and melancholic tunes.*

2. Detailed potentiation mechanism.

The mechanism of the long-term potentiation can be described in detail as follows.[22] The release of the neurotransmitter glutamate opens a non-(N-methyl-D-aspartate (NMDA) channel, allowing an influx of sodium, which depolarizes the neuron, i. e., the neuron becomes more sensitive to incoming stimuli. If a further release of glutamate occurs while the cell is depolarized, glutamate opens the ionic NMDA channels, which allows calcium to flow in. This results in a still greater sodium influx through the non-NMDA channels and a subsequent greater depolarization, which leads to long-term potentiation.This account is valid for normal conditions. Hence, it is understandable that LTP can easily arise with an extended glutamatergic activity.

4. Changing manic and depressive episodes.

An important heuristic problem is that the same person can develop mania at a certain period, and depression at another. I had some difficulty about this problem in my earlier paper in The ASCAP Newsletter. [23]

After reconsidering, I think a plausible answer can be given relating to two concepts:

1. The above described increased tendency to *depolarization* (~precondition of *triggering),* and *long-termpotentiation (rigorousmaintenance)* is the basis of mania or depression.

2. So-called *action-specific energies,* which means that certain stimuli are responsible for the stimulation of quite specific or typical nervous pathways.are the basis of what direction the extended depolarization takes: hypomania, mania, agitation, or depression. Rewarding stimuli might bring about mania, dejecting stimuli or long-term stress might release depression.

5. Specific nervous circuits and tentative physiological interactions of depression and mania.

Probably, rewarding energies affect certain nervous circuits in the brain, e.g., cortico-basal ganglia circuits (substantia nigra, nucleus accumbens, septum) related to rewarding feelings, and cortico-limbic circuits passing through amygdala that mediate fear, anxiety, and maybe also depression. Investigations have documented that depression is correlated to decreased dopamine levels,[24, 25] and probably also to an increased acetylcholine activity.[26, 27] The low dopamine levels may be explained by a considerable glutamatergic corticostriatai tone which stimulates putamen in such a way that the dopaminergic activity is suppressed. On the contrary, mania is correlated to elevated dopamine levels (higher than those of controls).[24]

This connection seems difficult to understand. However, the following seems a reasonable elucidation of it: like depression, mania is based on an increased glutamatergic activity and depolarization of certain neural circuits. Mania probably follows other pathways than depression. Tentatively, such other pathways might stimulate substantia nigra and maybe also nucleus accumbens and septum (center of reward). Although — like in depression—there

is still a rather great glutamatergic stimulation of putamen, the dopaminergic activity may prevail compared to the glutamatergic one. The fact that dopamine areas are stimulated accounts for the elevated dopamine level in the brain. An increased dopaminergic activity in thalamus will lead to an increased glutamatergic stimulation of the motor cortex that may contribute to extra motor energy. At the same time, dopamine inhibits acetylcholine. Although this explanation is tentative, the hypothesis might contribute to further experimental explorations of possible *specific* physiological interactions in depression and mania.

6. Kindling.

Kindling is a neural phenomenon I define as follows: when a number of attacks either of mania or depression have taken place, subsequent seizures will be released more easily, and eventually, they release spontaneously (i.e., without influence from external stimuli). In other words, the nervous system becomes more vulnerable. Episodes beget episodes.[2829]
Long-term depression or mania seem to reflect an evolution from

1. a stimulus-evoked stage *(developmental* stage) to
2. a full-blown stage after several stimulationsfcomp/etecf *stage)* to
3. a stage where seizures occur without the influence from external stimuli *(spontaneous stage).*

Thus a serious problem forthe central nervous system results from spontaneous depression or mania: during the gradual development from stimulus-evoked seizures to spontaneous seizures, an oncogene, c-fos, activates. This has a genetically determined influence on the nervous system, so that mania or depression can subsequently be more easily evoked.

In detail, the c-fos effects are the following: the mRNA for c-fos translocates to the ribosomes where the fos protein is sythesized. The fos protein feeds back on the nucleus where it activates an AP-1 binding site on DNA leading to transcription of mRNAs for peptides, neurotransmitters, receptors, enzymes, and growth factors. It is obvious that such a radical change may influence nervous circuits in a considerable manner.

This conceptual model suggesting that "episodes beget episodes" highlights the importance of early intervention. A continuous lithium treatment from the onset of the disorder has great importance. Discontinuation of lithium maintenance may indeed induce a lithium-refractoriness. Therefore, early treatment and maintenance apparently also constitutes long-term prophylaxis.

7. Suppression of affective disorders in their three phases.

The above account involves that it may be feasible to suppress affective disorders in their

1. early *developmental phase* and their
2. mid or *completed phase,* whereas it may be a problem to beat down the disorder in its
3. late *spontaneous phase.*

Atropine and the glutamate antagonist MK-801 inhibit the developmental phase, but not the completed phase. Carbamazepine and diazepam block the completed phase of amygdala-kindled seizures, but not the spontaneous phase. Thus, at this time, electroshock (ECT) seems the only treatment for the spontaneous phase of severe depressions.

Lithium has played a role as a mood stabilizer for about 50 years since Cade discovered its effects in 1949.[14] During some days, increased doses of lithium are able to stop a manic phase. And it has a prophylactic effect against depression. Lithium may act on the receptors of the cells and indirectly on phosphatidylinositol in the cell membrane thus making it less permeable.[36] A patient told me that he could relieve his depression by taking an extra amount of lithium. If this generally holds true it might be relevant for the various functional types of depression: completed and spontaneous types would need higher

doses of lithium than the developmental type.

8. Hypo-frontality.

Scannings have shown that depression or melancholy is characteristic of hypo-frontality, i.e. a relatively low blood flow in the frontal cortex.[30] However, the medial and the occipital cortex show an increased blood circulation and glucose metabolism. The reason forthe low blood flow in the frontal cortex is unknown, but one might speculate as follows:

1. The acetylcholine system may have been so highly aroused that it has inhibited itself to a certain degree by presynaptic, postsynaptic,[26] or negative feed back inhibition[13] This might reduce the frontal cortical blood flow.
2. The noradrenergic system may have been stimu lated to a high arousal level so that the contraction of the capillary vessels to the frontal cortex has become increased, thus in the same way reducing the frontal blood flow.

The high metabolism of the medial and the occipital parts of the cortex may influence pathways passing the amygdala (anxiety-depression). The long-term potentiated acetylcholine system (together with glutamate) also influences circuits which affect the basal ganglia (putamen and globus pallidus).Here they exert a powerful stimulation. But in thalamus this stimulation is converted to a weak one. Hence, the glutamatergic pathway leaving thalamus and proceeding to the motor cortex is weakened and not able to stimulate the motor cortex sufficiently-which might contribute to the well-known motor inhibition of depression.[12]
The frontal cortical inhibition probably represents intellectual retardation in depression (difficulty in making decisions, and retardation of answers). It may also contribute to the motor inhibition because of a weak stimulation of the motor cortex.

9. Diurnal rhythm.

A strange feature of major depression is that it manifests itself by diurnal rhythms showing morning agony and evening remission. A glutamatergic hypothesis might explain this phenomenon:

1. During the night/sleep there is probably an accumulation of glutamate in an increased number of vesicles in the glutamate producing cells.
2. In the morning when the depression vulnerable person wakes there will be an abnormally high release of glutamate causing a marked depolar ization and a long-term potentiation of depression pathways.
3. In the evening the release of glutamate vesicles has decreased which might be the background of remission. Of course such an explanation is tentative.

10. Suggested treatments.

Attacks of mania can be treated with large doses of lithium or haloperidol (in the last respect mania reminds one of schizophrenia that —among other agents — is also treated with haloperidol. This treatment should be followed up by anti-glutamatergic agents to reduce the glutamatergic activity. Mild to moderate depressions might be treated with TCA and SSRIs together with an anti-glutamatergic treatment. As for severe spontaneous depressions, ECT seems to be the best treatment. Probably, the working mechanism of ECT is a great release of NPY which inhibits the glutamatergic activity.

Possible Genetic Etiology

If manic-depressives have a glutamatergic activity higher than that of controls it may principally be caused by two dysfunctions:

1. A genetically determined fault in the enzymes glutaminase orglutamic dehydrogenase. Glutaminase converts glutamine to glutamate[13] and glutamic dehydrogenase converts alpha ketoglutaric acid to glutamate.[31] This fault might be responsible for an increased production of glutamate.
2. Another possibility might be a genetically deter mined fault in glutamate receptors so that there is an increased number of a certain type of receptor, e. g. N-methyl-D-asparte receptors.[18, 19, 20, 21]

The chromosomal mechanism responsible for both a glutaminase dysfunction and a glutamate receptor dysfunction might be a skew crossing-over between two homologous chromosomes in the meiotic phase: one chromosome would lose its glutaminase site (schizophrenia), the other would get an extra one (manic-depressive disorder). In the same way a skew crossing-over between two homologous chromosomes containing a site for the formation of a certain type of a glutamate receptorwould remove such a site from one chromosome (schizophrenia) and add an extra one to the other (manic-depressive disorder).

Whether the problem is an increased release of glutamate or a dysfunctioning glutamate receptor is difficult to determine. In schizophrenia it seems to be the amount of brain glutamate that is reduced.[6] Hence, manic-depressive disorder might be characteristized by an increased amount of glutamate. If this is the real situation we may return to the enzymes glutaminase or glutamic dehydrogenase as the possible molecular-biological background of the two diseases.

If a chromosomal mechanism like the above described (a chromosome anomaly) is really the origin of both schizophrenia and manic-depressive disorder, it may explain the fact that both diseases occur with a world prevalence of about 1% (each time a schizophrenic chomosomal anomality arises, then also a manic-depressive one is formed).

If for instance an abnormal male gamete with two glutaminase sites meets a normal female gamete, then the result will be a zygote with three glutaminase sites, i.e. a manic-depressive predisposition. If a gamete lacking a glutaminase site is combined with a normal gamete, then the zygote will only contain one glutaminase site corresponding to a schizophrenic predisposition.

The normal mutation rate is 1:10000.[32] Therefore, a world prevalence of 1:100 in schizophrenics and manic-depressives indicates that these diseases from an evolutionary point of view, at least in some respects, represent positive survival values.

Evidence Of A Glutamate Hypothesis

So far I think it is possible to state a few examples that might support a glutamate hypothesis of manic-depressive illness:

1. Electroconvulsant treatment (ECT) is the best treatment of severe depressions. It releases large amounts of neuropeptide Y (NPY) and hereby stops kindling[15] which is dependent on glutamate neurotransmission.[29] It might be the anti-glutamatergic effect that is responsible forthe improvement of both severe depression and mania
2. The antiepileptic agent lamotrigine, which stabi lizes the membrane of the glutamate cells, has been reported to have both antimanic and antide-pressant effects.[16]
3. Polish pharmacologists have demonstrated that after a veratridine evoked glutamate release in rat prefrontal cortex, three antidepressant agents, desipramine, imipramine, and citalopram, had a considerable inhibitory effect on the release of glutamate.[17] Although SSRIs may have a certain antidepressant effect via serotonin *perse* they might exert their principal antidepressant effect by inhibiting the release of glutamate.

4. Down-regulation of NMDA receptors seems to play an important antidepressant role.[18, 19, 20, 21]

5. Finally, Post mentions that glutamate neurotrans mission appears critical to the development, but not expression of the kindling process.[29]

Other Hypotheses

Since the establishment of the **monoamine theory** concerning depression and mania in the 1960s, depressions have been treated by monoamine oxidase inhibitors (MAO-inhibitors) andtricyclicantidepres-sants (TCA). Since the 1980s, selective serotonin reuptake inhibitors (SSRIs) have been used to an increased extent. Mania, equivalent to increased levels of dopamine, is normally treated with lithium or haloperidol.[24] With respect to haloperidol, its used for the treatment of mania resembles the treatment of schizophrenia.

During depression all three monoamine systems:

dopamine, serotonin, and norepinephrine show decreased amounts of brain monoamines or low values of their metabolites in the cerebrospinal fluid, which would correspond to a dysfunction of the systems. Moreover, it has been possible to treat depression by interfering with one of the amine systems selectively, only one at a time. But parsimoniously, it seems difficult to understand that all three transmitter systems should be dysfunctioning at once. In other words how can we understand all three monoamines to constitute a joint cause of depression. Contrariwise, I am inclined to follow Carisson et al.'s 1991 statement that glutamatergic-cholinergic pathways are capable of strongly suppressing the responsiveness of monoam-inergic receptors and monoaminergic transmitter release.[9] This means that the decreased monoaminergic activity is not itself a dysfunction *perse,* but rather a consequence of a superordinate depression factorthat influences each of them. *These phenomena in my view indicate a glutamatergic-cholinergic cause of depression rather than an unparsimonious monoaminergic one.*

The glutamate hypothesis emphasizes that the physiological core of depression is a glutamatergic dysfunction that involves psychomotor inhibition. According to Carisson et al, "glutamatergic pathways in cooperation with cholinergic pathways are capable of inhibiting psychomotor activity."

Janowsky et al in 1994 suggested an **acetylcholine hypothesis** as the dynamic cause of depression: a high arousal level of acetylcholine would be equivalent with depression.[26] They mention a Charles et al study that found patients with major depression responded more significantly than controls to physostigmine, an agent which increases central choline. "The study by Charles et al. therefore suggests that presynaptic cholinergic overactivity may be associated with depression." In this context I underline that such a presynaptic cholinergic overactivity might be identical with an increased activity of glutamate receptors situated on the presynaptic acetylcholine cells.

Summary

One might *tentatively suggest* that the mechanism of manic-depression illness as follows: during various stress situations the high glutamate level causes a depolarization, especially of acetylcholine. By further glutamate release, specific cholinergic circuits will become long-term potentiated, i.e., the pathways maintain their high arousal level and the process is difficult to stop. A certain cortico-limbic circuit might result in depression, and a cortico-striatal one in mania. According to El-Mallach et al., a mania starts with a weakly depolarized state, whereas the depolarization of depression is greater.[34] However, by repeated stimulation the depolarization of mania will be increased so that it resembles that of depression. In such a situation mania may switch over to depression as fast as during one night (information from a patient).[35]

The glutamate hypothesis *predicts* that depression or mania may be treated by

1. an efficient braking of the long-term potentiation of the respective nervous circuits (large, repeated doses of diazepam[29] or anticholinergica, e. g. scopolamine[26]), and
2. by simultaneous reduction of the outflux of glutamate by antiepileptica, e. g. lamotrigine16 and MK-801[29] (or SSRIs)[17] so that a following depolarization of depressive and manic pathways is less likely. Such a treatment may mainly be viable to patients in the early *developmental* phase or the mid *completed* phase where seizures are elicited by external stimulation.

However, there is a problem with patients who are in the late *spontaneous* phase where "exogenous stimulation is no longer necessary in order for seizures to be observed."[29] Probably, this state has been brought about by the consequences of the oncogene c-fos.[28] In such severe cases, ECT may be the only viable treatment. As mentioned above, ECT seems to exert its antidepressant and antimanic effect via neuropeptide Y (NPY) which stops kindling[15] that is dependent on glutamate neurotransmission.[29]

Thus, it seems possible that the inhibition of glutamate or glutamatergic receptors will be able to contribute to the treatment of manic-depressive disorder. Trullas et al suggest "that NMDA receptors may be involved not only in the mechanism of action of antidepressant drugs but also in the pathophysiology of affective disorders,"[18] and Papp mentions that "chronic antagonism at NMDA receptors may result in antidepressant effects."[19]

Conclusion

Based on the above, I conclude that a possible increased release of glutamate or a possible increased sensitivity of some kind of glutamate receptors may play an important role in mania and depression *together with* environmental action-specific energies that determine which neural circuits will be potentiated. As such, the hypothesis is consistent with the stress-diathesis theory.

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Article:

by Detlev W.Ploog

Psychiatry And Monkey Neuroethology

I began to study medicine In 1939, but was soon drafted and ordered to German-occupied France and into warfare against the Soviet Union. Despite the war I was able to complete my studies in March 1945 at the University of Marburg, the place where Luther and Calvin disputed about the iota. I did my medical thesis—an experimental study on thought processes—with Klaus Conrad, a professor of neurology and psychiatry and head of a unit for brain-injured soldiers, especially aphasics. This was the beginning of my life-long fascination with communication processes and their disorders.

One of the outcomes was an experimental paper on the time course of memory traces in brain atrophy and its relation to the unconscious. In the winter of 1948/49, during my training in neurology and psychiatry, I was sent to the Institute of Psychology at the University of Freiburg to study diagnostic testing. It was there that the turning point in my thinking occurred, and ethology came in. Konrad Lorenz and Erich von Hoist jointly held a one-week intensive course in ethology (Lorenz) and the brain mechanisms underlying innate species-specific behavior (von Hoist) such as swimming, flying, fleeing, attacking and ritualized behaviors of intraspecific communication (what Tinbergen called social signaling). I was very stimulated by this concept, went regularly to the nearby zoological institute to the seminars of Otto Koehler, who was then, in German circles, thought of as the father of ethology, and regretted not to be a zoologist.

Back in Marburg I tried to relate ethological concepts to psychiatry and psychopathology. My first presentation at a congress was on sleep and its relation to the major (endogenous) psychoses. I considered sleep to be an instinct whose disturbance is indicative of a cerebral mechanism that is also involved in psychotic behavior (1953). Afterwards there was a heated debate in which Richard Jung, the foremost neurophysiologist in Germany, attacked my concept. Nevertheless, he later asked me to write a comprehensive chapter on

Now what was the function of penile erection in the squirrel monkey? Was it used only for sex and reproduction, or was there more to it than that? I found a translucent cage that was well-suited for observing a group of six squirrel monkeys. A behavioral catalog was set up and a series of sociometric studies on two differently composed groups was conducted. Naturally, penile erection was used in copulatory behavior, but this was a comparatively rare event. In almost all cases penile erection occurred in conjunction with a rather conspicuous motor pattern: One thigh was bent, with supinated foot and spread big toe. No doubt this complex behavior pattern served as a social signal that was instrumental in establishing the hierarchical order in a group and each animal's individual role. Later on, in Munich, motion pictures of a newborn squirrel monkey showed the animal exhibiting the thigh-bending-big toe-spreading behavior from its mother's back towards an obtrusive group member on the day of birth (1963). This was further evidence that genital display is a ritualized behavior pattern evolutionally derived from sexual behavior but used as a powerful communicative social signal.

In 1962 I was able to establish the first laboratory for experimental studies on primate behavior and brain functions in Germany, at the Max Planck Institute for Psychiatry in Munich. There, in further brain stimulation studies, various types of vocalizations were elicited and animals next door responded to them. It became clear that vocalizations serve as social signals and are produced by specific brain structures. The first catalog of the squirrel monkey's vocal repertoire was worked out (1966). Among the great variety of calls, two warning calls were experimentally validated, one for aerial predators and one for terrestrial predators. Even newborn Caspar Hausers make this distinction (1973).

Concurrently the cerebral representation of vocal behavior was investigated (1970) and then further explored and refined by several co-workers for many years. Primates, including humans, share the phylogenetically old vocal cerebral system, which is hierarchically organized and leads from the anterior cingulate gyrus in midline structures down to the reticular formation, feeding oversome synapses into the nucleus ambiguus, which innervates the vocal cords. In humans, there is in addition a phylogenetically younger vocal system, running along the pyramidal motor pathway from the cortical laryngeal and oro-facial representation in the primary motor cortex to the respective motoneurons in the medulla oblongata. This direct connection serves as the neuronal basis for the voluntary control of the vocal folds and the articulators. This control appears to be a prerequisite for the evolution of speech. The monkey can use its whole vocal repertoire without the cortical primary motor system, but is unable to fractionate or segment its utterances into phoneme-like units. My hypothesis is that the last step in the evolution of the phonatory system is the outgrowing of the fine fiber portion of the pyramidal tract that serves the direct and fast innerva-tion of the speech apparatus. The (universal) phonemes in speech are species-typical articulatory gestures (1988).

In 1966, the research hospital of the Max Planck Institute for Psychiatry was opened. As its head I had the opportunity to put psychiatry, neurology and child neuropsychiatry, together with a department of psychology, under one roof. Baby talk and motherese was one of the major research topics in the children's department, along with speech disorders in preschool and school children. A neuropsychological research unit was concerned with phonatory and articulatory disorders in patients with neurological problems, and other groups investigated a whole spectrum of nonverbal communicative behavior patterns in patients with psychiatric disorders, including Parkinson's disease. The idea behind these and other programs was that a large proportion of mental and emotional disorders are disorders of the homo-typical communication system, which can become vulnerable in any of its different parts. I hoped that an evolutionary approach would help us to explain some of the mysteries in psychopa-thology.

In closing this brief sketch I'd like to mention someone whose visit to my office turned out to be a life event—as psychiatrists like to call events that are determining factors for the further course of a person's life. One day in 1963 a visitor named Schmidt announced his

visit over the phone. 1 had no idea who he was. It was Francis O. Schmitt, who had just created the Neuro-sciences Research Program at M.I.T. We talked for several hours, during which time I became very excited about his plans. Early in 1964 I was invited to give a talk. Thereafter the "Associates," the multidisciplinary advisory board of the NRP, voted for me and I too became an Associate. There were two meetings a year for reports, the exchange of ideas, and planning of work sessions. The two work sessions I held in 1967 and 1970 on "Primate Communication" and "Are Apes Capable of Language?" brought me together with the scientists in the forefront of the field. The Associates and their ideas were immensely important to me and the work in my institute. My deepest respect for and gratitude to the late Frank Schmitt.

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Sullivan A: What's so bad about hate? New ***York*** *Times Magazine Section,* Sept. **26,1999, pp.50**

Extract: Hate is everywhere. Human generalize all the time, ahead of time, about everyone and everything. A large part of it may even be hardwired. At some point in our evolution, being able to know beforehand who was friend or foe was not merely a matter of philosophical reflection. It was a matter of survival. And even today it seems impossible to feel a loyalty without also feeling a disloyalty, a sense of belonging without an equal sense of unbelonging. We're social beings. We associate. Therefore we dissociate. And although it would be comforting to think that the one could happen without the other, we know in reality that it doesn't. How many patriots are there who have never felt a twinge of xenophobia?

Of course by hate, we mean something graver and darker than this kind of lazy prejudice. But the closer you look at this distinction, the fuzzier it gets. Much of the time we harbor little or no malice towards people of other backgrounds or places or ethnicities or ways of life. But then a car cuts you off at the intersection and you find yourself noticing immediately that the driver is a woman, or black, or old, or fat, or white, or male. Or you are walking down a city street at night and hear footsteps quickening behind you. You look around and see that it is a white woman and not a black man and you are instantly relieved. These impulses are so spontaneous they are almost involuntary. But where did they come from? The mindless need to be mad at someone — anyone — or the unconscious of a darker prejudice festering within.

In 1993, in San Jose, Calif., two neighbors — one heterosexual, one homosexual — were engaged in a protracted squabble over grass clippings... The gay man regularly mowed his lawn without a grass catcher, which prompted his neighbor to complain on many occasions that grass clippings spilled over onto his driveway. Tensions grew until one day, the gay man mowed his front yard, spilling clippings onto his neighbor's driveway, prompting the straight man to yell an obscene and common anti-gay insult. The wrangling escalated. At one point, the gay man agreed to collecting the clippings from his neighbor's driveway but then later found them dumped on his own porch. A fracas ensued with the gay man spraying the straight man's son with a garden hose, and the son hitting and kicking the gay man several times, yelling anti-gay slurs. The police were called, and the son was eventually convicted of a hate-motivated assault. But what was the nature of the hate: anti-gay bias, or suburban property-owner madness? ....

[O]ne of the stranger aspects of hate is that the prejudice expressed by a group in power may often be milder in expression than the prejudice felt by the marginalized. After all, if you already enjoy privilege, you may not feel the anger that turns bias into hate. You may not need to. For this reason, most white racism may be more influential in society than most black racism — but also more calmly expressed.

Article:

by Russell Gardner, Jr.

Sex of Bronze Age Cretan Leadership

In August, Suzie and I joined her twin Lisa and my mother for travel to Athens, the Peloponnese, Delphi and Crete, thereby fulfilling a dream of a lifetime -- in my mother's words, but for me as well as her. There's no substitute for being there as the actual sculptures or frescoes bring home the fact of our cultural forebears either viewed still on site or nearby (as in the museums). Marvelous books seen in their museum bookstores may not be easily available here in the U.S. Things I learned in Greece connected nicely with previous professional meetings in Hamburg, Germany (Congress of the World Psychiatric Association).

For example, in a symposium put on by our psychotherapy section, Marco Bacciagaluppi told a more complicated story of social rank hierarchy stemming from agriculture and accumulated resources than the idea conveyed by Robert Sapolsky in a column of *USA Today* reprinted in part in a previous *ASCAP.* This generally believed formulation holds that the human accumulation of resources with the advent of agriculture fomented social rank distinctions in humans because such resources could foster those attaining alpha status to maintain it for themselves and their descendents. I noted in discussion of this that John Calhoun, a MacLean associate of 50 years ago, had showed this effect in rats though unwitting, he had taken the findings in another conceptual direction.

Marco introduced the following complexity: when the female goddesses (and female leaders perhaps) held sway — as was the case early on — the effect didn't show. That is, such early societies showed no evidence of warfare nor the need to fortify against the attacks of others. Hedonic societies apparently existed for several millenia after agriculture's advent in association with the worship of pregnant female goddesses. But then, later on, we presume that have-nots equipped with masculine leadership and the means to prevail - perhaps new warfare tactics -assaulted the grainery stores.

Here is the first way in which Grecian travels amplified this point about competitive societies: I found a quote of how this may have worked captured by this story about Sfakia, Crete, by Adam Harding quoted in the *Rough Guide to Crete,*[1] *"...God had given [many gifts] to other parts of Crete — olives to Ierapetra, Ayios Vasilis and Selinou; wine to Malevisi and Kissamou; cherries to Mylopotamos and Amah. But when God got to Sfakia only rocks were left. So the Sfakiots appeared before Him armed to the teeth. 'And us Lord, how are we going to live on these rocks?' and the Almighty, looking at them with sympathy, replied in their own dialect (naturally): 'Haven't you a scrap of brains in your head? Don't you see the lowlanders are cultivating all these riches for you?'"* Perhaps the "catastrophe" that characterized devastation of many cultures in 1200 B.C. by "The Sea-Peoples" reflected such harvest.

Agriculture began approximately 10,000 years ago. Crete was certainly settled from 6000 years forward (by emigrants) but left particularly significant traces of how the early ones lived after the beginning of the Bronze age about 3000 years ago. Linear A and B scripts that were baked in disastrous fires seem to have recorded agricultural accounts not stories of a more literary kind. Linear A has yet to be deciphered but seems to render numerical records also.

Different and fascinating to me was the as yet uncoded Phaistos disk of 1700 to1600 B.C., which I saw in the Heraklion Museum and which I've come to know better because I purchased a book describing and analyzing it in great detail by Louis Godart, a French Archeologist who specializes in Cretan work.[2] Has anyone heard of the disk? I had not and on return home could find little reference to it in any of the books on related topics that I have at home nor those that I later inspected in the Madison Borders Bookstore. The exceptions were Will Durant's *The Life of Greece*[3 p 15] and the *Encyclopedia Brittanica.*

The disk is of fine clay also used for the Minoan eggshell vases. Forty-five unique signs occupy 61 divided sets for a total of 242 figures that are decipherable (only one isn't). Signs pressed in the clay are sequenced spirally, going from outer-inner, 31 on one side and 30 on the other, with dividing lines incised between the stamped characters. The signs were probably printed with a gold stamp that anticipated Gutenberg by millenia. If these signs were also used on paper as well as on clay, we don't know, because the papyrus or other writing materials didn't last (as far as we know; more archelogical explorations may eventually turn up other such signs). Godart identifies one sign as the Egyptian papyrus plant, so possibly paper-like surfaces were used.

Godart believes that there was probably widespread familiarity with the signs and the story told, if that is what it was, although he also stresses that, from present evidence, *"These are truly few, [compared to the Linear B texts or the Rosetta Stone] for which reason, unless new texts in the script of the disc are found in quite great number, any attempt to decipher it is doomed to failure."*

We know from other sources that the spiral was used repeatedly in Cretan design. Some of the signs repeat like a poetic refrain perhaps. For me, better than any cross-word puzzle as a mindteaser, it seemed to tell a story more interesting than the property accountings of Linear A and B. Perhaps imaginative renderings would be interesting, as from contrasting male and female points of view, for instance.

Thus one of the puzzles hinges around the sexual identity of what seemed to me to be the primary sign, that of a face seen from profile with what we now think of as a Mohawk haircut (see figure at end of article). It could be a warrier with a plumed helmet (though the helmet part is not seen) or a woman with a upraised hairdo (although the characteristic band from Cretan frescos showing women with raised hairdos was not seen either). This sign recurs 19 times, more than any other and occupies the primary (first) position in each of the 19 sets in which it appears, again different from any other sign. The disk seems distinctly Cretan, not imported from elsewhere. Given the matriarchal heritage of the times and region, I personally think of the face as female and have familiarly named her Plumia . Ten of nineteen times this sign is followed by what may be a offering tray with seven compartments (from a less submissive and more masculine perspective, however, Godart notes it could also be a shield).

From reading accounts of life as it likely was in Minoan Greece, religious and submissive aspects of life clearly predominated. The people feared many things and propitiated the gods incessantly. Learning there was a future was helpful for humans as their brain developed into larger versions, but the dread of that future may have made the new information a problem. Memory has its curses. One imagines inhibitory GABA receptors working hard in expanded cerebral cortex.

Returning to the disk, the artisan fired it with a yellow glaze, a color connected with women in those times (depicting men as red probably stemmed from their tanned bare skin produced by their outdoor life). That Plumia might indeed be female fits with many other traces left in frescoes, vases, sculpture, tombs and architecture that indicate females ranked highly in Minoan Crete as priestesses and goddesses.[4] And in contrast to the aggressive image in Greek mythology of the Minotaur and the labyrinth that Theseus encountered in Minos, scenes from excavations by Sir Arthur Evans at Knossos showed seemingly carefree peoples who danced and liked flowers. A "Prince of the Lilies" graces the cover of Roger Castleden's recent book." Jacquetta Hawkes in 1968 developed the point that the Minoan society was likely a female-led one.[6]

Castleden presents a well considered argument that these Bronze Age Cretans were extremely religious and also peaceful. Their large temples had no fortifications (Castleden holds them to have been not "palaces" but religious temples, different from the view of the swashbuckling Sir Arthur Evans, the discoverer, excavator and "reconstnictor" of the Knossos site in the early 1900s.) More generally agreed is that there was likely no single King Minos but a series of people designated as such similar to the general term pharaoh in contemporaneous Egypt. In major contrast to contemporary Middle East and Egypt and later

Greece, there were no monuments to "great leaders." Echoing Marco Bacciagaluppi's point, Castleden summarizes evidence that this was a female-led society in that priestesses greatly outnumbered priests, female goddesses were greatly prominent, such as the famous snake goddess with snakes in her hands, a cat on her hairdo, and dramatically bared breasts. "Again and again, women are shown in dominant roles—in the Theran Naval Festival Fresco, and in the Knossos frescoes too. That priestesses were dominant in the temples cannot be doubted.... [I]t is tempting to see the powerless Wanax, with his mainly ceremonial role, living in the shadow of a Labyrinth run by powerful priestesses as an earthly parallel to the Minoan myth of an insignificant male god subordinate to a powerful goddess."[4,pp. 28-29]

Castleden develops further, "One peculiarity of Minoan society, even at [its] zenith stage, is that it shows no sign whatever of personal ambition. There are, in the archeological record, no signs at all of boastful, self-aggrandizing rulers or viziers, which is a striking contrast to the situation that prevailed in contempary Egypt or Anatolia."[4 p32] Yet, later he also makes clear that 'It was a ferociously aggressive world, and the Minoans lived successfully and competitively within it. There is no reason to suppose they were different from their neighbors in their attitude towards military aggression.[„4, p. 122]

A milk and water flower children society could not have survived in the Bronze Age Aegean. Probably because the Cretans had superb sea-going vessels and a corresponding dominance of the area, they needed little fortifications for their city states. Have-nots had not yet equipped themselves. Moreover, early on Cretans occupied various Aegean islands, not the other way around. This all ended not after an initial ruining of their cities and temples in 1700 probably from earthquakes (they rebuilt them even more splendidly), but several centuries later when the volcano north of Crete at Thera (Santorini) erupted (thereby preserving for posterity the Cretan colony at that island). Something happened to the Minoans about 1400 B.C., probably needing to yield to the Myceneans. They did, we know, take Cretan gold to the Peloponnese. Artefacts from there decorated graves. The Myceneans (think of Agammenon and his Troy-invading peers) seem to demonstrate the switch to a masculine led culture.

In summary, in early Bronze age Crete from 3000 to 1400 B.C., much laterthan the 10,000 to roughly 5000 B.C. that Marco discussed, a feminine dominance seems to have prevailed when Crete held strong in the central Mediterranean, the matriarchy making no difference in trading and exploitation, but without the males' vainglorious attitudes. Their peaceful trading may have carried the day along with their men who were not fighting the women but forthem.

Not that other complex things didn't happen. The classical Greeks gave Cretans credit for invention of homosexuality [7 pp. 194-5] and several cited the poppy-crowned goddess as background for the likely widespread use of opiates for religious ceremonies and perhaps some of the peculiarities of their thought content featuring fantastical dream-like creatures.

But back to Marco's point: here in the Bronze Age, we may see confirmation that ordered society might have been different with women leading. Not less equipped for aggression perhaps, but Crete might have been protected in part by its clevertraders and extensive colonization. And aggression might have been directed against pirates rather than focused on taking over others en masse. We don't know the details. But from what we do know we can see some confirmation of Durant's point about this: "use *of man* to signify all humanity reveals the prejudice of a patriarchical age, and hardly suits the almost matriarchal life of ancient Crete. ...[T]he Minoan woman does not put up with any Oriental seclusion, any purdah or harem; there is no sign of her being limited to certain quarters of the house, orto the home."[3 p 10]

Speaking sociophysiologically, we know now that women show more activity in their retrosplenial cortex than do men (men are more active in their medial temporal lobes). What does this region of the brain do that characterizes women more than men? Does a greater interest in collaboration and mutuality have its central nervous system counterpart or mediation taking place in this brain region? We look forward to

additional information on such matters.

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Figure: "Plumia." Is the 1700 B.C. Cretan profile that of a man or woman?

ARTICLE:

by Dan Wilson

Hypotheses, Evolutionary Science, and Psychiatry

Thanks both for publishing my letter in ASCAP V.12, #5, (May issue) as well as your (RG) editorial comment on 'hypothesis testing'. The comment caused me to think through a variety of new issues and review the philosophies, branches and methods of knowledge anew. It is amusing (to me at least) that this has occurred in the weeks before my 20th reunion at Yale College (where I studied Anthropology and the History of Science and Medicine). I am, therefore, re-raking some old leaves! So, I thank you for your stimulating if brief comments. To these I would like to reply at greater if yet insufficient length....

First of all, the word *hypothesis* derives from the Greek 'foundation, supposition'. In English it involves a conjecture put forth to account for known facts; especially in the sciences, a provisional supposition from which to draw conclusions in accordance with known facts. This serves as a starting point for further investigation by which the supposition may be *proved* or *disproved....* Meanwhile, *test* denotes action to ascertain the existence, genuineness or quality of...' (OED, First Edition).

In plain English, then, we have a quite reasonable and conventional request by Dr. Klein that evolutionary psy-chopathology not only base its suppositions in accord with known facts, but make better efforts to ascertain the genuineness of these suppositions. That is to say Don has, it seems, tarred the enterprise of evolutionary psychopathology with the brush of an insufficient empiricism.

Here I should emphasize my belief that he is not so much opposed to the Darwinian perspective, but that he is not well aware its claims to scientific validity exceed those of the (neo-) logical positivism both he and I much admire for its practical value. He would, I think, do well to take up the concerted study of evolutionary science to achieve an understanding of its processes and aims which is within at least an order of magnitude of his grasp of biomedical psychiatry. Thereby, his magnificent intellect and erudition could help guide what is, clearly, an accelerating transformation of psychiatry. The field is changing from a trade guild without necessary, sufficient and complete theoretic foundations into to an authentic science.

This transformation is only now in its infancy. The comprehensive reformation of psychopathology as a consequence of Darwinian principle and method will continue to gather momentum until it is the predominate and most valid bedrock of psychiatry. Yet while this quite salutary and seemingly inevitable trend progresses, it would be greatly aided by more informed input from such giants as Don is.

Be all that as it may, my reading of his comment about 'hypothesis testing' was (1) that it had to do more with the agenda of inductive empiricism, *senso stricto,* than epistemology or procedure in the larger sense, (2) that it was not a merely statistical concern and (3) that it was a call for this work to pursue an almost exclusively inductive approach in order to attain the esteem and status of 'science'. Hence, the discussion with Don, telegraphic and abbreviated though it has been thus far, entails considerably more than the fundamental statistics you (RG) mention.

It is, of course, a hopeless task to briefly consider the germane elements of scientific history, method and philosophy ... but here goes. There has been a long standing separation between two extremes. These extremes can be contrasted most vividly between those whose theoretic zeal and energy often eclipses the truth-seeking value of their work (Freud and Haeckel spring to mind) and those whose procedural compulsivities often reduce the aim of science to a neo-Baconian enumeration of facts. Often lifeless facts.

Between these two polarities there is the 'hypothetico-

deductive method' first engendered by Newton. This is not solipsistic jargon: the great steps in science over the past three hundred years have, almost invariably, occurred within the procedures of this method ... Newton, Kant, Darwin, Einstein and all of higher mathematics just for starters.

This is a procedure of science to account for *both* observation and experiment through *inference.* The method assumes proper theory arises from generalized *observation.* This is in keeping with Cartesian rationalistic aims by which theory is a deductive machine to explain particular *empirical phenomena with reference to general principles and definitions.* Yet the Newtonian hypothetico-deductive mode moves beyond Descartes in that it *hinges validity upon how robustly the consequences of its deductions can illuminate previously unexplained general phenomena or specific scientific questions.*

With this by way of a further background, it must be said much of evolutionary psychology and psychopa-thology suffers from insufficient rigor. Yet it must also be noted, often and firmly, that evolutionism is an inherently complex subject that is not likely reducible via the usual inductive experimental methods.

Besides the consensus that empiricism has lesser truth value than deductivity, the extra-inductive dimension of evolutionary analysis is all the more true with respect to human psychopathology. Indeed, within the living memory of Hitlerian excess one simply cannot insist upon experimentation with humans via molecular genomics, breeding intervention studies and so on and yet retain a moral ground. Therefore the highest ranges of empiric rigor is unavailable to evolutionary psychopa-thologists. Still, there is good hypothesis testing afoot. Nevertheless, if the last few hundred years of scientific history is any guide, the big knowledge is to be gleaned through cogent deduction not pedestrian experimentation.

Meanwhile, my own primary research interest in reconciling psychiatry—especially its *empirically generated* epidemiology, neurobiology and sociobiology—to evolutionary genetics has systematically tested at least one big, big hypothesis. This is to do with the prevalence of polymorphic traits. In this I have found no reason to conflict with Darwin: genes that are common were, with few and quite specific exceptions, selected due to advantageous traits conferred in phylogeny.

It is exactly this hypothesis that I have continued to test *(i.e.,* that several epigenetic psychopathological syndromes so far exceed likely mutation rate prevalence as to manifestly be genomic 'morphs[1]). Certainly, the "what[1], "when[1], "where[1], 'why' and 'how' of this natural selection is more debatable (though not merely 'auxilliary hypotheses'). Yet, in the absence of quite anomalous new evidence or the disconfirmation of Darwinian principles, I do not think we can argue the "whether".

Indeed, it is time for the nay-sayers to at least give voice to, if not test, a few hypotheses of their own. As the matter stands, an explanation, under the present evidence and within established biological principles, of their apparent adherence to the belief that deleterious psychopathogic epigenes accumulate greatly in excess of adjusted mutation rate prevalence has not yet been advanced, much less tested.

It will be interesting to consider such a hypothesis as it seems so profoundly illogical and unrelated to available evidence.

ARTICLE :

byAman U. Khan

EVOLUTIONARY HYPOTHESIS OF LONG-TERM MEMORY

Introduction:

Learning is concerned with the operations that place a relatively stable behavioral potential in memory. From this point of view, memory may be defined as the storage of learned behavioral potential overtime. Memory may also be defined as a persistent change in the CNS brought about by environmental input and by the activity of the organism (including the self-generation of an image, ideas, or thoughts that are retained as memory).

The operational definition of memory derives from the results of laboratory testing of individuals for memory processes. The individual is provided with some input and then tested forthe amount of retention in the memory, which is measured by determining how closely the output matches the input for various types of material over time.

Long term memory (LTM) implies a permanent record of events and learned material. Several synonyms include 'long-term storage', 'secondary memory', 'delayed memory', and 'distant memory'. Tulving[1] distinguished between two major forms of LTM: episodic memory and semantic memory. The episodic memory consists of the events that have been given a spatial and temporal coding - where and when something happened. The semantic (or categorical) memory contains stores of learned words, verbal symbols, and semantic relationships. Other classifications of memory may include declarative (memory of specific facts or events), and non-declarative memory (memory for skills and procedures).

Long-term memories are extremely resistant to erasure, persisting through sleep, unconsciousness, excitation, and seizures. It is reasonable to assume that long-term memories are laid down through some permanent changes in the structure and function of neurons. Search for the location and the mechanisms of LTM have generated large number of theories and hypotheses, which may be grouped into two broad categories:

(a) Molar Theories—focussing on events in the neuron at the molecular and structural levels.
(b) Holistic Theories—emphasizing changes in large clusters or ensembles of neurons

The molar theories have seized upon every newly discovered structure and function to explain the mediation or modulation of LTM. The holistic theorists do not dispute the importance of events and processes occurring at the molecular level, they believe that it is the patterning and sequence of events in large groups and systems of neurons that constitute the true and essential basis of memory. There is no necessary incompatibility between these types of theories since each deals with phenomenon at a different level of observation and analysis.

Synthesis of new proteins during learning has been the most popular hypothesis among molartheorists. Perhaps the first suggestion in the literature that macromolecules may be involved in processing LTM was made by von Forester[2] who pointed out that macromolecules or proteins within the cells offered a large capacity for information storage. Katz and Halstead[3] proposed a set of hypotheses suggesting that changes in the brain nucleoproteins might be the basis for LTM. Synthesis of new proteins has been demonstrated in association with learning in large number of studies. The most popular method has been the use of radioactive amino acids that are injected before, during and after a learning experience. These amino acids are incorporated in the formation of new proteins, which are presumed to indicate the influence of learning. A number of brain-specific proteins have been suspected to be related to LTM. For example, a brain-specific antigen" ,S-100 and 14-3-2[5], and synaptyn[6]. However, few investigators believe that protein molecules acted as storage bins

for long-term memory. Instead, these newly formed proteins may alter both structural and functional capacity of neurons. The proteins may be incorporated into neural membrane, changing its electrical properties; forming new synapses, and acting as enzymes involved in the metabolic processes of neurons.[7]

The mechanism by which a learning experience may induce production of new proteins has been studied extensively [8, 7]. It is now suggested that a sensory -motor experience occurring during a learning situation stimulates (or influences) surface receptors on appropriate neurons through release of various neurotrans-mitters and neuropeptides. The cells, in turn, produce several second messengers such as cAMP, cGMP, Ca, diacylglycerol. The second messengers influence DNA transcription, usually through phosphorylation of proteins, which then bind to DNA to initiate transcription of certain genes. For example, cAMP, whose intracellular concentration changes in response to stimulation from a variety of neurotransmitters and hormones, stimulates phosphorylation of many proteins. One such protein is CREB (cAMP response element binding protein). In its phosphorylated form, CREB binds to an 8-base regulatory sequence of nDNA called CRE (cAMP response element), which is present in several genes, whose transcription is increased by cAMP. Thus, increases in cAMP stimulate protein kinase A, which activates CREB, which stimulates transcription of genes.

Although most studies indicate significant changes in the incorporation of radioactive amino acids into proteins as a function of training, the precise role of the proteins in the establishment of LTM remains elusive. It is generally difficult to measure changes in any specific proteins during learning against the large background of protein synthesis that occurs normally in the brain. It is also possible that these changes result from some epiphenomenon associated with learning.

A major unanswered question is how memory is retained for long periods of time and frequently for the lifetime of an individual even without any periodic reinforcement. All structural and functional proteins of every cell are renewed periodically depending upon the need and metabolic activity of the cell. The new proteins formed during a learning experience would be lost by the process of recycling unless permanent alterations are made in the transcription mechanism, which would continue to transcribe and translate the same proteins over and over again. No such mechanism has yet been found. Even if there were a mechanism of transcription that was permanently activated by a learning experience, there would not be enough specific protein molecules to code each new learning experience. It is nonetheless possible that even a small number of protein molecules can work in combination to code a very large number of information items.

Two phenomena, long-term potentiation (LTP) and long-term depression (LTD) have been cited in support of prolonging the effects of a single learning experience. LTP has been demonstrated at several central and peripheral sites of neuronal systems. In a typical experiment, when different fibers to hippocampus (CA1 region) are stimulated electronically in close temporal proximity to depolarization of postsynaptic neurons, an increase in the sensitivity of the cell develops, which may persist for days and weeks[9]. Similarly, certain patterns of stimulation can produce long-term depression of the target neurons.

Holistic theories postulate that the most important factors in memory formation and retrieval are not the changes occurring in one neuron (which simply result in an increased or decreased probability/capacity of firing) but formation of neuronal networks with specific patterns and sequence of firing. Formation of neural networks has been suggested by many workers in the field, such as Hebb's neural assemblies,[10] Piaget's schema,[11] and neuronal ensemble of E. Roy John.[12] There are, however major differences among theoreticians in the way they have used these terms. In addition, there are numerous models of neural network formation. For a review, reader is referred to the writings of Anderson and Rosefield,[13] Shaw and Palm,[14] and Levine.[15] Most models assume some type of association or connection among neurons to form a network. Ramon Y Cajal[16] was probably the first to propose the formation of contacts among

neurons, as a consequence of learning and experience. However, Donald Hebb[10] is credited for formulat-ing a succinct theory of cell assemblies. He proposed : " *When an axon of cell A is near enough to excite cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A's efficiency as one of the cells firing B, is increased. ...*"

Experimental evidence from animal studies provides some support for formation of specific neuronal networks in simple forms of learning such as habitua-tion, sensitization, and classical conditioning. These studies show changes in the probability of firing in groups of neurons involved in specific learning[17 - 21].

Chronic electronic recording from cortical neurons indicates that memory is coded by groups (clusters or ensembles) of neurons which fire in a temporally correlated fashion[22 - 24]. Information appears to be processed in widely distributed parallel pathways where several neural ensembles are activated simultaneously. Individual neurons may participate in different ensembles to process different information[25]. Cell assemblies are considered as functional units, which interact and overlap with each other. They may recruit more neuron, drop other neurons, and join other assemblies to process complex information. When reactivated, these assemblies produce appropriate spatio-temporal output patterns that can "play back" the memory of the original event.

Evolutionary Hypothesis

Evolutionary process of brain development appears to be the process of encephalization , increasing capacity for learning and greater intelligence. During evolution, larger brain size has been achieved through both quantitative and qualitative changes. The quantitative changes have occurred through a steady increase in the number of neurons (and glial cells that support neurons) from lower species to man. Overall brain size, in relation to average body size, is a dimension upon which organisms can be ordered meaningfully between as well as within species.[26] The quantitative changes include increasing complexity of neuronal network and hierarchical organization. Larger brains allow greater interaction among neurons through extensive dendritic and axonal arborization, and formation of greater number of spines and synapses. On the evolutionary scale, brain size among various species appears to be well correlated with learning capacity, performance, and ability to process and utilize complex information.

Hierarchical organization of brain structures and functions has also become more complex during evolution. Nervous system functions as a hierarchy of semiautonomous subsystems whose rank order is variable. Any subsystem may take part in many types of interactions. Each subsystem is independent to a certain extent, being subordinate to the unit above it and modulated by inputs from its own subordinate subsystems and by other systems. Basic bodily functions, such as autonomic, appear to be less regulated by the hierarchical organization than complex behaviors. Neural networks, regulating autonomic functions, such as heartbeat, respiration, intestinal movements, are considered as hard-wired, that is, they generate their own rhythmic activity, and are subject to modulation to a limited extent. However, complex behaviors, including learning and memory, are considered to have no hard-wired circuitry, as they develop from experience and interaction of the organism with its environment.

Learning and memory are crucial for survival of many animals and humans. It is unlikely that billions of neurons added to mammalian brain, especially in the association areas, during evolution, were left to their own devices to regulate their functions. Current hypotheses of cell assembly formation during learning imply that it may be a random phenomenon, and that any group of cell stimulated during a learning task may code the memory of that event for short- and long-term storage. Such hypothesizing probably originates from our modem thinking that we humans have been "totally" liberated from our animal ancestry for development of complex behavior.

Evolutionary trends would suggest that complex functions such as learning and memory have evolved very gradually. New neurons and neural circuits developed to meet the new demands and challenges of

the environment, requiring new adaptations for survival. Most likely, the initial solutions were based on hard-wired circuitry. Subsequent addition of neurons provided flexibility of functions in the older circuits. It is generally believed that most of the hard-wired circuitry, developed during evolution, has survived in the mammalian brain. Its functions, however, are modified greatly by the subsequent development of other subsystems.

It is suggested that the hard-wired circuits, originally developed forstoring long-term memory still exist in the mammalian brain. They are, however, greatly modified through evolution to meet new challenges and to acquire new knowledge. These circuits act as small nuclei, or centers of rhythmic activity around which other neurons and elaborate assemblies of neurons are formed during learning. The rhythmic activity of basic hard-wired circuits is maintained by several mechanisms. Most commonly, the spontaneously active neurons (bursting or pacemaker neurons), that fire at a certain rate can maintain rhythmic activity in the circuits. Cortical and subcortical structures contain large number of spontaneously active neurons, which can easily maintain rhythmic activity in newly formed memory circuits.[27, 28, 29, 30] It may be that the processes of long-term memory formation involve recruitment of spontaneously active neurons in the memory circuits.

Discussion:

The current hypotheses are totally inadequate in explaining the lifetime persistence of long-term memories. It is generally assumed that clusters of neurons, which fire in a temporally correlated fashion, code memories. The clusters are maintained by an increased synaptic bias among the neurons of the cluster. The increased synaptic bias is brought about by synthesis of new proteins, which is stimulated by a learning experience.

Unfortunately, there are not enough new proteins to code every new learning situation. The haploid human genome consists of about $3x10^9$ nucleotide pairs. The brain as a whole transcribes only about 30% of genomic DNA sequences. The present estimates range from about 30,000 to 100,000 different genes expressed in coding brain proteins.[31] This hypothesis is also untenable because of periodic turnover of all structural and functional proteins of every cell, depending upon the need and metabolic activity of the cell. The new proteins formed during a learning experience would be lost by the process of recycling, unless permanent alterations are made in the transcription mechanism, which would continue to transcribe and translate the same proteins over and over again. No such mechanism has yet been demonstrated.

Other cellular processes such as long-term potentia-tion and long-term depression have also been cited in support of protein hypothesis. These processes increase cellular sensitivity to fire only temporarily, from a few hours to a few days. There is no known biochemical mechanism to support lifetime persistence of long-term memories.

It appears that for long-term memory to survive lifetime of an individual, even without periodic recall and reinforcement, it has to be coded in circuits that remain active permanently, more or less in the original configuration. Evolutionary theory suggests that hard-wired circuits, powered by spontaneously active neurons, that developed in the early mammalian brain, may have been involved in storing long-term memory. These circuits may act as small nuclei around which larger memory circuits are formed during learning. The spontaneously active neurons are ideal power source for keeping memory circuits alive for long periods of time.

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Dr. Khan has previously written a book addressing issues of human memory entitled:

Clinical Disorders of Memory. **New York: Plenum, 1986**

Article:

by Russell Gardner, Jr.

Empathy Must Enter Economic Thinking

Book Review of *The Reciprocal Modular Brain in Economics and Politics: Shaping the Rational and Moral Basis of Organization, Exchange and Choice,* by Gerald A. Cory, Jr. New York, NY: Plenum, 1999

I personally have two major reasons for being grateful that John Price began corresponding with Gerald Cory. The first and most obvious involved his joining the ASCAP Society and proposing to it that we sponsor the Paul D. MacLean Festschrift that occurred in July, and then joining me in co-editing the symposium proceedings.

The second stems from his slim but focused and articulate book that attacks the sufficiency of the self-centered economic man assumption of why people act the way they do in the markets and in other exchanges with each other. The imposing title looks almost longer than the book itself (134 pages). Its ponderousness in fact does a disservice because to me it indicates a more ponderous tome than the book in fact is. He states his points succinctly but clearly, and he also documents each thoroughly.

The approach should have great impact. As in the book itself or an expansion of it. He needs to make his statement in many venues. I strongly urge all ASCAP readers to absorb it but not only they; also the readers of The New York Times, Wall Street Journal, Atlantic Monthly, The New York Review of Books, Newsweek, Time and all venues for economists, politicians, thinkers and ordinary people.

Dr. Cory's fundamental point is that people are inherently not selfish only, but also and equally empathic. They thereby act according to algorithms of reciprocity with each other. He notes that these come from how the brain is wired. He argues strongly that we need a new model for the behaving economic and political human. Indeed, false and misleading models guide us as a public wrongly. Maslow's theory of personal fulfillment, for instance, may have led people falsely down a self-aggrandizing path in the 1970s. Rather, we are fundamentally social in our nature. This of course reflects sociophysiological thinking although from a view very different from the clinical that we frequently discuss in these pages. Interestingly, though, he has told me in personal discussions that he gained his young adult start as an assistant to a psychiatrist on an inpatient ward — priorto modem psychopharmacology. But though the sense of behavior stemming from the brain has stayed with him since, he has operated in the very different realms of business, economics and politics.

Thus, his thinking is solidly based in the brain though he calls his approach "interpersonal behavior ecology." His cross-disciplinary Stanford University Ph.D. encompassed biology, psychology, politics and sociology. Extensive business experience, including management of crowds at times, means that he brings an unusually informed experience from the real world to bear on the academic problems he has met. His analysis bears on the behavior of people in the political and economic spheres. Ecology for him extends beyond the physical environment to our social surround: *"It concerns our interpersonal... interactions at all levels, from simple dyadic one-to-one personal interactions to our larger, even global, social-economic, and political interactions."*

The organization of the brain determines this, he believes; it has within it what he calls algorithms that in turn influence how we behave with each other. *"Human society, to include the economic and political aspects, is a product o1 the the human brain interacting with like brains, under environmental constaints. There is no other possible source."* Also, he asserts that: *"The aspects of society that we term political and economic are .... products of the human brain. ... There are no political or economic essences or universals, independent of the human brain, existing out there in a positivist, mechanical world waiting to be discovered."*

He agrees, moreover, that how the brain does things in a ego-centered and selfish way in part, but not only in part.

He insists that empathic socially responsive and concerned algorithms constitute brain parts that are equal to the selfishness; this must be brought fully front and center. There are brain functions that mediate concerns for others; this biological fact must be reckoned with in a manner not yet clear to the economic thinkers although he found quotes from the most avid advocates of economic selfish man that demonstrated the inability of the selfish economic model to account for the generosity of people.

And most of all, Cory is grateful to Paul MacLean for conceptualizing, researching and elaborating the importance of a brain region in humans and other mammals that manages that attribute. I sense that when he encountered this conception, he must have felt it to be revelatory, echoing the sense he already had but fleshing it in with neurobiological realities of how the brain must work in human interactions. Cory acquainted himself with the neurobiological factors, read widely about them, and noted criticisms of MacLean as he encountered them. He assessed these using his own independent view of things. Then he took measures to correct what he perceived as injustice. Cory become one of MacLean's most effective advocates in rehabilitating his reputation. This reputation was sullied unfairly, trivialized and demeaned in an offhanded manner, Cory has documented, by a reviewer in *Science* who hadn't read the book. Despite this, this opinion has been uncritically accepted in the neurobiological world.

In doing this, Cory hid his personal light (his own theory) under a bushel at the Festschrift where he spent his minutes on the podium in defence of MacLean's theory. Last year he developed these arguments in *ASCAPs* July, 1998 issue, and additionally makes the point in the book's third chapter. He wonders if we need an addition to our ethical code that might address "review malpractice."

Cory presents an intraindividual conflict theory although he doesn't mention Freud. Surely he must certainly have encountered the famous theoretician, but of course Freud had delinked his observations from neurological realities despite his neurological training. Cory in contrast found that the very brain modules that he most works with are responsible for internal conflicts and their resolution. These were evolutionary determined. He notes that *"Behavioral tension serves as an internal emotional compass that we can use to guide ourselves through the often complicated and treacherous pathways of interpersonal relations. Behavioral stress tells us that we are exceeding safe limits for ourselves and others and for our larger social, economic, and political structures."*

Cory uses 18 short chapters to tell his story. In chapter 4 after he deals with MacLean and his critics, he sets out a "new modular model of behavior" that he calls the "conflict systems neurobehavioral model.'A first component, MacLean's lizard brain in the striatum, he calls the self-preservational module, and the second the paleomammalian or limbic level, he relates to maternal nursing and long-term infant-parent-family bonding. The neocortex of neomammalians with language and thought, he notes, has the capacity and responsibility for rational thought, needing to make rational choices from among often conflicting behavioral priorities.

Cory fundamentally uses equilibrium equations as the classical economists do. As already noted, what he does that is different, is add the empathic element, noting that the cold-blooded reptilian model is not the accurate one for how people operate despite its hoary pervasive tradition.

More extensively, Cory develops that there are *"two master, inclusive and modular programs of self-preservation and affection that have been wired into our brain structure [that] operate dynamically according to a set of subjectively experienced and objectively expressed behavioral rules, procedures, or algorithms."*

The egoistic range dominated by self-preservational programming has empathy within it but taking a back seat. The empathetic range can go to the extremes of self-sacrifice and submission if ego is minimal. A dynamic balance range represents a working relationship between the two. When there exists conflict, out of balance, or pulls against the other amongst the major modules, there is stress and tension. I now quote without qualifiers or examples his rule statements core to the book:

1) Self-interested egoistic behavior, because it lacks empathy to some degree, creates tension within ourselves and between ourselves and others. The tension increases from low to high activity levels. And it increases as we move toward the extremes of ego.

Within ourselves, the tension created by the tug of neglected empathy is experienced as a feeling of obligation to others or an expectation that they might wish to "even the score" with us.

Within others, the tension created by our self-interested behavior is experienced as a feeling of imposition or hurt, accompanied by an urge to "even the score."

The reactions that build in ourselves and others do potentially proportion to the behavioral tension created by the egoistic, self-interested behavior.

2) Empathetic behavior, because it denies ego or self-interest to some degree, also creates tension within ourselves and others. This tension, likewise, increases as activity levels increase and as we move towards extremes of empathy.

Within ourselves, the tension created by the tug of neglected self-interest (ego) is experienced as a feeling that "others owe us one" and a growing need to "collect our due." This tension, especially if it continues over time, may be experienced as resentment at being exploited, taken for granted, not appeciated, or victimized by others.

Within others, the tension created is experienced as a sense of obligation toward us.

The reactions that build in ourselves and others, again, are in proportion to the behavioral tension created. And again, the unmanaged, or excessive tensions is experienced as behavioral stress.

3) Behavior in the range of dynamic balance repre sents an approximate balance of ego and mutuality. Within ourselves and others, it creates feelings of mutuality and shared respect.

Nowto provide a sense of the usefulness of this approach, I now turn to his contrasting of his theory to that of Nobelist Oliver Williamson who has popularized the "new institutional economics" aimed at integrating classical economic theory with institutional theory. Williamson stressed that the basic unit of analysis is the transaction. He maintains the standard assumption of opportunism, meaning self interest practiced with guile (deceit), including a premise of wealth-maximizing. Heirarchies exist in part to contain the opportunism.

Cory notes that Williamson's examples are ridden with exemptions and highlights *"some of the frustrating and Ptolemaic epicycle-like exceptions that spin off from the assumption of the exclusively self-interested, wealth-maximizing economic man that underpins and pervades the paradigm of our current economic science."*

Then neatly Cory opens up or unpacks the basic atom of the transaction. He notes that it is ***"fundamentally a unit of reciprocity,****.... of the tug and pull of ego and empathy.* "These two elements exist in negotiated tension or cooperation. *"Opportunism, or the unbalancing tug toward self-interest, then is* ***deviancy*** *within the* ***centrality of cooperation and reciprocity."***

He further develops that transaction cost economics "is, in fact, a self-defeating, counterproductive artifact because it unnecessarily legitimizes, reinforces, and perpetuates the very transaction-costly behavior that it wishes to control and reduce."

I believe that this will become a classic book. Gerald Cory does have a sense of where the center of the economic universe is, not selfish economic man but the evolved human brain. I feel most fortunate to have become one of the first to have read it and predict that it will become a new and important intellectual tool for the better implementation of our economies and politics. Though far from the sociophysiology that involves clinical matters, Gerald Cory illustrates how puzzling out how the brain works in social relationships can be an extraordinary tool for the better understanding of how we function in all relationships, including those involving our banks, purchases, inheritances, loans and how we vote.

ABSTRACTS & EXTRACTS...

Gladwell M: The physical genius. *The New Yorker* 1999, August 2 issue, pp. 57-65.

Extract: ... The puzzling thing about physical genius, however, is that the closer you look at it the less can be described by... cut-and-dried measures of athleticism....

Timing... appears to be controlled by the cerebellum. Richard Ivry... has looked at patients who suffered cerebellar damage as a result of a stroke. He had them pronounce the words "bah," "pah," and "dah."The difference between the "b" sound and the "p" sound is primarily a matter of timing. "To make the 'b'sound, you put your lips together and as you open them you immediately vibrate the vocal chords," Ivry said. "For 'p' you open the lips thirty to forty milliseconds before the vocal chords vibrate." Stoke patients with cerebellar damage, Ivry found, make lots of "b"-"p" mistakes: "baby: comes out "paby.'Their timing is off. But they don't have trouble with "p" and "d," because the time of lips and vocal cords for these two sounds is exactly the same. The difference is simply in the configuration of your tongue. "You never hear them say 'dady' instead of 'baby,'" Ivry said.

Force regulation appears to be controlled by another area of brain entirely, the basal ganglia. "I like to think of the basal ganglia as a gate to the motor system," Ivry said, although he cautioned that the work on force regulation is still a good deal more speculative than the work on timing. "At any point in time, I have a few actions that I'm thinking about, and the basal ganglia are monitoring all the potential ones, then choosing one. The question is, How quickly does that gate open up?" He devised a study in which subjects were asked to press a lever with their index finger over and over again, with the same degree of force each time. Patients with Parkinson's disease, which is a degenerative condition affecting the basal ganglia, had relatively little trouble with the timing of the movement, but they had great difficulty controlling the force of the tapping. At one moment they were pressing too hard, and the next they weren't pressing hard enough. The "gate" wasn't working property....

[T]here is probably a natural variation on the efficiency of these motor-control functions.... Clumsy kids are at one end of the coordination bell curve ... [A]t the other end you find [superb hitters as in baseball]"

[OJbsessive preparation does two things. It creates consistency.... More important practice changes the *way* a task is perceived.... [F]or example ... hours and hours of chess playing have enabled [chess masters] to do what psychologists call "chunking."... [W]hen [they] see the board from a real game, they are able to break the board down into a handful of chunks—two or three clusters of pieces in positions that they have encountered before.... Peter Gzowski argues that one of the principal explanations for the particular genius of Wayne Gretzky was that he was hockey's greatest chunker.

Mazure CM: Life stressors as risk factors in depression. *Clin Psychol Sci Prac* 1998;5:291-313.

Abstract: Compelling evidence for an association between major adverse life experience and subsequent major depression is reviewed. Determining individual vulnerability to life stress and the effect of stressors on treatment outcome in depression are highlighted as the next major targets for contemporary stress research. Methodological concerns in the evaluation of stressors are detailed, and available data on variables that may influence the stress-depression relationship are presented. The critical importance of multivariate models in understanding individual vulnerability and outcome is emphasized. As methods for ascertaining stressful life events and chronic stressors continue to be refined, and models addressing the complex relationship of stressors and depression continue to be developed, prediction of stressor effects in onset and outcome of major depression will become increasingly precise.

Holden C: Notes. Extra neurons for the chase? *Science* 284;39.

Extract: [Anthropologist Dean Falk of the University at Albany of SUNY... with her team analyzed data on 414 male and 390 female brains. Instead of following the usual procedure of dividing brain size by body size, they compared males and females of the same body weight. Falk says she was "surp4ised" to find that "at any body weight, men have bigger brains than women." For example, at a weight of 60 kiliograms, Caucasian women's brains weigh about 1256 and men's about 1373 grams.... [C]omparable data [stemmed from comparisons of] 39 male and 44 female rhesus monkeys, a species in which males leave their groups at puberty in search of mates [in a] pattern 'remarkably consistent" with that seen in humans. Because human males outscore females on visual spatial tests, Falk's team suspects that in both men and monkeys all those extra male neurons may be dedicated to navigational skills. There's more evidence in the works: Falk's graduate student J. Redmond...ound no sex differences among gibbons, where males are monogamous stay-at-homes.

The conclusions bolster similar findings reported in 1992 by zoologist Dave Ankney of the University of Western Ontario, who found the same human brain size difference and who believes the male surplus is for "dynamic" spatial tasks, as in football passing.

Other scientists say the findings make sense. Anatomist Jim Cheverud of Washington University School of Medicine says ... that Falk's observations fit with the fact that in primates, most male features are larger than females'.

Dehaene S, Spealke E, Pinel P, Stanescu R, Tsivkin S: Sources of mathematical thinking: behavioral and brain-imaging evidence. *Science* 1999;284:970-974.

Abstract: Does the human capacity for mathematical intuition depend on linguistic competence or on visuo-spatial representations? A series of behavioral and brain-imaging experiments provides evidence for both sources. Exact arithmetic is acquired by language-specific format, transfers poorly to a different language or to novel facts, and recruits networks involved in word-association processes. In contrast, approximate arithmetic shows language-independence, relies on a sense of numerical magnitudes and recruits bilateral areas of the parietal lobes involved in visuo-spatial processing. Mathematical intuition may emerge from the interplay of these brain systems.

Roche H, Delagnes A, Brugal J-P, Feibel C, Kibun-jia M, Mourre V, Texier P-J: Early hominid stone tool production and technical skill 2.34 Myr ago in West Turkana, Kenya. Mature 1999;399:57-60.

Abstract: Well-documented Pliocene archaeological sites are exceptional. At present they are known only in East Africa, in the Hadarand Shungara formations of Ethiopia and in the Nachukui formation of Kenya. Intensive archeological survey and a series of test excavations conducted in the Nachukui formation since 1987 have led to the discovery of more than 25 archeological sites whose ages range from 2.34 to 0.7 million years before present (Myr), and to the extensive excavation of two 2.34-Myr sites, Lokalalei 1 in 1991 and Lokalalei 2C in 1997. Lokalalei 2C yielded nearly 3,000 archaeological finds from a context of such good preservation that it was possible to reconstitute more than 60 sets of complementary matching stone artefacts. These refits, predating the Koobi Fora refits by 500 Kyr are the oldest ever studied. Here we describe a technological analysis of the core reduction sequences, based on these refits, which allows unprecedented accuracy in the understanding of flake production processes. We can thus demonstrate greater cognitive capacity and motor skill than previously assumed for early hominids, and highlight the diversity of Pliocene technical behavior.

Engert F, Bonhoeffer T: Dendritic spine changes associated with hippocampal long-term synaptic plasticity. *Nature* 1999;399:66-70.

Abstract: Long-term enhancement of synaptic efficacy in the hippocampus is an important model for studying the cellular mechanisms of neuronal plasticity, circuit reorganization, and even learning and memory. Although these long-lasting functional

changes are easy to induce, it has been very difficult to demonstrate that they are accompanied or even caused by morphological changes on the subcellular level. Here we combined a local superfusion technique with two-photon imaging, which allowed us to scrutinize specific regions of the postsynapticdendrite where we knew that synaptic changes had to occur. We show that after induction of long-lasting (but not short-lasting) functional enhancement of synapses in area CA1, new spines appear on the postsynaptic dendrite, whereas in control regions on the same dendrite or in slices where long-term potentiation was blocked, no significant spine growth occurred.

Simpson J, Ickes W, Blackstone T: Where the head protects the heart: empathic accuracy in dating relationships. *J Personality and Social Psychology!* 995;69:629-641.

Abstract: This study investigated circumstances in which romantic partners may be motivated to /naccu-rately infer each other's thoughts and feelings. Dating couples rated and discussed pictures of opposite-sex people with whom they might later interact in a dating context. Couples evaluated either highly attractive persons or less attractive persons. As predicted, dating partners who were close, who were insecure about their relationship, and who evaluated highly attractive opposite-sex persons displayed the *least* accuracy when they tried to infer each other's actual thoughts and feelings from the videotape of the rating and discussion task. The effects of these variables were additive, and they were mediated by the degree of perceived threat to the relationship. Theoretical implications of these findings are discussed.

Flint J, Corley R, DeFries JC, Fulker DW, Gray JA, Miller S, Collins AC: A simple genetic basis for a complex psychological trait in laboratory mice. *Science* 1995; 269:1432-1435.

Abstract: Psychological traits are commonly inferred from covariation in sets of behavioral measures that otherwise appear to have little in common. Emotionality in mice is such a trait, defined here by covariation in activity and defecation in a novel environment and emergence inot the open arms of an elevated plus maze. Behavioral and quantitative trait analyses were conducted on four measures obtained from 879 mice from an F_ intercross. Three loci, on murine chromosomes 1,12, and 15, were mapped that influence emotionality. This trait, inferred from studies of strain, sex, and individual differences in rodents, may be related to human susceptibility to anxiety or neuroti-cism.

Ruse M: Stories from the front. Review of Brown A: The Darwin Wars: How Stupid Genes Became Selfish Gods, NY: Simon & Schuster, 1999. *Science* 1999; 284:923

Extract: Well before Charles Darwin put pen to paper, men were arguing bitterly over organic origins. Although the great Georges Cuvier was a sincerely practicing Protestant, the things he said about his fellow Frenchmen, Jean Bapiste de Lamarck and Geoffery Saint Hillaire, were really quite unchristian.

This tradition continues. The most recent eruption has been over the extension of Darwinian selection theory to ... animal social behavior.... [I]nthe early 1960s, when a number of people developed new models for the evolution of behavior,... the field really caught fire. By the 1970s "sociobioiogy," as it was then called, was quickly moving forward....

Yet, at the same time, criticism of this approach was building and then exploded.... Richard C. Lewontin and Stephen Jay Gould led a band of radical biologists in condemning every aspect of Wilson's thought: the fondness for Darwinian explanations, the extension of the science to humankind, the belief that now we have a new ideology leading us progressively upwards to a brighter future. In England, Dawkins came under fire from ... Mary Midgley, who dipped their pens in purest venom and then wrote polemics with a sarcasm index almost equaling Jonathan Swift's....