NORMAL AGING OF THE HUMAN BRAIN POTENTIATES THE NEUROPATHOLOGIES OF PARKINSON'S DISEASE, DEPRESSION, AND ALZHEIMER'S DISEASE: BEHAVIOURAL IMPLICATIONS

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Abstract

The normal aging process of the human brain involves neuropathological changes which potentiate the progress of Parkinson's disease, depression and Alzheimer's disease. Thus the old person is not just a younger person afflicted with an especially stressful array of environmental contingencies. The professional should be prepared for the insidious development of milder forms of the symptoms of these diseases, in normal aging persons. As a corollary Parkinsonism, depression and Alzheimer's disease may be viewed as an acceleration of normal aging.

Résumé

L'évolution normale du vieillissement du cerveau humain entraîne des changements neuropathologiques qui intensifient le développement de la maladie de Parkinson, de la dépression, et de la maladie d'Alzeimer. Donc les stress de la viellesse ne proviennent pas uniquement des nouvelles exigences du milieu. Les professionnels impliqués dans des domaines associés à la gérontologie devraient être sensibilisés aux possibilités des dévoloppements insidieux des formes moins sévères de la maladie de Parkinson, de la dépression, et de la maladie d'Alzeimer.. L'auteur suggère que ces trois maladies représentent une accélération de l'évolution normale du vieillissement.

While we are all aware that *normal* senescence is accompanied by dimming of the senses, muscular weakening and digestive upsets, we are inclined to ignore the physical and chemical changes in the brain. Age related changes in cognitive and motivational behaviours are often ascribed to social factors, such as loss of job, bereavement, frustration with infirmity and relocation away from familiar surroundings (Baltes & Willis, 1977; Lawton, 1977). One might conclude from such emphasis on environmental factors that the oldster's behaviour would be the same as that of a young person subjected to the same horrendous stressors. The assumption is that the brain of the normal 80 year old is the same as the brain of the normal 20 year old. The knowledgeable professional might cavil remembering that brain cells do not replace themselves and that there is a loss of approximately 80,000 cells per day and therefore the normal old brain would have fewer cells. But because brain cell connections have a high degree of redundancy and because the net loss of brain cells over a lifetime has been placed at less than 1% (Brizee, Sherwood & Timiras, 1968), the observer would probably feel safe in concluding that the old brain is essentially the same as a young brain and that therefore, the burden of the age-related behavioural variance should be attribured to environmental factors.

However, evidence will be presented in this essay that there are significant physical and chemical differences between mature young and old brains and that these differences are signalled by pathological symptoms in specific parts of the brain. The expected behavioural correlates of these pathologies will be enumerated. Acceleration of these normal age-related pathologies has been proposed as an etiological factor in several neurological diseases. A corollary of this proposition is that the normal aging process exacerbates the same neurological diseases. An implication for psychological theories of aging is that environmental factors etiologically implicated in the onset of the diseases will have greater impact on the behaviour of an old person than on the behaviour of a mature younger individual. The description of the symptoms of these diseases will illuminate latent symptoms of a similar nature in the aged.

Motivation and Aging

Several brain neurotransmitter systems have been implicated in motivation. One of these systems involves the neurotransmitter dopamine and another system secretes the neurotransmitter noradrenalin. The dopaminergic nigrostriatal systems contain neurons which support electrical self-stimulation (Crow, 1971; German & Bowen,

1974). The implication is that normal physiological activation of these pathways is positively reinforcing. There is also evidence that this dopaminergic system is the neural substrate for heightened general activity and investigative behaviour (Randrup & Munkvad, 1974; Snyder, Banerjee, Yamamuro & Greenberg, 1974).

The aging mammalian brain undergoes a significant decline in the functional effectiveness of the dopamine system (Finch, 1973; Govoni, Loddo, Spano & Trabucci, 1977; McGeer, McGeer & Suzuki, 1977). The dysfunction may be measured as frank neuronal loss (McGeer et al., 1977) and as a compensatory denervation supersensitivity to released dopamine (Govoni et al., 1977; Spano, Kumakura, Tonon, Govoni, & Trabucchi, 1975). The ergot alkaloids, e.g., dihydroergotoxine, which stablize the terminal membranes of dopaminergic neurons (Goldstein, Lew, Hata, & Lieberman, 1978; Spano & Trabucchi, 1978) alleviate the complaints of the aged (Bazo, 1973; Hoffbrand, Maclay & Turner, 1976). Age pigment or lipofuscin accumulates in an age-related fashion in normal human brains. It consists of oxidized nerve cell membranes (Dayan, 1970; Gellerstedt, 1931; Matsuyama, Namiki, & Watanabe, 1966). Chronic chlorpromazine administration reduces neuronal lipofuscin accumulation (Samorajski & Rolsten, 1976). Chlorpromazine has multiple effects on release and uptake of dopamine (Snyder et al., 1974).

The dopaminergic system dysfunction in the normal aging brain mimics Parkinson's disease. The aging process moves the normal brain toward the Parkinsonian ratio of excess acetycholine to dopamine in the nigrostriatal system (McGeer et al., 1977). Conversely Parkinson's disease has been described as an acceleration of the normal aging process (Barbeau, 1976). The motor symptoms of the dopaminergic dysfunction in Parkinsons' disease e.g., tremor, rigidity and akinesia tend to obscure the motivational components, e.g., loss of initiative, decline in investigative and manipulative behaviour and avoidance of effort. The cognitive implications of the Parkinson model for the aged will be discussed in the cognitive section of this paper.

Neuronal secreting noradrenalin forms a second part of the motivational system. The dorsal noradrenergic bundle originates from cells in the locus ceruleus and has terminals in limbic system structures, as well as throughout the neocortex. This system has been implicated in the positively reinforcing goal oriented behaviours (Crow, 1972; Wise, Berger & Stein, 1973). Concentrations of noradrenalin (norepinephrine) decrease with age in the human brainstem (Robinson, Sourkes, Nies, Harris, Spector, Bartlett, & Kaye, 1977). Thus the locus ceruleus which is located in the dorsal aspect of the brainstem suffers noradrenalin depletion. Enzymes necessary for the synthesis of noradrenalin decline with age (Freedman, Onuchis, Goldstein, Axelrod, Fish & Dancis, 1972), whereas the level of enzymes which inactivate norepinephrine, such as monoamine oxidase and catechol-o-methyl transferase, increase with age (Broch, 1973; Robinson et al., 1977). There are also morphological signs of degeneration observable under the light microscope in the locus ceruleus of old people and in patients with Parkinsonism (Forno & Alvord, 1974; Forno & Goebel, 1974). Senescent mouse brains are impaired in ability to repair damage to noradrenergic cells of the locus ceruleus compared to young brains (Scheff, Bernardo, & Cotman, 1978). Specifically, very few of the degenerated axons subsequently regenerate to send branches to link up with the original target cells.

It is possible that this age-related neuropathology of the noradrenergic system contributes to the likelihood of behavioural depression in the aged. There is substantial evidence that behavioural depression in younger patients involves the same noradrenergic system. Drugs which decrease the activity of norepinephrine at central synapses induce depression in normal humans (Kety, 1967). Depressed patients have lowered levels of norepinephrine activity in the brain (Kety, 1971). Cerebrospinal fluid concentrations of norepinephrine metabolites increase in depressed patients who respond favourably to chemotherapy (Goodwin, Post, & Sack, 1975). Electro-convulsive shock, which is probably the most effective treatment for depression, increases the availability of norepinephrine at synapses in the brain (Kety, Javoy, Thierry, Julou & Glowinski, 1967). Tricyclic antidepressants which are effective therapeutically for many depressed patients inhibit the reuptake of norepinephrine in the locus ceruleus (Svensson & Usdin, 1978). The same drugs reduce the sensitivity of presynaptic receptors of noradrenergic neurons (Crews & Smith, 1978). These receptors provide a signal which blocks futher norepinephrine production in a negative feedback fashion. The net effect of both actions of the antidepressants is agonistic to the noradrenergic system. It is obvious that the age-related deterioration of the noradrenergic system would potentiate noradrenergic depressive pathology. Thus, one would expect an increase in the likelihood of depressive disturbances in old people beset by social deprivation, economic uncertainty and worries about infirmity, *beyond* that which one would expect in normal young people afflicted by the same difficulties.

Indeed, review of the behavioral literature suggest that older people are more susceptible to depressive disorders (Lewisohn & MacPhillamy,

1974; Lipton, 1976; Mendlewicz, 1976). Many institutionalized aged show an excess disability, apathy and excess dependence. Kahn (1971) has termed this avoidance of reality, "unoriented behavior." In the depressed elderly symptoms of memory loss and cognitive dysfunction have been severe enough to merit designation as pseudodementia, in that the symptoms resemble an organic psychosis (Post, 1975). The dopaminergic system evidence presented earlier in this paper suggests that the organicity may not be so pseudo after all. Similarly, evidence is available that depression and hence noradrenergic system dysfunction may underlie some instances of reported forgetfulness. In a remarkable study, it was found that the severity of memory loss as measured by objective tests in the elderly was correlated with neuropsychological tests of brain dysfunction but not with complaints about memory impairment by the elderly. The incidence of complaints about forgetfulness was correlated significantly with the degree of depression, not with the actual memory deficit (Kahn, Zarit, Hilbert, & Niderehe, 1975). If both members of an elderly couple complained about one member's forgetfulness, the designated individual was the more depressed and not necessarily the more mnemonically impaired. The breadth of this phenomenon is indicated by Lowenthal, Berkman, Buehler, Pierce, Robinson and Trier's (1967) observation that 66% of the non-institutionalized elderly over 75 years of age have complaints about memory loss. Thus in some cases, complaints of memory loss by the elderly are related to degree of depression and thus by inference to noradrenergic system dysfunction. The facts supporting the inference are detailed in the preceeding paragraph. The subject of genuine memory loss in the aged will be dealt with in the section of the essay on cognitive dysfunction.

If activity gives pleasure as the data on the dopaminergic system suggest, then behavioral corroboration should be available. Happy or successful, depression-free aging has been found to correlate positively with greater social participation (Graney, 1975), increased recreational activity (De Carlo, 1974), scheduling of social commitments (Schonfield, 1973) and adaptive outgoing personality factors (George, 1978). Heightened activity estimated by measures of physiological arousal correlated positively across individual elderly with performance on the Benton Visual Retention Test, and the Trail Test and inversely with Geriatric Scale rating (Poitrenaud, Hazemann, & Lille, 1978). Increased anxiety and open mindedness correlated positively with shorter reaction times and better recognition recall (Costa & Fozard, 1978). Type A individuals are more active and live longer than type B persons (Cohen, 1977). Physical exercise definitely facilitates physiological performance (Retzlaff & Fontaine, 1965; de Vries, 1971) and reaction time (Spirduso, 1975; Spirduso & Clifford, 1978). The last study is especially provocative because exercising men in their sixties had reaction times comparable to men in their twenties.

Conversely greater unhappiness and dissatisfaction is associated with reduced general activity and perception of reduced self-control over events (Kuypers, 1972; Reid, Haas & Hawkings, 1977). The aged compared to the young engage in fewer events they classify as pleasant (Lewinsohn & MacPhillamy, 1974).

If the reinforcement system for goal-oriented behaviour is impaired in the elderly, one would expect a tendency to ignore information conveyed by reward contingencies. Compared to the young, the aged exhibit a reduced sensitivity to the introduction of reward to a task (Sanford & Maule, 1973a) and shifts in reward value in a task (Sandford & Maule, 1976). The aged have difficulty choosing which source is supplying the best information feedback, a knowledge of results, form of rewards, and consequently, adopt less than optimal search strategies (Sanford & Maule, 1973b).

To summarize, parts of the dopaminergic and the noradrenergic neurotransmitter systems, both of which show age-related deterioration have been implicated in motivation. Damage to the dopaminergic system results in a loss of pleasure from being active, a decline in general and investigative activity and in extreme cases, the Parkinsonian pathology. Disease in the noradrenergic system results in loss of pleasure derived from accomplishment, unrealistic complaints, insensitivity to reward contingencies and eventually behavioural depression. The degreee to which behavioural regimens involving social and recreational activities can reverse these physiological trends is unclear since studies of the effects of such therapy on the aged afflicted with varying degrees of age-related brain damage have not been reported. The correlations cited do not rule out this interpretation.

Cognition and Aging

In an article titled "On Watching Myself Grow Old," Donald Hebb (1978) described three changes he observed in his own aging. These included difficulty in recalling a word he wished to use, persistence of unwanted, irrelevant thoughts, and a reduced interest in and motivation for tackling new problems. In the previous section of this paper, the age-related neuropathology relevant to decreased motivation was discussed. This portion of the paper deals with the neural mechanisms of memory and persistence.

Age-related damage in three neural systems may contribute to the memory deficits of the aged. Animal studies suggest the integrity of the noradrenergic system, previously discussed, is important for normal recall (Kety, 1971). Young depressive patients have impaired memory (Sternberg & Jarvik, 1976; Walton, 1958) but not as severe an impairment as that of the depressed elderly (Post, 1975; Zung, Rogers, & Krugman, 1968). Some of the forgetfulness of Parkinson patients (Bowen, 1976) may be the result of the degeneration of noradrenergic cells in the locus ceruleus (Forno & Alvord, 1974; Forno & Goebel, 1974). The precise aspect of memory to which the noradrenergic system contributes has not been established. Possibly the noradrenergic system guides the mechanism for retrieval from memory. Its dysfunction would contribute to the failure of the elderly to adopt optimal search strategies (Sanford & Maule, 1973b).

The dopaminergic pathology of the aged and the Parkinson patient may also contribute to the memory deficits of both. The hypothesis here is that both Parkinson patients and the elderly experience a general slowing of information processing. The most obvious sign of this basic deficit is the slowing of gross movements. As regards to memory dysfunction, slowed processing would be expected to result in slowed retrieval search of both primary and secondary memory (Anders & Fozard, 1973) and improvement in performance when total learning time available is increased (Adamowicz, 1976). Before this implication is pursued further, it should be noted that the present neural model of aging suggests that the forgetfulness of the senescent should be no worse than that of the depressed Parkinson patient, which is not the case (Craik, 1977; cf. Bowen, 1976).

In addition to the Parkinsonian and depressive pathologies, the normal aging brain is saddled with a latent form of Alzheimer's disease (presenile dementia). This disease is characterized by forgetfulness, as well as other signs already mentioned as either Parkinsonian or depressive (Kolb, 1968). There is morphological evidence supporting the contention that the normal aging of the brain approximates a mild form of Alzheimer's disease. There is a positive correlation between age related (1) nerve cell loss, (2) severity of helical tangles of neurofibrils, normally longitudinally arranged in the nerve fiber and thought to participate in the transport of vital substances along neurons, and (3) degree of granulovacuolar degeneration in the brain cells in both normal and Alzheimer patients. However, the yearly rate of cell loss is five times as great in the Alzheimer patient as in the normal aged person (Ball, 1977; Ball & Lo, 1977). Although these morphological signs have been found in many parts of the brain, in aged mammals (Scheibel, Lindsay, Tomiyasu & Scheibel, 1975; Scheibel, Tomiyasu & Scheibel, 1976; Stein & Firl, 1976; Vijayan, 1977) the magnitude of the cell loss is most severe in the hippocampus (Brizzee, Ordy & Kaack, 1974; Gellerstedt, 1931). Damage to the hippocampus results in memory deficits in humans (Milner, 1970). The magnitude of the hippocampal cell loss by 70 years of age is fairly substantial. There is approximately 12% cell loss in the normal elderly and 60% loss in Alzheimer patients of a similar age (Bael, 1977). It should be noted that substantial deterioration can occur before a neuron dies. Prior to the disintegration of the nerve cell body, there is an aged-related deterioration of dendritic (input) and axonal (output) terminal processes (Bondareff & Geinisman, 1976; Machado-Salas, Scheibel & Scheibel, 1977; Scheibel et al., 1975, 1976).

There is an age-related shortage of the enzymes necessary to synthesize acetylcholine, a principle neurotransmitter of the hippocampus (Spillane, White, Goodhart, Flack, Bowen & Davison, 1977; Vijayan, 1977). Chemical blocking of pathways requiring acetylcholine impairs performance on memory tests. The deficits were similar to those observed in normal old people (Drachman & Leavitt, 19740. In Alzheimer patients the decline in enzyme levels is significant in the hippocampus and the neocortex. Normal old people experience a significant decline in the enzyme levels only in the hippocampus (Perry, Perry, Gibson, Blessed & Tomlinson, 1977). This evidence implicates a failure of acetylcholine synthesis rather than lowered receptor site sensitivity (White, Goodhardt, Keet, Hiley, Carrasco, Williams & Bowen, 1977) as the critical mechanism. This speculation is corroberated by electron microscopic evidence of gross degenerative changes in presynaptic but normal postsynaptic structures (Wisniewski & Terry, 1976). The greater the depletion of the cholinergic enzyme, the more neurofibrillary tangles are evident (White et al., 1977). Geinisman, Bondareff and Telser (1977a, 1977b) suspect that the tangles may be partly responsible for reduced availability of the enzyme at the presynaptic membrane. Their evidence for a 25% slower rate and a 50% reduced volume of axonal transport of substances from the cell body to the presynaptic membrane supports this hypothesis.

The neurofibrillary tangles may be caused by the deposition of metallic ions in the nerve cells. The occurrence of neurofibrillary tangles is proportional to the pathological accumulation of aluminum in the brain cells (Crapper, Krishnan & Quittkat, 1976). The concentration of aluminum in Alzheimer patients is four times that in normal

aged people (Crapper, 1974; Crapper, Krishnan & Dalton, 1973). Implantation of aluminum into the brains of animals results in neurofibrillary tangles similar to those in aged human brains (Terry & Pena, 1965).

Accumulation of aluminum in brain cells during the aging process may be the result of altered levels of endocrine hormones. Fluctuations of adrenal cortex liberated corticosterone is correlated with the degree of gliosis and therefore neuron degeneration in the hippocampus (Landfield, Waymire & Lynch, 1978). Corticosterone modulates enzyme synthesis in the hippocampus via receptor sites in the hippocampus (Lee, Etgen & Lynch, 1977). A similar endocrine involvement in aging has been postulated regarding melanocyte stimulating hormone and the death of dopaminergic cells in the substantia nigra and noradrenergic neurons in the locus ceruleus in the aged and in Parkinson patients (Barbeau, 1976).

In summary, an endocrine hormone X brain interaction may be responsible for age-related morphological and biochemical changes in normal old people. Alzheimer's disease is seen as an acceleration of this normal aging process. The behavioural implications for memory and persistence will now be discussed.

The memory deficit of the aged is *not* specific for any particular mnemonic subfunction, such as memory storage capacity (Erber, 1976; cf. Salthouse, 1978); level of memory processing (Eysenck, 1974; Zelinski, Walsh & Thompson, 1978; cf. Mergler, Dusik & Hoyer, 1977); ignoring irrelevant stimuli (Rabbitt, 1965; cf. Klauser & Kleim, 1978); registration as opposed to retrieval (Adamowicz, 1976); long versus short delays of recall (Schneider, Gritz & Jarvik, 1975) or short versus long term memory (Squire, 1974; Warrington & Sanders, 1971). Both professionals and patients persist in believing that short-term memory is more adversely affected than long-term memory. This is probably the result of the difficulty in checking the patient's long-term memory accuracy. In addition, the elderly patient prefers to dwell on the golden past and to avoid the unpleasant realities of the present.

Rather than a deficit in a specific aspect of memory, forgetfulness in the elderly appears to be the result of a general slowing of information processing (Adamowicz, 1976). If the slowed processing were a general characteristic, one would expect an increased deficit with an increase in amount of information processed on verbal tasks (Anders & Fozard, 1973; Klauser & Kleim, 1978) and on nonverbal tasks (Benton, 1977; Fozard & Waugh, 1976); slowed retrieval search of both primary and secondary memory (Anders & Fozard, 1973; Waugh, Thomas & Fozard, 1978) and slowed rotation and comparison of spatial depth figures (Gaylord & Marsh, 1975). The studies cited have demonstrated these effects with the normal aged. When given time to reach the same original learning criteria, young and old are no different on subsequent recall (Hulicka, 1965). When allowed to pace themselves, the elderly took longer to learn the task than did the young persons but did just as well as the young on recall tests (Adamowicz, 1976). Total learning time available rather than rate of presentation is the critical variable (Winn & Elias, 1977).

Two main categories of subtest of traditional intelligence tests are age sensitive. These are the speeded subtests and the memory subtests (Birren & Morrison, 1961; Shader, Harmatz & Salzman, 1974; Williams, 1970). The present hypothesis suggests that the speeded and memory subtests are measuring the same thing. Memory tests would produce "speed" deficits if the pace of stimulus presentation and response production were too rapid for the slow rate of information processing of the old person.

Timed subtests of the intelligence inventories usually do not distinguish between a cognitive or reaction time component and a motor or movement time component. Both times are slow in the aged (Spirduso, 1975) and in Parkinson patients (Brumlick & Boshes, 1966). Retarded movement times in the aged are attributable to slower motoneuron conduction velocities (Norris, Shock & Wagman, 1953), loss of muscle fiber mass (Gutmann & Hanzlikova, 1976) decreased frequency of miniature end-plate potentials and slowed contraction coupling time (Gutmann & hanzlikova, 1972). Slowed reaction times on the other hand are of such magnitude that raised sensory thresholds (Clark & Mehl, 1971; Dyck, Curtis, Bushek & Offord, 1974; Dyck, Schultz & O'Brien, 1972; Harkins & Chapman, 1976; Kokmen, Bossemeyer & Williams, 1978; Whanger & Wang, 1974) and slowed sensory neuron conduction rate (Retzlaff & Fontaine, 1965) would account for only a small portion of the slowed reaction time. Slowed information processing seems to be the hypothesis which best fits the data (Simon & Pouraghabagher, 1978).

It is possible that the slowness of the aged is partly the result of a prolongation of the neural response to internally or externally generated stimuli (Axelrod, 1963; Botwinick, 1973). If the subsidence of the neural response to the initial stimulus is slow, the perception of the second stimulus would be retarded and slowed processing of information would result. If this were the case, one would look for evidence in the aged of the persistence of brief images at the registration level and for the perseveration of sets at the cognitive level.

Exaggerated persistence of the iconic trace has recently been demonstrated to result in superior performance in the recognition of fragmented words in the aged compared to the young (Kline & Orme-Rogers, 1978). Complementary halves of a single word were flashed on a screen one after the other. If the persistence of the trace of the initial word half in the mind of the viewer was superimposed on the flash of the second half of the word, recognition of the word would result. Old people were especially superior for the longer intervals between word fragments. In addition, old persons show enhanced persistence of complementary after-images (Kline & Nester, 1977), and as one might expect, poor temporal resolution of shocks to the skin (Axelrod, Thompson & Cohen, 1968); showed temporal processing of auditory stimuli (Corso, 1975); lowered visual critical flicker fusion thresholds (McFarland, 1951; Misiak, Warren & Kavis, 1958), as do Parkinson patients (Riklan, Levita & Misiak, 1970); lowered auditory click fusion thresholds (Weiss, 1959), protracted susceptibility to backward masking (Kline & Szafran, 1975) and longer lasting visual evoked responses to photic stimulation (Mundy-Castle, 1953). It is easy to see how such persistence, if also applicable to items retrieved from primary or secondary memory, would slow down retrieval search time (Anders & Fozard, 1973).

When one speaks of secondary and permanent memory operations, one usually speaks of perseveration of sets rather than persistence of traces, even though the nature of the deficit is the same. Old people perseverate in viewing ambiguous figures in only one mode (Botwinick, Robbin & Brinley, 1959), persist in viewing the Necker cube in only one view (Heath & Orbach, 1963) and fail to reverse the figure-ground relationship in order to read ambiguous words (Kline, Culler & Sucec, 1977). Parkison patients persist in an error response for a longer duration on tracking tasks than do normal individuals (Angel, Alsten & Higgens, 1970; Bowen, Hoehn & Yahr, 1972). Tasks requiring a shifting of problem solving set are especially taxing for the aged (Botwinick, Brinley & Birren, 1975; Botwinick, Brinley & Robbin, 1958, 1959; Goodrick, 1972; Heglin, 1956). Old people have anecdotally described the persistence with which unwanted tunes and thoughts run through their minds (Hebb, 1978).

It should be emphasized that perseveration of sets implicates expressive, as well as receptive processes as deficient. The slowed processing seems to implicate all aspects of information manipulation. The examples of the previous two paragraphs provide evidence for slowed receptive functioning. The best example given to this point for the retardation of response processes is the slowed retrieval of items from lexical, primary and secondary memory (Anders & Fozard, 1973; Waugh, Thomas, & Fozard, 1978). Retrieval of items from environmental sources of information by the elderly is slow as well. The slowness has been linked to the old persons' tendency to use less than optimal search strategies. This inefficiency in the utilization of strategies has been observed in a wide variety of situations: failure to use clustering (Denney, 1974; Hultsch, 1971) or imagery mnemonics (Hulicka & Grossman, 1967; Rowe & Schnore, 1971) or incidental cues (Perlmutter, 1978) to ease verbal learning; failure to use systematic search of several sources when looking for a hidden visual object (Sanford, 1973); the same difficulty on a haptic match to sample task (Kleinman & Brodzinsky, 1978); and failure to adopt the optimal maximizing strategy on a probability learning task (Sanford & Maule, 1973a). Conversely on tasks in which the material was not amenable to strategic organization, the differences between the young and the elderly were small (Craik & Masani, 1967; Heron & Craik, 1964).

Young persons adopt strategies by responding selectively to clues abstracted from the task situation. Old people are also aware of these clues (Sanford, 1973) and can benefit from strategies derived from the clues when instructed to do so (Canestrari, 1968; Hulicka & Grossman, (1967), but they do not voluntarily use the strategies. The failure to use strategies is probably the result of an interaction of several neuropathologies. Dopaminergic dysfunction may contribute directly to slowed processing and thus render the simultaneous handling of multiple stimulus inputs difficult. For example, in the haptic match to sample task (Kleiman & Brodzinsky, 1978) an optimal search strategy involved sweeping both hands simultaneously — one over the standard stimulus and one over the comparison stimulus to detect abstracted general features. The old person by contrast used one hand to palpate successively the standard and comparison stimuli for unabstracted details. It is apparent that simultaneous bimanual sweeping of two different objects would be very difficult for a brain coping with memory traces of extended duration. Hebb (1978) believes that closed circuits of cortical cell assemblies failure to inhibit such extraneous traces would be a contributing factor to the persistence phenomena in the elderly. Either the dopaminergic or the noradrenegic system could be responsible for such changes in cell connections because portions of both systems project diffusely to the neocortex.

The noradrenergic system pathology may contribute to the deficit by making the individual

less sensitive to reward contingencies. Examples of the oldsters' failure to respond to shifting contingencies were provided in the motivation section of this paper. As a consequence, one would expect that the elderly would not be sensitive to reward increments achievable with more optimal strategies (Sanford & Maule, 1976). If the noradrenergic pathology is important here, one would expect corroborative behavioural evidence from depressed patients. An interesting parallel was found in the case of probability matching tasks. Old people persisted in using a matching strategy whereas, young persons preferred the more efficient maximizing strategy (Sanford & Maule, 1973a). The matching strategy involved predicting which of two keys would light up next, at a frequency indentical to that at which the keys were actually lighting up. The strategy was inefficient because although probabilities of prediction of event and event occurrence match, the trials of occurrence of the two do not match. The optimal strategy is to maximize, that is to always predict that the more frequent of the two events will occur. Depressed persons were tested in a slightly different situation. They were told they could control the occurrence of the lights by pressing the respective keys whereas in actuality the lights were controlled by an independent program. The subjects were then asked to estimate the degree to which they controlled the light probabilities. The normal individuals had a significantly exaggerated perception of their degree of control whereas the depressed individuals had a very realistic impression of their control. This intriguing result may reflect the same process as that basic to the elderlys' probability matching (Alloy & Abrahamson, in press). Perhaps Seligman's (1975) view of the depressed person as one suffering from an illusion of lack of self control should be one of suffering from the lack of an illusion of self control. Hebb (1978) spoke of old age as characterized in part by an absence of "arrogant confidence that I can master the new ideas and developments in the field." The totalitarian ego of the normal young individual capable of distortion of belief in one's own power, goodness and stability (Greenwald, in press) gives way with advancing age to a mellow ego with a more limiting but perhaps more realistic view of things.

Finally the pathology of the cholinergic system in the hippocampus most certainly contributes to the elderlys' difficulty in using strategies. Studies of hippocampal damage in man (Sidman, Stoddard, & Mohr, 1968) and animals (Kimble & Pribram, 1963) reported deficits on tasks requiring codes or strategies.

To summarize, the old person is not just a younger person facing a more stressful array of environmental contingencies. In fact, the normal aging process is accompanied by neuropathological changes which would clearly potentiate the progress of Parkinson's disease, Alzheimer's disease or depression should the appropriate precipitating virus, toxin or behavioural stress occur. Further one should be prepared for the insidious development of milder symtoms of these diseases (and probably others) in normal aging persons. Finally Parkinsonism, depression and Alzheimer's disease may be viewed as accelerations of normal aging.

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