Some manifestations of the J-reflex

A. S. Paintal

Centre for Visceral Mechanisms, Vallabhbhai Patel Chest Institute, Delhi University, Delhi 110 007, India

The discovery of the J-reflex and how it helped to understand the cause of the muscle weakness in the victims of the Bhopal gas tragedy is described. Secondly, it was found that intravenous injections of lobeline stopped muscle clonus in a patient.

A discussion of the area of J-reflex is incomplete without discussing the contributions made by Devanandan to this area nearly thirty years ago[1]. How Devanandan got involved in this area at a time when his attention was directed at studying spinal reflexes by the monosynaptic technique deserves a mention. At that time, I was conducting experiments on the mechanisms of stimulation of J-receptors, then called alveolar receptors. I was struck by the fact that anaesthetized cats would relax completely for a short period after an intravenous injection of phenyl diguanide (PDG). I also observed that whenever the cats overcame the effects of the anaesthesia, another intravenous injection of PDG resulted in calming down of cats and all signs of muscular movements ceased. These observations and the role of the J-receptors in animals led to the following questions: (i) What is the physiological stimulus for the J-receptors? (ii) What is the actual mechanism for their stimulation? (iii) What physiologically useful reflex do they produce as a consequence of their activity? It seemed quite clear that the J-receptors were stimulated as a result of pulmonary congestion[2]. The next question was what were the physiological conditions under which pulmonary congestion would occur, leading to the stimulation of the J-receptors. Muscular exercise seemed to be the only physiological condition under which pulmonary congestion could occur. If this was indeed the case, I concluded that the central effect of impulses from the J-receptors was to produce muscular relaxation and thereby terminate exercise. But, proof for this was lacking at that time, although Kalia's on-going contemporary work[3] on the knee jerk suggested that this indeed could be the case. The proof came in July 1968. I had to go to Lucknow for a meeting at the Central Drug Research Institute. Before going I gave Devanandan a solution unknown to him (actually it was PDG, 100 µg/kg) and asked him to inject 2 ml of it intravenously into a cat while recording the monosynaptic reflex. Upon returning after two days, I was met at the door by Devanandan and Deshpande. 'What was the solution you gave us' asked Devanandan. 'Why' I said – 'was the monosynaptic reflex abolished'. 'How did you know' asked Devanandan excitedly. I knew then that we had discovered an important reflex – later called the J-reflex.[4]

A major observation by Deshpande and Devanandan was that the effect of PDG which inhibited the monosynaptic reflexes of various muscles tested, was abolished after mid-collicular decerebration (Figure 1). This meant that certain higher pathways were involved in the reflex inhibition. This was studied in detail by Kalia using a simpler approach, i.e. by recording the knee jerk of the cat[5] and seeing the effect of PDG on the size of the knee jerk before and after making certain lesions in the cerebrum. Specifically, her aim was to see which lesions did not abolish the knee jerk. It was essential for her to pursue the enquiry along this line, because making lesions in any part of the brain tends to depress the function of the other parts of the brain. Using this approach she found that making lesions in various parts of the brain, except the caudate nucleus and cingulate gyrus, permitted the J-reflex to survive, i.e. the knee jerk was still diminished after injecting PDG.

Schiemann and Schomburg[6] found that there were three components of central motor actions of the J-receptors: (i) inhibitory effects mediated by structures rostral to the intercollicular level, (ii) excitatory effects from structures caudal to this level, and (iii) certain

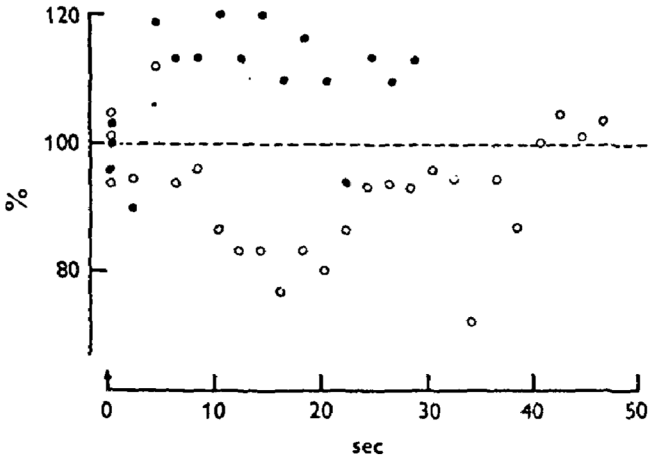

Figure 1. Gastroncnemius soleus monosynaptic reflex on right atrial injection of PDG at zero time. Following intercollicular decerebration, injection of PDG no longer depresses the reflex as shown by the filled circles. Ordinate, size of monosynaptic reflex as percentage of control = 100% (from ref 1.)

depressing effects upon brain stem responsiveness. At about the same time, Kalia *et al.*[7] showed in a film to the German Physiological Society, how a moving cat stops walking on injecting PDG through an intravenous catheter. Rao and Devanandan[8] explored the spinal pathways involved in the J-reflex and Ahluwalia *et al.*[9] also made related observations. Kalia[10] reported observations on the reflex effects of J-receptors on kittens and showed that the J-reflex appeared only three weeks after birth, whereas the respiratory and cardiac reflexes were present a week after birth. Satchell[11] showed how the J-reflex affected the swimming ability of fishes.

Later it was found that receptors other than J-receptors, e.g. those located in the heart, could also depress the knee jerk, since injecting PDG into the left atrium depressed the knee jerk, an effect that could be abolished by injecting xylocaine into the pericardial sac[12].

The Bhopal gas tragedy of 1984, involving methyl isocyanate affected several thousand individuals. Those that survived complained, in addition to the complaint of breathlessness, a feeling of marked muscular weakness. This appeared to be due to the operation of the J-reflex because the motor cortex had to produce greater activity to overcome the inhibition, by the greatly increased activity of J-receptors, exerted at lower spinal levels[13] (Figure 2). However, one should keep in mind that although impulses from the J-receptors may be of primary importance during muscular exercise (Figure 2), other pathways in the brain may also be involved during the execution of muscular movements. This is confirmed by the observations of Pickar *et al.*[14], who showed that the walking movements produced by stimulation of

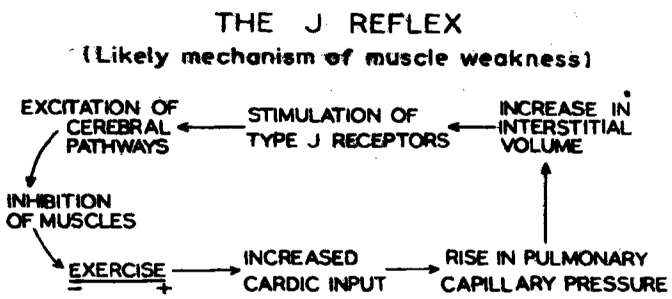

Figure 2. Sequence of events in the J-reflex showing how exercise is terminated by stimulation of the J-receptors during exercise. The reflex is also the likely basis for the feeling of muscle weakness in pathophysiological conditions leading to interstitial oedema (from ref. 13). This is a modified version of an earlier figure in ref. 4.

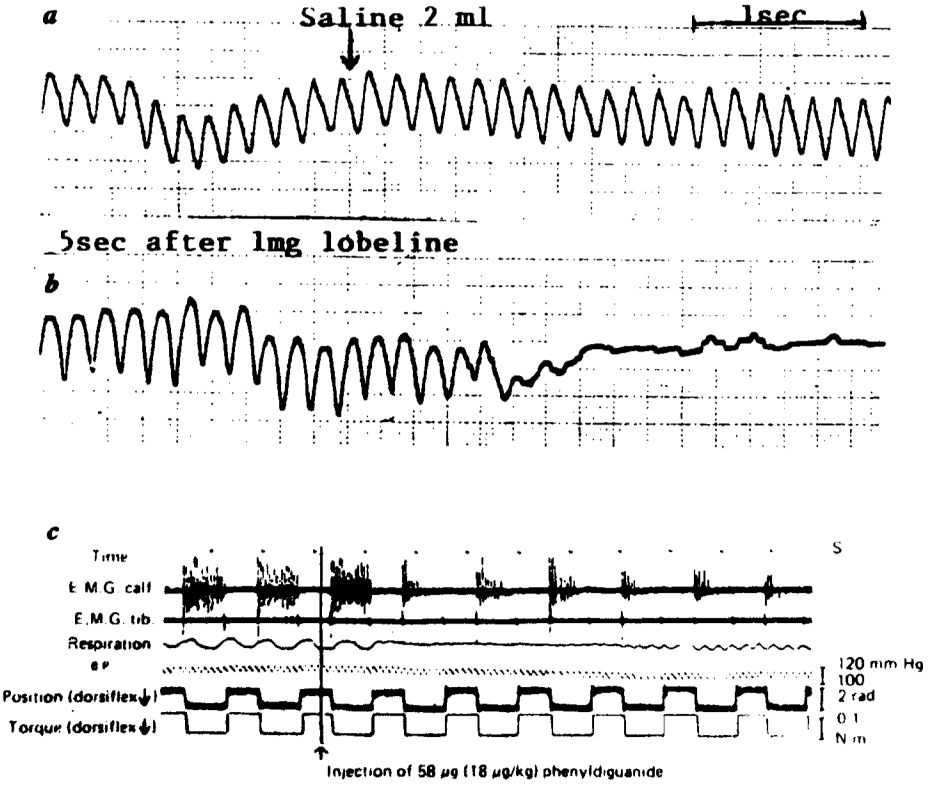

Figure 3. Effect of lobeline on muscle clonus in a female patient with upper motoneurone lesion. *a*, shows that injection of 2 ml saline had no effect on the clonus elicited by dersiflexion of the foot. *b*, 1 mg lobeline was injected i.v. before start of the record. This abolished the clonus. (Paintal *et al.*, 1981, unpublished observations). *c*, Corresponding effect on a cat: Stretch activity in the calf emg (topmost trace) is seen when the foot is dorsiflexed rhythmically. On injection of 18 µg/kg PDG there is opnoea and the calf emg is reduced (from ref. 19).

midbrain structures in decerebrate cats were greatly inhibited, following stimulation of the J-receptors by injections of phenybiguanide or congestion of the lungs produced by raising the left atrial pressure. (Kalia[15] had also reported earlier that pulmonary congestion inhibited the knee jerk of cats.) Clearly in these decerebrate cats the higher cerebral pathways had been cut. This recalls the original observations of Ginzel and Eldred[16], showing that decerebrate rigidity of cats is abolished by injecting PDG, although at that time the authors did not know that this effect was through the stimulation of J-receptors.

A critical evaluation of the J-reflex and other aspects of somato–motor inhibition by stimulating J-receptors, is available in a more recent review by Coleridge and Coleridge[17], and it is clear that the reflex sometimes operates in a dramatic way in various animals from fishes to mammals. Although it has been postulated that in certain conditions stimulation of the J-receptors in humans produces a feeling of muscle weakness (Figure 2), direct stimulation of J-receptors of man by injections of lobeline does not give rise to motor inhibition in normal humans unequivocally as shown recently by certain observations by Raj and Agrawal[18]. Clearly much more work needs to be done in this area of great clinical importance. For example, in certain neurological conditions involving upper motoneurone disease, the clonus produced by dorsiflexion of the ankle in humans is dramatically reduced by injections of lobeline (Figure 3 *b*), reminding one the corresponding situation seen in cats wherein the rhythmically produced stretch reflex of the soleus muscle (Figure 3 *c*) is reduced by i.v. injections of PDG[19].

Injection of PDG also depresses the activity of the muscles involved in coughing produced by touching the carina of the cat's trachea with a thin nylon fibre[20]. It has been suggested that this depression of muscle activity may be a manifestation of the J-reflex[21]. This needs to be confirmed in humans because of its clinical importance[21]. As concluded earlier[22], the cough that appears after lobeline injections is not a reflex act following stimulation of the J-receptors. Recently, Widdicombe[23] has also pointed this out and so it seems appropriate to term the cough response after stimulating the J-receptors with lobeline, or by any other way, such as pulmonary congestion[13] as a behavioural cough.

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