Abstract

Repeated administration of dopaminergic agents such as L-dihydroxyphenylalanine (L-DOPA) or apomorphine in hemiparkinsonian rat model enhances the rotation response induced by subsequent administration of dopaminergic agent. This phenomenon is known as "priming" and comparable to drug induced dyskinesia in human Parkinson's disease. This study was designed to investigate the electrophysiological changes of the substantia nigra pars reticulata (SNpr) neurons and their response to selective D2 agonist corresponding to the behavioral changes following priming.

6-hydroxydopamine (6-OHDA) was stereotactically injected into the nigrostriatal pathway of the adult rats to make hemiparkinsonian model. After 3 weeks from lesioning, apomorphine was administered repeatedly for 1 week with measurement of rotation response. Also rotation response to selective D2 agonist quinpirole was measured before and after apomorphine administration. After completion of behavioral test extracellular single unit recording was done in SNpr. Baseline firing rate, firing pattern and response to systemically administered quinpirole were analyzed.

Repeated administration of apomorphine caused significant increase in rotation response. The number of rotations/hr at first test was 341/hour and 755/hour at the last session. The number of rotation induced by equipotent amount of quinpirole was less than by apomorphine, however, it also showed significant increase after repeated apomorphine administration. Baseline firing rates of SNpr
neurons in ipsilateral and contralateral side of the lesion did not showed significant difference. Priming did not make any difference either. SNpr neurons were classified according to the firing pattern into burst and non-burst unit. Frequency of burst units was significantly higher in the ipsilateral side than the contralateral side of the lesion (19/49 vs. 0/47). Also frequency of burst units in the ipsilateral SNpr was higher in the animals with repeated administration of apomorphine than the animals with no subsequent treatment after 6-OHDA-lesioning (13/28 vs. 6/21). Firing of the SNpr neurons was more frequently and strongly suppressed by quinpirole in the animals treated with apomorphine.

In conclusion, the increase of burst units among SNpr neurons and enhanced suppression by selective D2 agonist are the significant electrophysiological changes corresponding to behavioral changes after priming.

Key word : Parkinson's disease, priming, single unit recording, substantia nigra pars reticulata, quinpirole
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