ASCAP NEWSLETTER

Across-Species Comparisons And Psychiatry Newsletter
Volume 2, No. 5, 15 May 1989

..the cubist had convinced [her] to pose for a still life and, with his typical abstract conception of objects, began to break her face and body down to its basic geometrical forms until the police came and pulled him off. Woody Allen [1]

(c/o Russell Gardner, 1.200 Graves Building (D29), University of Tens Medical Branch, Galveston, TX 77550)

ATTENTION! IF YOU HAVEN'T YET SENT IN THE SURVEY FORM ON THE LAST PAGE OF A RECENT ISSUE, BUT YOU WISH TO CONTINUE READING ASCAP, PLEASE SEND THE LAST PAGE OF THIS ISSUE. Details in ASCAP Volume 2, #3, 15 March 1989.

For the philosophy guiding this newsletter, see footnote on p. 9[2]. Newsletter aims: 1. A free exchange of letters, notes, articles, essays or ideas in whatever brief format.
2. Elaboration of others' ideas.
3. Keeping up with productions, events, and other news.
4. Proposals for new initiatives, joint research endeavors, etc.

Feature: This issue is devoted to Roger Master's summary of an important conference on serotonin and behavior directly associated with ASCAP aims despite focusing on law. Psychiatrists are most interested in the pathophysiology that may be reflected, and psychiatrists in the courtroom must talk about the recidivists here featured.

Announcements: » Napoleon Chagnon has created a Yanomamo Survival Fund to help Yanomamo groups in Venzuela and would be glad to send a description of that nonprofit, tax-exempt fund to interested colleagues. For the controversy surrounding his work and their dilemma, see his letter in the 7 Apr 89 Science [3]. He has studied them for 25 years [4] and points out that over the past 5 centuries, about 80-90% of native American cultures existing in 1492 have disappeared. He feels that his scientific approach to hunter-gatherer behaviors is compatible with humane goals associated with their survival if not in Brazil (where their ways seem doomed) then in Venzuela. NA Chagnon, Dept Anthropology, U Cal, Santa Barbara, CA 93106.
» U Mich Evolution and Human Behavior Program is looking for postdoctoral fellows: Warren Holmes, 1524 Rakham Building, Ann Arbor, MI 48109-1070 Tel: (313) 936-2526
» First Annual Meeting of The Human Behavior and Evolution Society, is on 25-27 Aug 1989:Northwestern U, 1810 Hinman St, Envanston, Ill, 60208-1310 Tel: (312) 491-5402

Notes: The biochemistry of the cell is of course involved with across-species comparisons of animal communication and other behaviors as well as issues important to psychiatry. This being the case, the interesting G proteins continue to be a hot area of biochemical research and to be surprising instances of nature's economy and resourcefulness. (We've been following them from a distance in ASCAP since finding out [ASCAP Vol 1 #7] that the lithium that treats mania affects them.) They are components of a "second messenger" system that provide communication within the cell, as between receptors inputting messages received at the cell wall from neurotransmitters/hormones ("first messengers") and other cellular parts, eg, effector proteins. Target effectors include adenylyl cyclase and calcium channels, two of about

eight such proteins used for information transfer. .

In Science we read [5] that they operate with greater efficiency than had been envisioned: "Although one G protein can interact with several receptors, a given G protein was thought to interact with but one effector.. By using recombinant DMA techniques, three..variants were synthesized in E Coli and each variant was shown to stimulate both adenylyl cyclase and calcium channels, [underlinings added]..a particular G protein can serve as a branch point in pathways of tranmenbrane signaling and suggest that the networks "wired" in the plasma membrane may be quite complex..."

From an evolutionary point of view, we wonder if here again nature did not invent something new when something near at hand would do — recall Jacob's "tinkering" metaphor in ASCAP Vol 1 #13? Nature didn't make it any easier for the decoders of the "complex" membrane networks by using such homily tactics of course. The creative tracks of a tinkerer may be hard to follow also!

Moreover, it turns out that G proteins are structurally related to protein products of the so-called "ras oncogenes" found in 40% of colon cancer cells. Normal ras variants help regulate growth and development. A 3-dimensional molecular portrait of "the backbone structure of [a] human oncogene protein" decorated the cover of Science on 11 Feb 88 [6].

SEROTONIN. SOCIAL BEHAVIOR AND THE LAW: A SUMMARY. by Roger D Masters

A workshop at Dartmouth on "Serotonin, Social Behavior, and the Law" [7] featured legal implications of research in behavioral neurochemistry, with attention to the effects of serotonin on social behavior in humans and nonhuman animals. Unlike other conferences linking research in life sciences to study of human behavior,this workshop began not from the framework of biological research, but from a legal one.

Legal Concepts in the Face of Research on the Neurochemical Substrates of Social Behavior.

Michael Shapiro argued against the need for radical changes in our concept of social responsibility [8]; Ray Jeffery made a case for the "medicalization" of crime and abandonment of the mens reas concept as both unscientific and impractical [9].

Shapiro noted the legal system typically assumes human behavior is "caused." On this premise new scientific findings provide details concerning causation but need not be grounds for radical changes in law. After surveying the varied theories of freedom and responsibility, he suggested that knowledge of the "physical substrates" of behavior would not be likely to change the concept of culpability unless it could be shown that an individual lost "pre-existing" capacities for reason and deliberation." From this perspective, although nothing in new research compels a move toward a "therapeutic" model of jurisprudence, future biological discoveries could lead us to modify or "reassemble" our notions of guilt, confidentiality, and other basic norms.

Jeffery's contrasting view put the issue of our legal tradition in the context of the increasing strains on our criminal system. For Jeffery, our approach to criminal justice combines "an irrational model based on revenge and retribution with a rational model based on..deterrence." The failure of this approach to confront crime effectively has combined with the emergence of new, biomedical sciences of behavior to make possible a "medicalizatlon" of crime. More specifically, discoveries concerning the role of amino acids in the brain makes it possible to move from ineffective punishment to prevention defined coherently and treatment of individuals at risk of violence.

For Jeffery, the inability of our prisons to function either as rehabilitative environments or as effective deterrents increases the relevance of therapeutic alternatives. If attention is shifted to "crime prevention," a prisoner's "right to treatment" might become more salient than such issues as "informed consent," which now often dominate discussions of medical treatment of prisoners. While mentalist approaches to crime and mental illness persist, discoveries in the physical and chemical basis of normal as well as abnormal behavior have spread rapidly. Given the likely impact of findings based on new scientific theories and techniques, Jeffery argued in favor of moving from punishment to prevention and treatment for crime.

The positions of Shapiro and Jeffery, though not completely opposed, set forth rather different ways of responding to the data emerging from biobehavioral studies of serotonin and other neurotransmitters. In discussion, other participants pointed to the risks of seeking to define a "perfect" legal "solution" to the ambiguities of apparently contradictory doctrines. E.Donald Elliot [101 noted, for example, that attempts to change the law by means of frontal assault have typically had the opposite effects from those intended. Hence, before deciding to modify such a fundamental concept as "responsibility," the next step required detailed consideration of scientific evidence.

Serotonin and Aggressive Behavior.

Four papers examined serotonin levels and functioning:(1)M Linnoila: Low serotonin activity and hypoglycemia as factors predictive of recidivism for arson and impulsive homicide [11]. (2)M&B Stanley: Low serotonin and suicide(121. (3)B Ginsburg: Ontogeny, social experience, and serotonergic function ing [13]. (4) M Raleigh: High serotonin levels as a correlate of social dominance [141

The work of Linnoila and colleagues illustrates both the extraordinary promise of research on the biochemistry of human behavior and the danger of public misunderstanding of complex scientific findings. Studies in a number of countries have now shown that low serotonin levels associate with many impulsive behaviors, including unpremeditated homicide, arson and suicide. To explore the mechanisms, the group followed 58 Finnish arsonists and homicidal males in a prospective study to ascertain whether lower levels of CSF 5-hydroxyindolacetic acid (5-HIAA), (a principle metabolite of serotonin which is also known as 5-hydroxytryptamine or 5-HT) would associate with recidivism.

The remarkable findings showed that a combination of a low glucose level after a glucose tolerance test (GTT) and a low 5-HIAA at time of original assay correctly classified 84.2% of 58 subjects in predicting recidivism (vs non-recidivism) over the next 36 months. Other behavioral and diagnostic factors do not accurately predict repeated criminal acts among dangerous offenders. Of particular interest is the fact that Linear discriminant analysis showed no false negatives, suggesting that even if this method did not predict recidivists with total certainty, it night be used to identify persons presenting a low risk of repeated offenses and hence likely to benefit from rehabilitation or parole.

However, this work points to three crucial considerations that should hold off premature interpretations of relationships between neurotransmitter activity and criminal behavior. First, the aggressivity of behavior may be secondary to other factors in several categories of "violent crime." Thus, despite focusing on

violence as a "cause" of criminality, mechanisms implicated in this study seem to be associated with poor impulse control rather than aggressiveness per se, eg,low serotonin metabolism was evident in persons displaying impulsive arson (without other aggressiveness) as well as in unipolar depressives who attempted or committed suicide.

Second, despite an early focus on serotonin, low 5-HIAA alone did not sufficiently predice impulsive and antisocial behavior, but only the combination of hypoglcemic response to glucose load and low 5-HIAA. Two rather distinct mechanisms seemed implicated. Also there was a lack of correlation between the glucose lowering and CSF 5-HIAA or other metabolites of monoamine neurotransmitters norepinepherine and dopamine.

Finally, alcoholism seems to play a role in the etiology and functioning of those individuals at risk for repeated impulsive offenses: the recidivists are likely to be Cloninger's type 2 alcoholics (a pattern associated with impulsive drinking not associated with guilt). This type of alcoholism, moreover, may be a sex-linked familial trait, since typically it is found in the father or grandfather of the investigated recidivists.Why should such alcoholism be associated with low 5-HT turnover and low glucose with the GTT?

Linnoila suggested an intriguing hypothesis: although alcohol in the short term releases 5-HT, it also depletes it in the long term. Since low serotonin correlates with depression, alcoholism may in effect be a crude "self-medication." Thus (goes this story), drinking produces immediate disinhibition and release from depression (positive reinforcer), but alcoholics over the long run not only further reduce the rate of serotonin turnover, but, at least in persons with a tendency to hypoglycemia, suffer from acute losses of impulse control.

Such considerations should importantly qualify popular reactions to reports that serotonergic functioning and possible heritable variants in one or more neurochemical processes may associate with criminal behavior. The findings hardly suggest biological or genetic determinism;indeed, serotonin levels can be treated. To the contrary, the greatest danger may rise from premature attempts to use scientific findings as a means of behavior control. Not only ace measures of single neurochemical systems risky, but complex interactions seem to vary with differences in individual behavior and subject to treatment and control.

Such complexities are evident in the Stanleys' research on low levels of 5-HT with suicide (particularly in those attempting/completing violent suicide). Controlled research on humans to unravel effects of social experience and individual development on neurotransmitter systems; and social behavior is difficult. For this reason the Ginsburg and Raleigh reports were useful.

Ginsburg explored experimental studies of social behavior in several mammalian species. Although some individuals in species as diverse as wolves, dogs, mice and chimpanzees exhibit "hyperaggressive" behavior that appears heritable. genetic mechanisms associated with behavioral tendencies are normally quite sensitive to individual development and social context.

One example is the defensive threat behavior of the coyote, an innate reponse not found in dogs. But, despite different behavioral repertoires, coyotes and dogs can mate; experiments in cross-breeding can therefore illuminate relationships between genetic and developmental factors in the expression of the defensive threat.Ginsburg found that in some interbred coyote-dog strains,

there are "animals carrying the genetic capacity for the coyote defensive threat behavior, along with the genetic system of the dog, [who] ..spontaneously switch from the dog behavior to the species-typical coyote behavior during or after puberty." An explanation is that "coyote genes have, in this instance, been brought to active expression by the sex steroids in both sexes," even though the coyote behavior itself is not expressed until "the animal is aggressively challenged."

In this case, an experiment shows the combined roles of genetic inheritance, hormonal priming during development, and social context. Any one of these factors in isolation is not sufficient to produce the particular form of threat behavior. Ginsburg warned that simplistic extrapolations from a single genetic or hormonal factor might be dangerous. Evidence from experimental studies on mice reinforced this cautionary note; they showed that effects of serotonin on aggression may be due to specific serotonergic receptor sites (rather than from the serotonin levels themselves) as well as to interactions between dopamine and serotonin (rather than to a single neurotransmitter system acting in isolation).

These conclusions stemmed in part from studies of two strains of mice differing dramatically in aggressive behaviors. C57BL/6 individual male mice reared in isolation and introduced to a dyadic situation show far more aggression than do BABL/c mice in parallel circumstances. Moreover, mouse of each strain tended to show different aggressive behaviors, with "attack and chase" accounting for 90% of C57BL/6's but only 28% of the BABL/c's (in which "wrestle and tail rattle" accounted for 70% of the agonistic actions).

Since males of the two strains thus appear to have different innate behavioral repertoires, cross-breeding the two provides an elegant way of studying the interaction of experience, individual development, and social context in the expression of aggressive behaviors. Experiments using amphetamines that act as dopamine agonists produced marked effects upon aggressive behavior - but responses were diametrically opposite: "where the effect on one genotype is to increase aggression, the effect on another is to decrease it." As a result, a statistical prediction of neurotransmitter influence on a broadly defined category like aggressiveness is "simply a statement of odds that cannot serve as a predictor for any specific instance."

Such need for caution was reinforced by M Raleigh's report on studies conducted with M McGuire on vervet monkeys. This group found that individual experience and social environment have important effects on expression of aggressive behaviors associated with serotonergic functioning. By using various drugs, this group found that in vervets, as in humans, reduction of serotonin turnover is associated with increases in aggressive behavior - but the relationship is far from simple.

Over years Raleigh and McGuire have found that even though dominant and subordinant vervets do not differ physiologically, the dominant male in a group has higher serotonin levels and lower rates of aggressive behaviors than subordinates. The effects seem to be mediated by social interations; sight of submissive behaviors by others triggers the neurohormonal changes leading to enhanced serotonin turnover and dominant social behaviors. Similar changes in other species confirm that social experience and group structure may be extremely important in the functional relationship between serotonin and behavior.

Of particular relevance in these experimental findings to the human

issues raised by Linnoila was social rank's effect **ON** the target of aggressive responses within the group. In a vervet band, some individuals - such as the young - are not typically "appropriate" as targets of aggression or threats. When serotonergic functioning was experimentally reduced, subordinate vervets - but not dominants - were more likely to attack socially "inappropriate" individuals. Might the subordinate vervets whose serotonin is artificially lowered be having difficulties with "impulse control" comparable to Linoila's recidivists? Since similar treatments of a dominant male do not have this effect, functional consequences of serotonin on behavior seem to depend both upon the individual's rank and social situation.

Evolution of Legal Doctrines

Discovery that some persons may have genetic predisposition to violent or deviant behaviors caused by neurotransmitters like serotonin could have far-reaching effects, particularly if the many qualifications noted above are not considered as this research enters criminal law. Two papers focused on on the best ways to integrate scientific data into the legal system.

Donald Elliott surveyed the concept of evolution in legal theory, noting that Oliver Wendell Holmes' celebrated analysis of common law explicitly relies on the Darwinian theory of evolution. In Holmes' thought, this analogy did not imply a perfect adaptation of the law to environmental change; like the process made famous by Stephen Jay Gould's analysis of the panda's "thumb," legal practice typically works "primarily by adapting existing legal structures to perform new functions." Considering areas of civil procedure in the law, Elliott noted that legal evolution is a kind of artificial intelligence system akin to what Claude Levi-Strauss
described as "bricolage": an imperfect, sometimes jerry-built structure that cannot be entirely explained by the simple cost-benefit considerations of economic theory.

William Rodgers [15] produced evidence of this general point. Models in game theory that have been used to describe animal behavior can equally well be applied to legal decsions and doctrines such as those in the area of environmental law. In predator-prey relations, deception is highly advantageous - at least until counter-deception evolves to counteract the fake.

Confronted with predation from an owl, for example, crows "developed a strategy of wandering into easy range, 'pretending' to be wholly unaware of the presence of the owl, only to sidestep..futile strikes with disdain and ease." In much the same way, Rodgers showed the development of environmental statues has been marked by strategies of deception, using techniques like procedural entitlements, ambiguity, delegation of authority, postponements, and self-nullifying legislative provisions.

If the law is a jerry-built system of bricolage in which the legislative process is typically characterized by deception and counter-deception, simple adjustments to the new scientific evidence concerning social behavior are unlikely to be productive. On the contrary, seeing indirect means of integrating new Information into the legal system will be most valuable. In no area is this more likely to be sound advice than the biological correlates of criminal behavior, if only because enormous passions are evoked by fears of violence and by anger at seemingly ineffective judicial procedures,

conclusion

In the extraordinary range of issues discussed, the most interesting questions concerned how to minimize dangerous error and misunder-

standing. Many defense lawyers have already sought to benefit from the data correlating low serotonergic functions (accompanied by hypoglycemic rebound from sugar load) with violent social behavior; if the public were convinced of such findings, the consequence might well be a demand for genetic screening combined with economic, social and legal discrimination against persons with these supposedly "defective" genes.

The scientific evidence demonstrates that loss of impulse control associated with neurochemical changes depends greatly on individual experience or social situation and it produces diverse forms of deviant behavior (alcoholism, arson, suicide, and homicide). Insofar as knowledge of the biological causation of behavior is being advanced, we learn more about how to control outcomes; rather than genetic determinism or biological reductionism, the complexities of the serotonergic system point to possibilities of prevention and treatment that require caution if they are not to undermine our traditions of legal procedure.

A major suggestion arose from the meeting with legal procedure unassociated with criminal law: Roger Masters proposed that insofar as some persons may be genetically at risk for low serotonin turnover and hypoglycemic rebounds from glucose loads, and hence more likely to commit crimes of impulse, this condition should be considered an entitlement for Special Education rather than a matter of reduced criminal responsibility. Indeed, persons with the recidivist profile have typically exhibited great difficulties with impulse control in elementary school; such behavioral problems are often associated with poor educational results, marginality within school, and persistent social failure.

Evidence of serotonergic functioning and hypoglycemic conditions pose thorny problems in the context of legal responsibility and guilt, but the same information is less likely abused as an entitlement for educational benefits for the young child. Introduction of neurochemical and genetic information in criminal proceedings is likely to produce diverse and passionate emotional responses from judges and juries, thereby reducing the liklihood that social and developmental factors probably involved in the expression of genetic propensities can be weighed carefully or accurately. In contrast, a gene for low serotonin turnover (if ultimately there turns out to be such a DNA sequence) is likely comparable to genes that may bias some children to forms of dyslexia.

To restate the issue: scientific information of this sort should provide parents with entitlement to special education, not to diminish adult responsibility. This avoids the risk of "genetic screening" as a mode of "criminal labeling," and would more directly address the finding that the recidivist's behaviors are primarily impulse control; and that aggression (as such) is secondary.

Need to avoid "genetic engineering" and stigmatization of persons with the serotonin-glucose finding argues for this approach. Such genes may have been maintained in the human gene pool for some adaptive reason that could still exist. Perhaps males affected are more likely to engage in risk-taking behaviors, as in the altruistic bravery of war. Whatever such hypothesized reinforcing factors might have been and/or are, ill-conceived attempts to "cure" crime by genetic engineering could backfire.

Despite the wide range of disciplines represented, conference participants agreed emphatically on the dangers of assuming that simple legal solutions are possible with future developments in the neurochemistry of behavior.

The May issue features John Price's "A Note on Hamburg's Hypothesis on the Function of Anger and Depression."

1. Allen W: Getting Even. NY: Random House, 1971, p 91

2. ASCAP philosophy and goal. High scientific importance rests on comparing animal behaviors across-species to understand better human behavior, knowing as we do so that evolutionary factors last be considered for understanding properly such behaviors. To accomplish these comparisons, very different new ways of viewing psychological and behavioral phenomena are required This in turn explains why we need new words to define and illustrate new dimensions of comparisons across species, we expect that work in natural history biology combined with cellular -molecular biologic research will emerge as a comprehensive biologic basic science of psychiatry. Indeed, this must happen if we are to explain psychiatric illnesses as deviations from normal processes, something not possible now. Compare to pathogenesis in diseases of internal medicine.

Some neologisms that hopefully will help implement these goals are those of:
a| Michael R. A. Chance: 'hedonic' and "agonic" refer to the tone of groupings of conspecifics (members of a same species) i.e., relaxed and fan-loving versus tense and competitive. First initiated with CJ Jolly in 1970, this term is referenced fully in ASCAP #1, Footnote 1.
b) John S. Price: "anathetic2 and "catathetic" describe conspecific comminications. Catahetic messages "put down' whereas anathetic signals 'build-up* the resource holding potential (R) of target individuals.
c) Russell Gardner, Jr.: "psalic" is a 2 way acronym: Propensity States Antedating Language In Communication and Programmed Spacings And Linkages In Conspecifics. This describes communicational states conjecturely seen with psychiatric disorder and normality (human and non-human), ie, alpha psalic seen in manics, high profile leaders and dominant non-human animals. Eight psallcs are named alpha (A), alpha reciprocal (AR), in-group omega (IGO), out-group omega (0G0), spacing (Sp), sexual (S), nurtarant (N), and nurturant-recipient (NR).

All of the above new or renewed terms are initiated or elaborated in Chance, MRA (Ed) Social Fabrics of the Hind, due out in 1981, published by Lawrence Erlbaum Associates, Hove and New York.
d. Paul Gilbert: Social Attention Holding Power/Potential (SAHP) focuses upon the non-aggressive facets of leadership when this is deployed in the hedonic mode. See ASCAP v.2, #1 and his new book: Human nature and Suffering, Hove, East Sussex: Lawrence Erlbaum, 1989.

3. Chagnoa MA: Letter - Yanomamo survival. Science 1989;244:11.

4. Chagnon MA: Yanomamo: The Fierce People IT: Holt, Rinehart & Winston, 1968, 1983.

5. Mattera R, Graziano HP, Yatani A, Zhou Z, Graf R, Codina J, Birnbaumer L, Gilman AG, Brown AM: Splice variants of the a subonit of the G Protein GS activate both adenylyl cyclase and calcium channels. Science 1989;243(llPeb):l04-l

6 de Vos AM, Tong L, Milburn MV, Matias, Jancarik J, Moguchi S, Nishimura S, Miura K, OhtsuKa E, Kim S-K: Three-dimeisional structure of an oncogene protein: catalytic domain of human c-H-ras p21. Science 1911;239:888-893.

7. Dates: November 3-5, 1988; Co-sponsored by the Rockefeller Center for the Social Sciences at Dartmouth and the Gruater Institute for Law and Behavioral Research.

8. Shapiro M: Law, culpability and the neural sciences: The conceptual and normative effects of enhanced knowledge of the causes of human action, (from USC Law School, LA CA

9. Jeffery R: The Brain, the Lav, and the Medicalization of Crime, (from University of Florida School of Criminology)

10. from Tale Lav School, lev Haven, CT 06520

11. front National Institute of Alcoholism and Alcohol Abuse, Bethesda, MD

12. from Columbia Medical School, IT, IT (Unfortunately, due to unforeseen illness the Stanleys were forced to leave the workshop before presenting materials based on papers circulated in advance.

13. from University of Connecticut, Hartford, Conn

14. from UCLA Medical School, Los Angeles, CA

15. Rodgers WH: The Lesson of the Owl and the Crows: The Sole of Deception in the Svolstion of the Environmental Statutes (from Law School, University of Washington, Seattle, WA 98105).

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