(-)-Epigallocatechin gallate, the most active polyphenolic catechin in green tea, presynaptically facilitates Ca2+-dependent glutamate release via activation of protein kinase C in rat cerebral cortex.

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Abstract

(-)-Epigallocatechin gallate (EGCG), the main polyphenolic constituent of green tea, has been reported to improve cognitive decline. Considering the central glutamatergic activity is crucial to cognitive function, the objective of this study was to investigate the effect of EGCG on the release of endogenous glutamate using nerve terminals purified from rat cerebral cortex. Results showed that the release of glutamate evoked by 4-aminopyridine (4AP) was facilitated by EGCG in a concentration-dependent manner, and this effect resulted from an enhancement of vesicular exocytosis and not from an increase in Ca2+-independent efflux via glutamate transporter. Examination of the effect of EGCG on cytoplasmic free Ca2+ concentration ([Ca2+]c) revealed that the facilitation of glutamate release could be attributed to an increase in Ca2+ influx through N- and P/Q-type voltage-dependent Ca2+ channels. Consistent with this, the EGCG-mediated facilitation of 4AP-evoked glutamate release was significantly prevented in synaptosomes pretreated with a combination of the N- and P/Q-type Ca2+ channel blockers. Additionally, inhibition of protein kinase C (PKC) by treatment with Ro318220 significantly reduced the facilitatory effect of EGCG on 4AP-evoked glutamate release and phosphorylation of PKC or its presynaptic target myristoylated alanine-rich C kinase substrate (MARCKS). These results suggest that EGCG effects a facilitation of glutamate release from glutamatergic terminals by positively modulating N- and P/Q-type Ca2+ channel activation through a signaling cascade involving PKC. In this EGCG/PKC signaling cascade facilitating glutamate release, the regulation of cytoskeleton dynamics was also indicated to be involved by disruption of cytoskeleton organization with cytochalasin D occluded the EGCG-mediated facilitation of 4AP-evoked glutamate release.