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Do mental events cause neural events analogously to the probability fields of quantum mechanics?

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If non-material mental events, such as the intention to carry out an action, are to have an effective action on neural events in the brain, it has to be at the most subtle and plastic level of these events.

In the first stage of our enquiry an introduction to conventional synaptic theory leads on to an account of the manner of operation of the ultimate synaptic units. These units are the synaptic boutons that, when excited by an all-or-nothing nerve impulse, deliver the total contents of a single synaptic vesicle, not regularly, but probabilistically. This quantal emission of the synaptic transmitter molecules (about 5000–10000) is the elementary unit of the transmission process from one neuron to another.

In the second stage this refined physiological analysis leads on to an account of the ultrastructure of the synapse, which gives clues as to the manner of its unitary probabilistic operation. The essential feature is that the effective structure of each bouton is a paracrystalline presynaptic vesicular grid with about 50 vesicles, which acts probabilistically in vesicular (quantal) release.

In the third stage it is considered how a non-material mental event, such as an intention to move, could influence the subtle probabilistic operations of synaptic boutons. On the biological side, attention is focused on the paracrystalline presynaptic vesicular grids as the targets for non-material mental events. On the physical side, attention is focused on the probabilistic fields of quantum mechanics which carry neither mass nor energy, but which nevertheless can exert effective action at microsites. The new light on the mind–brain problem came from the hypothesis that the non-material mental events, the 'World 2' of Popper, relate to the neural events of the brain (the 'World 1' of matter and energy) by actions in conformity with quantum theory. This hypothesis that mental events act on probabilistic synaptic events in a manner analogous to the probability fields of quantum mechanics seems to open up an immense field of scientific investigation both in quantum physics and in neuroscience.

1. Introduction

All attempts to formulate a dualist hypothesis on brain–mind interaction are met with the strong criticism that such an hypothesis violates the conservation laws of physics. On this basis it is maintained that the World of matter-energy (the

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World 1 of Popper) is completely closed to the action of any non-material agency such as the subjectively experienced mind (the World 2 of Popper). These critics as a rule do not deny their mental experiences. They are dualists of a sort, but they deny the effectiveness of mental events, such as an intention to move, in causing or modifying neural events in the motor centres of the brain. There are many versions of such parallelist or identity or physicalist theories in which it is proposed that the mental events 'somehow' are identical with a special class of neural events as was first proposed by Feigl (1967). Such theories lack precision in their formulations, but have been generally accepted because they do not violate the *closedness of World 1*.

Similarly the dualist–interactionist theory of Popper & Eccles (1977) lacked a precise formulation of the site and manner of the postulated mental–neural interaction. Its appeal lay in its explanatory power of our experiences, particularly in respect of voluntary movement, where we seem indubitably to bring about actions at will.

In recent years investigations on the brain events in voluntary movements have defined with some precision the neural events which are triggered by the mental events of intending to move, as will be described below. This work has been recently reviewed (Eccles 1982*a*, *b*), but the enigma of the manner of the mental–neural interaction remained. It was suggested (Eccles 1982*b*) that the mental influence of intention to move might be able to change dynamic patterns of interacting nerve impulses and that this may not involve a net change in the matter–energy system of the brain. Three very recent happenings have shed new light on these hitherto unsatisfactory theoretical concepts.

2. Probability of quantal emission from a synaptic bouton

Figure 1*a* illustrates a simple synaptic system where many nerve fibres make synaptic contact with a neuron. The brief electrical message or impulse in a nerve fibre travels to the ending (synapse) of this fibre on a neuron (cf. figure 2*k*) and by a chemical transmitter mechanism, it there sets up a brief depolarization of the surface membrane of that target neuron. A single impulse sets up a very small excitatory postsynaptic potential (EPSP), as it is called, but there is an approximately arithmetical summation of the EPSPs simultaneously produced by impulses in other fibres (figure 1*b–g*) converging on that neuron, as is illustrated in figure 1*k–n*, where $k+l+m=n$.

We must now focus attention on EPSPs produced by a single presynaptic impulse (figure 2*a*). Figure 2*k* shows a synaptic ending (a bouton) on a dendrite of a neurone. A bouton is a structural unit, and they are shown as small swellings on many fibres in figure 1*a*, where each presynaptic fibre makes several synapses on the neurone. In the bouton of figure 2*k* there are many small vesicles which contain the synaptic transmitter substance. For any one presynaptic fibre, this array of its synapses can be identified on the dendrites of a neurone by special labelling techniques (Brown 1981). A diagram of one such fibre, with its five boutons, is shown in figure 2*b*. It was surprising to discover that a single presynaptic impulse generates the wide fluctuation of EPSPs illustrated in figure 2*c*. However, when

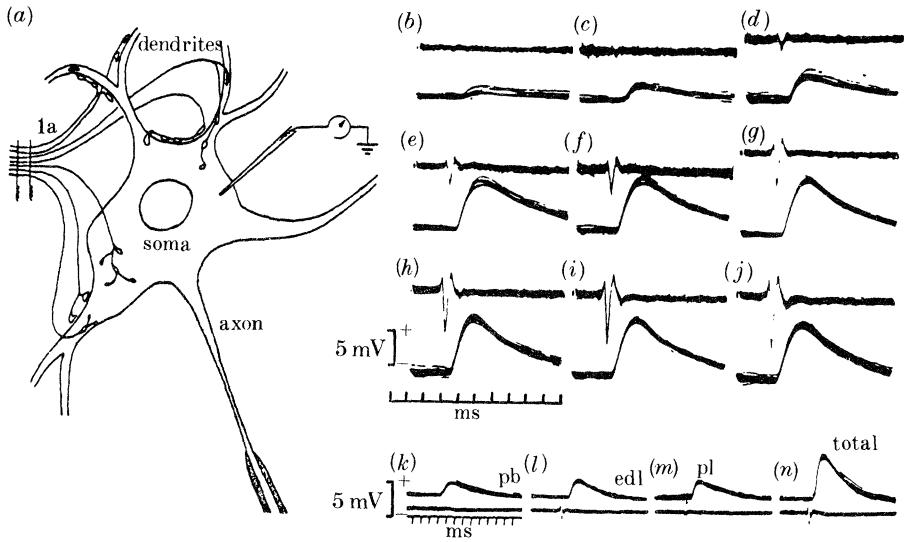

FIGURE 1. Monosynaptic excitation of motoneurons by the group Ia afferent pathway. (*a*) Drawing of a motoneuron showing the central dendritic regions, the soma, the initial segment of the axonal origin and the beginning of the axonal medullation. On the dendrites and soma are shown the excitatory synaptic endings of seven group I*a* afferent fibres that have an applied stimulating electrode (actually in the peripheral muscle nerve). The intracellular microelectrode recording is shown diagrammatically. (*b*)–(*j*) The upper traces give the size of the afferent volley as it enters the spinal cord, and the lower the simultaneously recorded EPSPs. All records are formed by the superimposition of about 25 faint traces. (*k*)–(*m*) The EPSPs recorded in another motoneuron (peroneus longus) in response to maximum group I*a* volleys in the nerves to three muscles: peroneus brevis, extensor digitorum longus and peroneus longus. (*n*) All three muscles combined (Eccles *et al.* 1957).

there is averaging of a large number (800) of such EPSPs, a smooth simple EPSP is recorded (*d*) much as in figure 1*b–j*. The fluctuations in the EPSPs of figure 2*c* are attributable to two factors: to fluctuations in the EPSPs produced by a single bouton, and to fluctuations in number of the boutons generating the EPSPs.

By a sophisticated technique of fluctuation analysis (Jack *et al.* 1981*a*) it has been possible to derive the averaged unitary EPSPs produced when a single impulse invades each one of the four boutons on that neuron (figure 2*e–h*). The EPSP is produced by the emptying into the synaptic cleft of synaptic vesicles (*k*) containing the transmitter substance. This complete emptying of the 5000 to 10000 transmitter molecules in a vesicle is a quantal emission (Hubbard 1970). The fluctuation analysis reveals that never more than the contents of one vesicle is emitted from a bouton and that there is a probability of emission of one vesicle (quantum) from each of the four boutons, as is indicated: *e*, 0.29; *f*, 0.5; *g*, 0.16; *h*, 0,05. Allowing for these probabilities, *e*, *f*, *g*, *h* can be added to give the EPSP (*i*) which is identical with *d* when allowance is made for the different scaling. The probability of emission is usually about 0.4.

A similar fluctuation to that of figure 2*c* was observed for a granule cell of the hippocampus activated by a single presynaptic impulse (McNaughton *et al.* 1981).

By a binomial method of analysis the mean probability, of vesicular emission was calculated to be 0.3, but with other methods, values of 0.9 and 0.4 were calculated. Further investigation is needed for a reliable estimate, but at least there is agreement that the probability is less than 1.0, or even much less. In a further study the highest probabilities with boutons on two CA_1 pyramidal cells of the hippocampus were 0.363 and 0.365, respectively (Dr P. Andersen, personal communication).

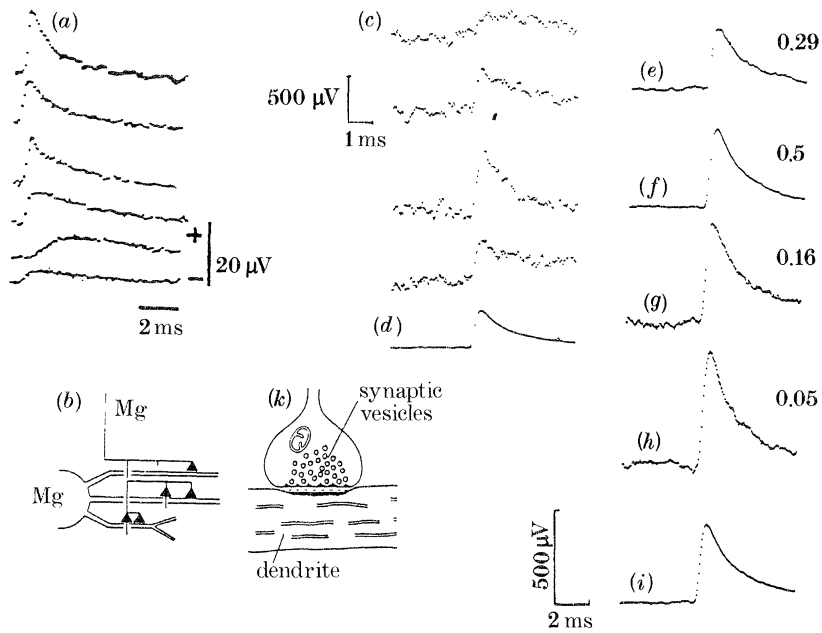

FIGURE 2. (*a*) Averaged recordings of EPSPs produced by impulses in the same I*a* fibre terminating on six different motoneurons (Mendell & Henneman 1971). (*b*) Summary diagram of the location of I*a* synapses from a single medial gastrocnemius I*a* fibre on to a medial gastrocnemius motoneuron at five sites on three different dendrites as indicated (Brown 1981). (*c*) Four individual EPSPs selected from a population of 800 responses. (*d*) The average of all the 800 responses. *e*, Component 1 of the EPSP derived from fluctuation analysis. (*f*)–(*h*) Components 2, 3 and 4 of this same fluctuation analysis. The probabilities of the occurrence of these components are indicated to the right of each. (*i*) The reconstructed EPSP obtained by adding the weighted sum of (*e*), (*f*), (*g*), (*h*); $0.29\,(e)+0.5\,(f)+0.16\,(g)+0.05\,(h)$ (Jack *et al.* 1981*a*). (*k*) Drawing of a synapse on a dendrite to show the bouton with vesicles and the synaptic cleft.

The only other central synapses studied in this unitary analysis are the very different synapses, the inhibitory synapses on the Mauthner cell of a fish spinal cord (Korn & Faber 1986). The synaptic potentials showed a fluctuation comparable with that of figure 2*c*, and a binomial method of analysis gave essentially the same results, namely that for a single bouton there was never more than a probability of emission of a single vesicle, which usually was about 0.3 to 0.4.

The observed fluctuations of unitary EPSPs as in figure 2*c* can be accounted for

on the basis of the four quantal EPSPs of *e–h*, either alone or in every possible combination at a frequency governed by the mean probabilities of each. This probability of emission of quanta of transmitter from single boutons represents a fundamental unit of synaptic action in the brain.

3. The structural basis of the quantal probability

Since our enquiry concerns the mode of operation of the cerebral cortex at the ultimate micro-level, attention will be concentrated on the spine synapses discovered by Gray in 1957 and illustrated in figure 3, his most recent drawing (Gray 1982).

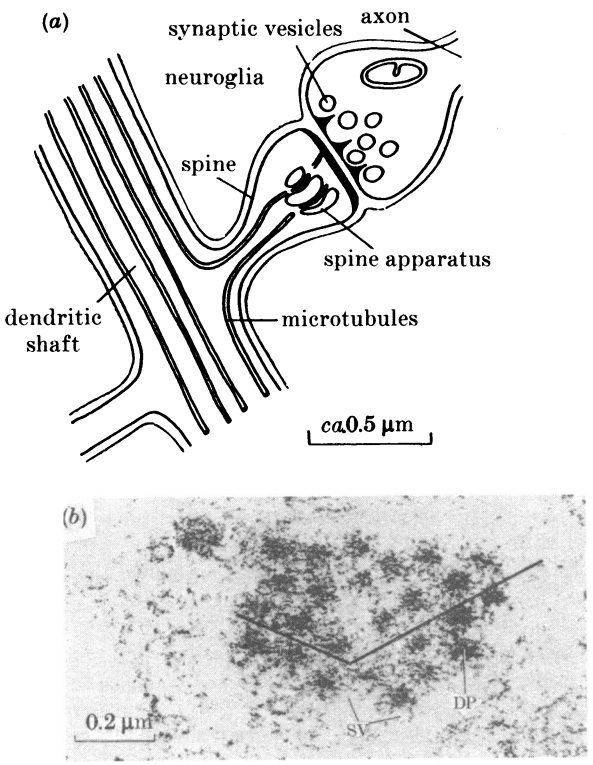

FIGURE 3. (*a*) Drawing of an synapse on a dendritic spine. The bouton contains synaptic vesicles and dense projections on the presynaptic membrane (Gray 1982). (*b*) Presynaptic dense projections (DP) seen *en face* on the presynaptic membrane; SV, synaptic vesicles (Gray 1982).

Almost all of the cortical excitatory synapses are in this form, there being about 10^{14} in the human cerebral cortex. The bouton is shown as a terminal swelling of the axon (the presynaptic fibre) and it contains synaptic vesicles partly arranged in relation to presynaptic dense projections (*b*) that arise from the presynaptic membrane in the region of its confrontation with the synaptic spine across the synaptic cleft, which is about 20 nm wide.

Further structural analysis, particularly by the freeze–fracture technique of

Akert and associates (1972, 1975), has led to the construction of a diagram of an idealized spine synapse (figure 4), which is shown in perspective with partial excisions to reveal the deeper structures. The relatively loose arrangement of synaptic vesicles and presynaptic dense projections (figure 3) is shown in figure 4 as the precise packing illustrated in the inset on the left, with the synaptic vesicles

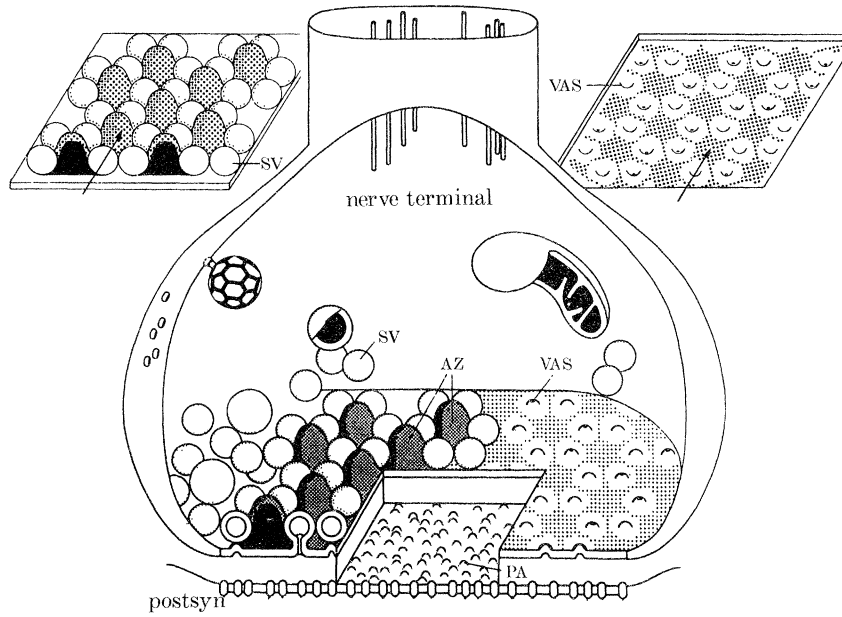

FIGURE 4. Schema of the mammalian central synapse. The active zone is formed by presynaptic dense projections (AZ). The postsynaptic aggregation of intramembraneous particles is restricted to the area facing the active zone. SV, synaptic vesicles; PA, particle aggregations on postsynaptic membrane (postsyn.). Note synaptic vesicles (SV) in hexagonal array, as is well seen in the upper left inset, and the vesicle attachment sites (VAS) in the right inset. Further description in text (Akert *et al.* 1975).

in hexagonal array packaged between the presynaptic dense projections in triangular array. This composite structure is termed a presynaptic vesicular grid and it can be regarded as having paracrystalline properties (Akert *et al.* 1975; Triller & Korn 1982). The boutons of brain synapses have a single presynaptic vesicular grid, as is indicated in figures 3 and 4. Thus the probability of quantal (vesicular) emission is a holistic property of the presynaptic vesicular grid of a bouton. Actually this probability is not a fixed number for a bouton. By physiological and/or pharmacological treatment it can be increased or decreased (Jack *et al.* 1981*b*; Hirst *et al.* 1981; Korn & Faber 1985).

There are only approximate figures for the number of synaptic vesicles incorporated in a presynaptic vesicular grid. The usual number appears to be 30–50 from the illustrations of Akert *et al.* (1972, 1975). Triller & Korn (1982) give the number as 44–83 for the boutons on Mauthner cells. Thus only a very small proportion of the synaptic vesicles of a bouton (about 10000) is embedded in the firing zone of the presynaptic vesicular grid. The remainder are loosely arranged in the interior of the bouton, as is partly shown in figures 3 and 4.

Figure 5*a* well illustrates the packaging of transmitter molecules into a synaptic vesicle, its movement up to the presynaptic vesicular grid with locking into a presynaptic density of the presynaptic grid. Finally (figure 5*b*) there is apposition to the presynaptic membrane under the influence of Ca^{2+} ions, and the total release of the transmitter molecules into the synaptic cleft. The very close contact of the vesicle to the presynaptic membrane (figure 5*b*(ii)) is also depicted in the left of figure 4 with the two little bulges and one vesicle apparently ready to discharge, while to the right of figure 4, after the vesicles and the dense projections have been stripped off, the vesicle attachment sites (VAS) are seen in hexagonal array, as also in the inset diagram to the right.

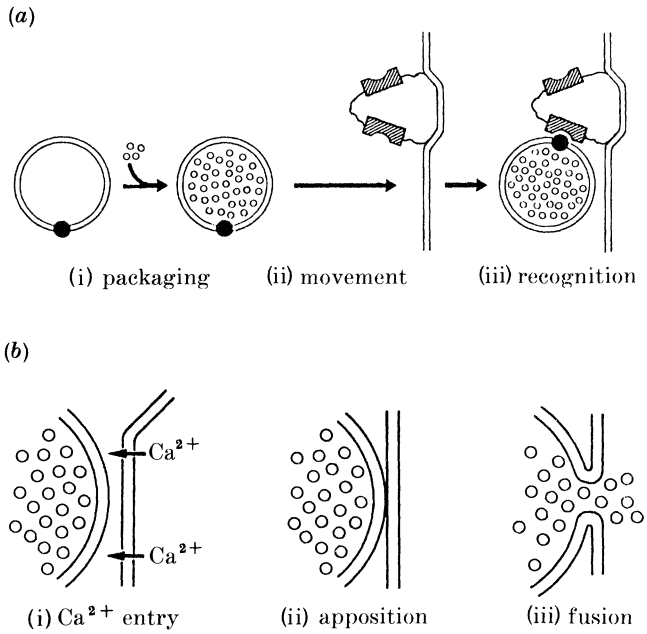

FIGURE 5. Stages of synaptic vesicle development, movement and exocytosis. (*a*) The three steps involved in filling a vesicle with transmitter and bringing it to attachment to a presynaptic dense projection of triangular shape. (*b*) Stages of exocytosis with release of transmitter into the synaptic cleft, depicting the essential role of Ca^{2+} input from the synaptic cleft (Kelly *et al.* 1979).

4. THE POSSIBLE ROLE OF A NON-MATERIAL MENTAL EVENT ACTING AT BRAIN MICROSITES ANALOGOUSLY TO THE PROBABILITY FIELDS OF QUANTUM MECHANICS

In a recent book the quantum† physicist Margenau (1984), has suggested that a non-material mental event such as an intention to move could influence neural events at microsites without violating the conservation laws of physics. He states

† It should be pointed out that there are two distinct uses of the word *quantum*: that in quantum physics, and that in neuroscience for the unit of synaptic transmission (a synaptic vesicle).

(p. 96): 'In very complicated physical systems such as the brain, the neurons and sense organs, whose constituents are small enough to be governed by probabilistic quantum laws, the physical organ is always poised for a multitude of possible changes, each with a definite probability; if one change takes place that requires energy, or more or less energy than another, the intricate organism furnishes it automatically. Hence, even if the mind has anything to do with the change, that is, if there is a mind-body interaction, the mind would not be called upon to furnish energy'. In summary Margenau states (p. 97): 'The mind may be regarded as a field in the accepted physical sense of the term. But it is a nonmaterial field, its closest analogue is perhaps a probability field. It cannot be compared with the simpler nonmaterial fields that require the presence of matter (hydrodynamic flow or acoustic) ... Nor does it necessarily have a definite position in space. And so far as present evidence goes it is not an energy field in any physical sense, nor is it required to contain energy in order to account for all known phenomena in which mind interacts with brain.'

Hitherto such postulated microsites have had no specific identification, but now the evidence presented in §2 and §3 suggests that, because of the probability of vesicular emission, the presynaptic vesicular grids are ideally fitted to be the targets for the non-material mental events such as the intention to carry out some movement. It is *not* proposed that the mental events initiate activity at a synapse by an excitatory action either on the presynaptic or postsynaptic elements of a synapse such as figure 3*a*. On the contrary, the hypothesis is that the mental events merely alter the probability of a vesicular emission that is triggered by a presynaptic impulse. This action of a mental event would be exerted on the paracrystalline presynaptic vesicular grid that acts in a global manner in controlling the probability of emission of one vesicle from its array of many embedded vesicles.

The first question that can be raised concerns the magnitude of the effect that could be produced by a probability wave of quantum mechanics. Is the mass of the synaptic vesicle so great that it lies outside the range of the uncertainty principle of Heisenberg? Margenau (1977, p. 384) adapts the usual uncertainty equation for this calculation of non-atomic situations:

$$\Delta x\, \Delta v \geqslant k/m, \quad \text{where } k = 1.06 \times 10^{-27} \text{ erg s. } (1 \text{ erg} = 10^{-7} \text{ J.})$$

The mass (m) of a synaptic vesicle 40 nm in diameter can be calculated to be 3×10^{-17} g. If the uncertainty of the position Δx of the vesicle in the presynaptic vesicular grid is taken to be 1 nm, then Δv, the uncertainty of the velocity, comes out at 3.5 nm in 1 msec, which is not far from the right order of magnitude. The presynaptic membrane (figures 4 and 5) is about 5 nm across and the time of emission of a vesicle is many tenths of a millisecond (Katz & Miledi 1965).

However, this calculation assumes that the synaptic vesicle is freely moving, which is certainly not the case when it is embedded in the presynaptic vesicular grid (figure 4). Since that grid is a paracrystalline structure, it could have special resonance relations with a mental influence operating analogously to a probability field. A valuable insight into the manner of operation of the presynaptic vesicular grid could come from the quantum mechanics of microcrystalline structures. As

illustrated in figure 5*b*, the postulated mental influence would do no more than alter the probability of emission of a vesicle already in apposition.

It can be concluded that calculations on the basis of the Heisenberg uncertainty principle show that the probabilistic emission of a vesicle from the presynaptic vesicular grid could conceivably be modified by a mental intention acting analogously to a quantal probability field.

The second question raises the order of magnitude of the effect, which is merely a change in probability of emission of a single vesicle (figure 5). This is many orders of magnitude too small for modifying the patterns of neuronal activity even in small areas of the brain. However, there are many thousands of similar boutons on a pyramidal cell of the cerebral cortex. The hypothesis is that the probability field of the mental intention is widely distributed not only to the synapses on that neurone, but also to the synapses of a multitude of other neurones with similar functions. The next section will treat this problem with special reference to the cerebral response to the mental intention to carry out a voluntary movement.

5. Amplification of the postulated action of a mental intention in changing the probability of emission of a synaptic vesicle

Figure 6 shows the position of the supplementary motor area (SMA) of the left cerebral hemisphere in the medial part of the frontal cortex just anterior to the motor area of the hind limb and extending deep on the medial side. By a radio-Xenon technique, Roland *et al.* (1980) recorded the regional blood flow (rCBF) over

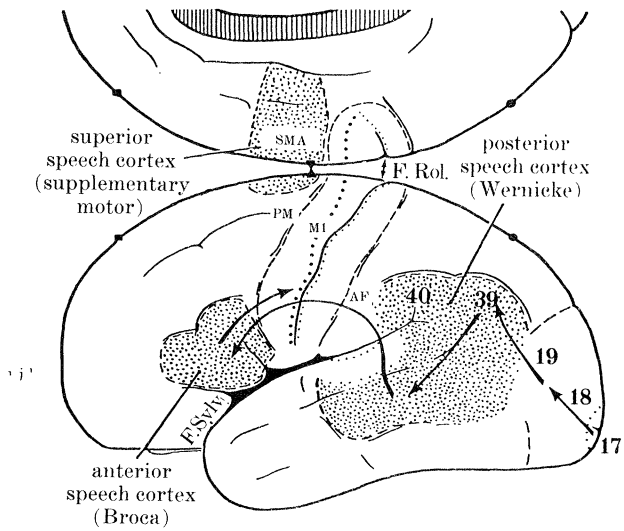

Figure 6. The left hemisphere from the lateral side with frontal lobe to the left. The medial side of the hemisphere is shown as if reflected upwards. F.Rol. is the fissure of Rolando or the central fissure; F.Sylv. is the fissure of Sylvius. The primary motor cortex, M1, is shown in the precentral cortex just anterior to the central sulcus and extending deeply into it. Anterior to M1 is shown the premotor cortex, PM, with the supplementary motor area, SMA, largely on the medial side of the hemisphere (modified from Penfield & Roberts 1959).

a cerebral hemisphere, there being an assembled pattern from 254 Geiger counters for recording the detailed spatial pattern of radio-emission following a brief injection of radioXenon into the internal carotid artery. It is now established that any regional increase in rCBF is a reliable signal of an increased neuronal activity in that area. The subject was trained to make a complex pattern of finger-thumb movements for the full duration (45 s) of the Geiger counting. In figure 7*a* there was a strong activation of the contralateral motor and sensory areas for the thumb and fingers, as would be expected, but there was just as strong an activation of the SMA, and that was bilateral. The primacy of the SMA is revealed in figure 7*b*,

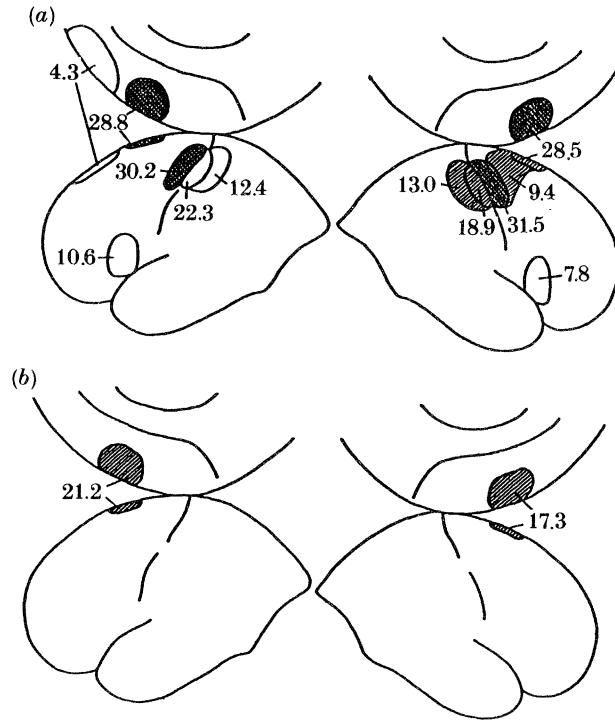

FIGURE 7. (*a*) Mean increase of the rCBF (%) during the motor-sequence test performed with the contralateral hand, corrected for diffuse increase of the blood flow. Cross-hatched areas have an increase of rCBF significant at the $p = 0.0005$ level. Hatched areas have an increase of rCBF significant at the $p = 0.005$ level; for other areas shown, the rCBF increase is significant at the level $p = 0.05$. Left: left hemisphere, five subjects. Right: right hemisphere, ten subjects. (*b*) Mean increase of rCBF (%) during internal programming of the motor-sequence test; values corrected for diffuse increase of the blood flow. Left: left hemisphere, three subjects. Right: right hemisphere, five subjects (Roland *et al.* 1980).

when during the radioXenon test the subject was making no movement but merely carrying out the learned motor task mentally. A highly significant (20%) increase in neuronal activation was restricted to the SMA on both sides, and was nowhere else. The subject was at complete rest with eyes and ears closed. This rCBF increase is an index of an increase in neuronal activity of the SMA under the influence of

a mental intention by the subject. Evidently the mental intention was bringing into action an immense ensemble of neurons, which of course would be essential if it is to cause the desired movement.

By means of an implanted microelectrode it has been possible to study the responses of single SMA neurons of a monkey while it was carrying out a voluntary movement (figure 8*a*, *c*; Brinkman & Porter 1979). There was an increase in the discharge rate of many neurons at about 50 ms before the discharge of motor cortical neurons that eventually would cause the willed movement as signalled by the electromyogram of figure 8*b* (cf. Eccles 1982*a*, *b*). Ethical considerations preclude the carrying out of such an experiment on a human subject. However, the recording of electric and magnetic fields over the human scalp during repetitive voluntary movements (Deecke & Kornhuber 1978) also point to the neurons of the SMA as the site of strong activation by the mental intention.

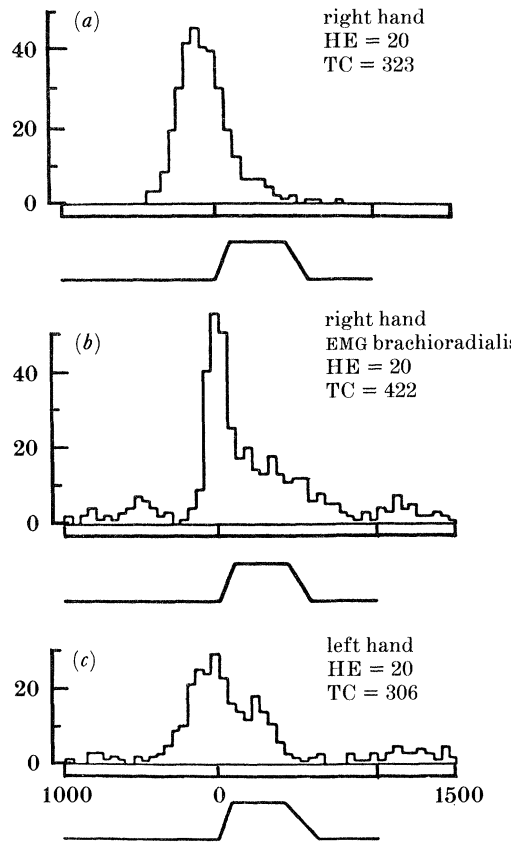

FIGURE 8. Illustration of the discharge patterns of a neuron associated with flexion of the elbow during the lever pull for both the right (*a*) and left hand (*c*). (*b*) is the periresponse time histogram demonstrating the EMG activity of a representative elbow flexor, m. brachioradialis, in the right arm during the same 20 pulls as those in (*a*), and shows that the neuron increased its discharge well before EMG activity increased. This was the case for the majority of neurons in which the discharge pattern could be compared with EMG changes (Brinkman & Porter 1979).

According to the hypothesis the presynaptic vesicular grid provides the *chance* for the mental intention to change *by choice* the probability of its synaptic emission. This would be happening over the whole ensemble of spine synapses that are activated at that time, probably even thousands, since there are about 10000 on a single cortical pyramidal cell (Szentágothai 1978*a*). It would be expected that a mental influence analogous to a probability field would exert a global influence on the synapses of an appropriate neuron, modifying up or down the probabilities of vesicular emission by incoming impulses.

So the *reliability* of mental intention is derived from integration of the *chance happenings* at the multitude of presynaptic vesicular grids on that neuron. In order to bring about some chosen movement, such as bending one's finger, the mental intention has to select the correct pyramidal cells for its action in modifying the probability of vesicular emissions. This selection is accomplished according to the learned inventory of SMA cells for a particular movement. It can be effective only when there is a background synaptic barrage on those cells, because all it can do is to modify the probability of vesicular emission of the activated synapses. Tanji & Kurata (1982) have demonstrated the wide convergence of sensory inputs onto SMA cells. All such activated boutons can be regarded as presumptive sites for modification of the probability of vesicular release by the mental intention.

This may seem a clumsy method for initiating a movement, but it must be recognized that we do have the ability to carry out at will an immense range of movements, and this necessitates a most complex strategy of selection of SMA neurons from the enormous inventory of about 100 million pyramidal cells in perhaps 30000 modules. All we experience is how mentally to initiate the skilled movement. It is essential that the mental intention causes the activation of packages of SMA neurons in correct time sequence for the different muscles concerned in the motor act, as has been demonstrated for SMA neurons by Brinkman & Porter (1979, 1983). In the simplest explanation these SMA cells project to the other cortical and subcortical areas in order to have the learned motor programmes incorporated into the eventual activation of the motor pyramidal cells with discharge down the pyramidal tract.

In summary it can be stated that it is sufficient for the dualist–interactionist hypothesis to be able to account for the ability of a non-material mental event to effect a changed probability of the vesicular emission from a single bouton on a cortical pyramidal cell. If that can occur for one, it could occur for a multitude of the boutons on that neuron, and all else follows in accord with the neuroscience of motor control. The closedness of World 1 has been opened and by a mental intention we genuinely are able to bring about movements at will.

6. The action of silent thinking on the cerebral cortex

Figure 9*a* illustrates a remarkable finding of Roland (1981) that, when the human subject was attending to a finger on which a just-detectable touch stimulus was to be applied, there was an increase in the rCBF over the finger touch area of the postcentral gyrus of the cerebral cortex as well as in the mid-prefrontal area. These increases must have resulted from the mental attention because no touch

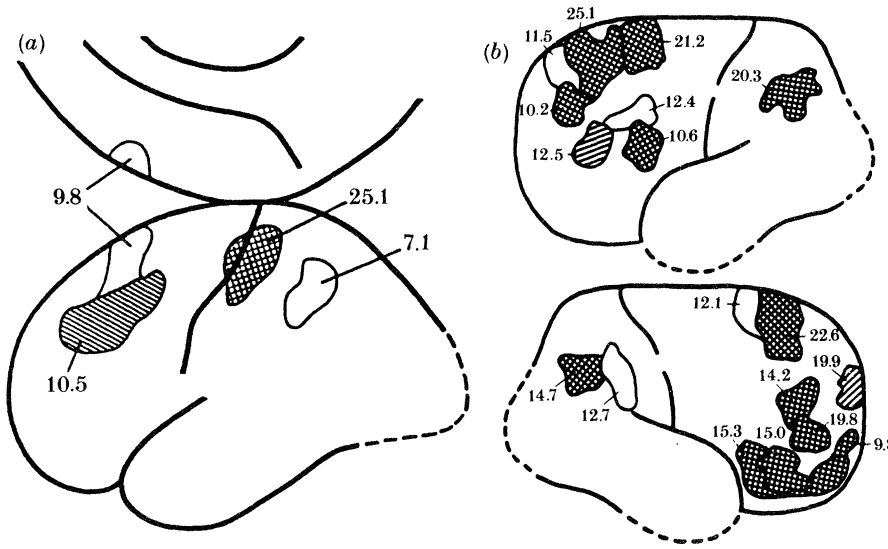

FIGURE 9. (*a*) Mean increase of rCBF (percentage) during pure selective somatosensory attention; that is, somatosensory latent sensing without peripheral stimulation. The size and location of each focus shown is the geometrical average of the individual focus. Each individual focus has been transferred to a brain map of standard dimensions with a proportional stereotactic system. The cross-hatched areas have an increase of rCBF significant at the $p = 0.0005$ level (Student's t test, one-sided significance level). For the other areas shown the rCBF increase is significant at the $p = 0.05$ level. Eight subjects (Roland 1981). (*b*) Mean increases of rCBF (percentage) and their average distribution in cerebral cortex during silent arithmetic with successive subtraction of threes from 50. Left hemisphere six subjects, right hemisphere five subjects. Cross-hatched areas have rCBF increases significant at the $p = 0.005$ level. With hatched areas $p < 0.01$ and with outlined areas $p < 0.05$ (Roland & Friberg 1985).

was applied during the recording. Thus figure 9*a* is a clear demonstration that the mental act of attention can activate appropriate regions of the cerebral cortex. A similar finding occurs with attention to the lips in expectation of a touch, but of course the activated somatosensory area is now for the lips.

The effect of attention in causing an increased cerebral electrical response to finger touch has been demonstrated by Desmedt & Robinson (1977). In a very ingenious investigation they discovered that with touch to the attended finger there was a large increase in the late N 140 and P 500 evoked potentials relative to controls with touch to unattended fingers. This may be correlated with the increased rCBF that attention produced in the finger area of figure 9*a*. In both these investigations the mental event of attention is effecting selective neuronal responses.

A related finding is that, when the subject was attending to simple counting or other arithmetical mental activities during complete relaxation with eyes and ears closed, there was an increased rCBF in many cortical areas, but not in the primary sensory or motor areas (Roland & Friberg 1985). As illustrated in figure 9*b* for both the left and right hemispheres with the silent mental arithmetic of successive subtractions of 3 starting with 50, there was an increased rCBF in a medial strip

of the frontal cortex anterior to the SMA, and also in other areas of the prefrontal cortex on both sides, as well as in the supramarginal and angular gyri of both parietal lobes. The patterns are more complex than for the silent thinking of a motor movement in figure 7*b*. Still more complex patterns were revealed with a memory sequence based on a nonsense word sequence and with the visual imagery of route-finding.

It can be predicted that the immense range of silent thinking of which we are capable will be found to initiate activity in such a wide variety of specific regions of the cerebral cortex that the greater part of the neocortex will be found to be under the mental influence of thinking (Ingvar 1985). Of course there is as yet no criterion for demonstrating a direct influence. The areas of direct activation can immediately influence other areas, as occurred with the SMA (figure 7*b*) activating the motor cortex (figure 7*a*).

The hypothesis that non-material mental events alter the probability of vesicular emission by presynaptic vesicular grids can account for all these influences of silent thinking.

7. The mind–brain problem

In formulating more precisely the dualist hypothesis of mind–brain interaction, the initial statement is that the whole world of mental events (World 2) has an existence as autonomous as the world of matter–energy (World 1) (figure 10). It can be mentioned that we only know of World 1 through sense organs. Sense organs provide the data by which we perceive, and act and think and remember, and hence for all of human activity including science and technology. The present interactionist hypothesis does not relate to these ontological problems, but merely to the mode of action of mental events on neural events, that is to the nature of the downward arrows across the frontier in figure 10. The hypothesis is that the mental influence modifies the probability of vesicular emission from an activated bouton in a manner analogous to the probability fields of quantum mechanics.

Since it is postulated that mental events can influence only those neural events engaged in the probability of quantal (vesicular) emission by presynaptic impulses, it would be predicted that the effectiveness of mental events would be reduced to zero when the presynaptic background was reduced to zero. Loss of consciousness would occur, and would be irreversible unless there were revival to a considerable degree of the impulse discharge in the cerebral cortex. An example is 'vigil coma' that supervenes when injury to the mid-brain turns off the reticular activating system (Hassler 1978; Eccles 1980). In fact the principal role of the reticular activating system may be to provide a background of excitatory impulses into the cerebral cortex with an immense array of probabilistic vesicle emissions that are targets for the quantal probabilistic fields of mental influence.

So we can assume that, in a global manner, the mental events achieve interaction with the neural events of spatiotemporal patterns of activity (Eccles 1982*b*) of the awake cerebral cortex. Even in one cortical module with its 4000 or so neurones, there must be an ongoing intense dynamic activity of unimaginable complexity. Although we know the outlines of the neuronal structure of a module (Szentágothai 1978*a*, 1983), there has as yet been only a very limited study of the physiology.

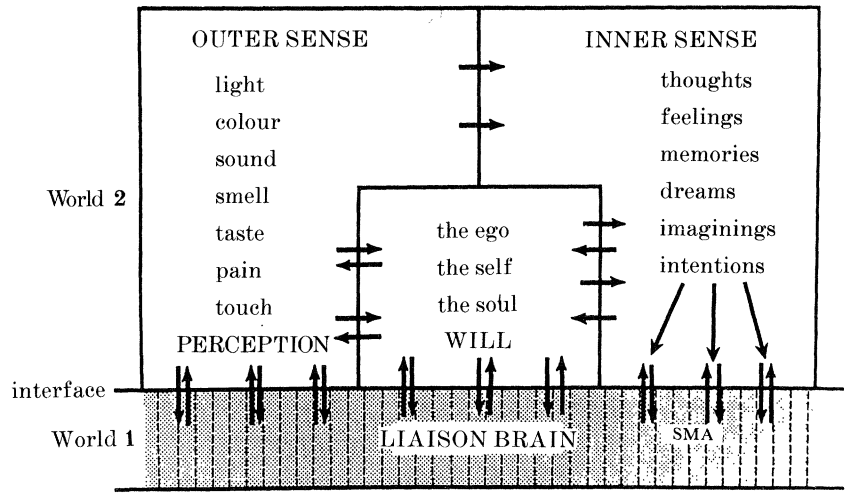

FIGURE 10. Information flow diagram for mind–brain interaction in human brain. The three components of World 2 (outer sense, inner sense and the ego, self or soul) are drawn with their communications shown by arrows. Also shown are the lines of communication across the interface between World 1 and World 2, that is from the liaison brain to and from these World 2 components. The liaison brain has the columnar arrangement indicated by the vertical broken lines. It must be imagined that the area of the liaison brain is enormous, with open or active modules numbering over a million, not just the two score here depicted. The supplementary motor area, SMA, is shown specially related to intentions of World 2, with the three arrows giving some suggestion of the potential specificity of action of the intention on the modules of the SMA, as discussed in the text. World 2 is shown above World 1, but this is a diagrammatic device without spatial significance. If World 2 is to be given any spatial location, it will be placed where it acts, which is shown by the arrows to be in the modules of the liaison brain.

All that we can surmise is that mental events acting as a field in the manner postulated by Margenau (1984) could effect changes in the spatiotemporal activity of a module by changing the probability of emission in many thousands of active synapses. There need be no violation of conservation laws.

One can ask how the monkey sets up the immense synaptic barrage that results in the neuronal firing in figure 8*a* and *c* and that through the well-known complex pathways results in the desired motor action. The only answer is that this performance is at the end of a long line of training sessions. Motor learning is essential for all skilled actions devolving from the cerebral cortex, and this is particularly true for human actions (Eccles 1986). Memory of some kind is required for all conscious experiences and actions.

A final consideration relates to the reverse arrows in figure 10, from cerebral cortex to mind, as for example in perception to the left of the diagram. Is it possible that the discharge of a vesicle from a presynaptic vesicular grid can cause a mental event by a quantum probability wave in the reverse direction? Such vesicular emissions would occur in immense numbers in the perceptual areas of the cerebral cortex. Hence there could be an immense summation of 'unitary' mental events in order to surpass the threshold for a perception.

A general observation is that hitherto all hypotheses attempting to give some

explanation of how conscious experiences derive from or relate to neural events concentrate on the extreme complexity of the neural events in the active cerebral cortex, as was done by Feigl (1967) in the introduction. Sperry (1976) proposed that mental events are holistic configurational properties of the brain process. Mountcastle (1978) developed the concept of distributed systems which are 'composed of large numbers of modular elements linked together in echeloned parallel and serial arrangements', and are thought to provide an objective mechanism of conscious awareness. Edelman (1978) suggested that 'the brain processes sensory signals and its own stored information upon this selective base in a phasic (cyclic) and re-entrant manner that is capable of generating the necessary conditions for conscious states'. Szentágothai (1978*b*) suggested that 'dynamic patterns' offer 'superstructures' and might be helpful to give a scientific explanation on the higher functions of the brain, including even consciousness. Eccles (1982*b*) suggested that 'the mental influence is exerted on an extremely complex dynamic system of interacting neurones'.

The extreme alternative to these 'nebular' hypotheses is now proposed, namely that the essential locus of the action of non-material mental events on the brain is at individual microsites, the presynaptic vesicular grids of the boutons, each of which operates in a probabilistic manner in the release of a single vesicle in response to a presynaptic impulse. It is this probability that is assumed to be modified by a mental influence acting analogously to a quantal probability field in the manner described above. The manner in which effective action at microsites becomes amplified by conventional neuro-circuitry will be dependent on the complex circuits envisioned for example by Feigl (1967), Sperry (1976), Mountcastle (1978), Edelman (1978), Szentágothai (1978*b*) and Eccles (1982*b*). *The microsite hypothesis* can be proposed as a tentative beginning of a scientific study of the reflective loop proposed by Creutzfeldt (1979) as opening up the independent symbolic world of the mind, which is the World 2 of Popper & Eccles (1977). In contrast to the 'nebular' hypotheses, it offers a unique challenge to molecular neurobiology.

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