

due to such confounding factors.

In conclusion, we have shown that low frequency rTMS over the DLPFC could produce rCBF changes in the distant paralimbic areas. We conclude that antidepressant effects of rTMS over the right DLPFC could be produced by modulation of the meso-limbic dopaminergic system as well as influence on the local and distant paralimbic regions.

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Legend for figures

Fig. 1 A schema of rTMS/PET protocol

A total of 9 PET scans consisted of 3 conditions, sham condition before rTMS, during_rTMS and sham conditions before and after rTMS. In each condition, three scans were performed. In rTMS condition, 100 trains of rTMS were administered during each PET acquisition. Further, subjects received 100 trains of rTMS during each inter-scan interval. Subjects received 100 trains of rTMS every 5 min 8 times under rTMS condition, therefore, a total of 800 trains of rTMS were delivered to each subject.

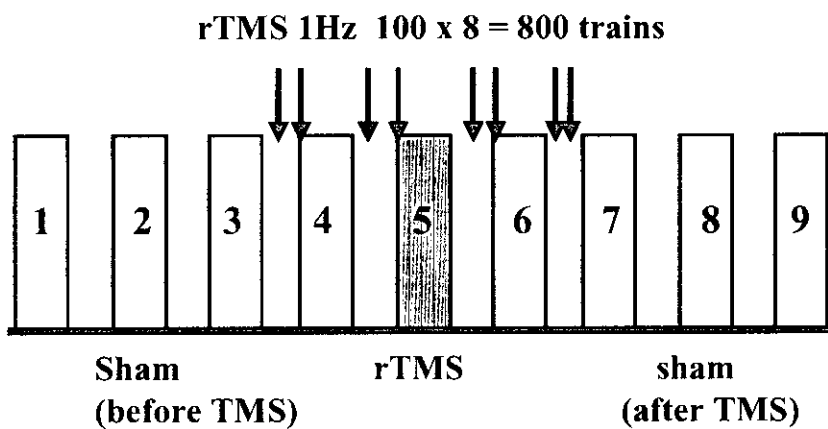


Fig.2 Fixation of a rTMS coil in the PET scanner.



Fig.3 To determine the site of stimulation, a transmission image was coregistered and superimposed on an anatomical MR image. The black image outside the skull is a rTMS coil. See details in methods.

Fig.4 An area showing rCBF increase during 1Hz rTMS over the right dorsolateral prefrontal cortex.

4a. The 3-dimensional "look-through" projections of SPM with brain regions that were significantly active during rTMS as compared with sham condition (before rTMS) ($p = 0.001$ with correction for multiple comparison). Significant activation was noted in the right anterior cingulate cortex and medial prefrontal cortex (BA10).

4b. The orthogonal view. The activation was located at the ACC (BA32 and 24a) and BA10.

Fig.5 An area showing rCBF decrease during 1Hz rTMS over the right dorsolateral prefrontal cortex. The 3-dimensional "look-through" projections of SPM with brain regions where rCBF significantly decreased during rTMS as compared with sham condition (before rTMS) ($p = 0.001$ with correction for multiple comparison). Significantly decreased rCBF was noted in the left cuneus.

Fig.6 Areas where rCBF increase lasted even after 1Hz rTMS over the right dorsolateral prefrontal cortex.

6a. The 3-dimensional "look-through" projections of SPM with brain regions that were significantly more active after rTMS condition ($p = 0.001$ with correction for multiple comparison) than the condition before rTMS. Significant activation was noted in the left ventral striatum, ventral prefrontal areas (BA45, 47) and right medial prefrontal cortex (BA10).

6b Activated areas superimposed on transaxial T1 weighted MR images.

6c Activation in the ventral striatum is superimposed on a coronal T1 MR image.

The activation is seen in the ventral part of the putamen and nucleus accumbens (NAc).

Table 1 Coil locations in each subjects

| Subject No | Talairach cordinate | | | Broadman area |
|------------|---------------------|-------------|-------------|---------------|
| | x | y | z | |
| 1 | 34 | 25 | 32 | 9 |
| 2 | 38 | 41 | 38 | 9 |
| 3 | 28 | 35 | 36 | 9 |
| 4 | 34 | 38 | 36 | 9 |
| 5 | 39 | 35 | 38 | 9 |
| 6 | 28 | 35 | 30 | 9 |
| 7 | 40 | 30 | 22 | 46 |
| Mean (s.d) | 34.4(4.96) | 34.14(5.24) | 33.1 (5.76) | 9 |

Table 2 rCBF changes associated with rTMS over the right DLPFC

| Anatomical region | Brodmann's area | Talairach coordinate | | | t value |
|--------------------------------------|-----------------|----------------------|-----|-----|---------|
| | | X | Y | Z | |
| Increased activity during TMS | | | | | |
| R Anterior cingulate cortex | 24, 32 | 14 | 42 | -5 | 6.53 |
| Decreased activity during TMS | | | | | |
| L Cuneus | 18 | -7 | -89 | 12 | 7.17 |
| Lasting effect of activation | | | | | |
| L Putamen, nucleus accumbens | | -16 | 7 | -7 | 8.16 |
| L Inferior frontal gyrus | 45 | -53 | 29 | 4 | 9.43 |
| L Inferior frontal gyrus | 47 | -32 | 28 | -18 | 7.8 |
| R Medial frontal gyrus | 10 | 8 | 39 | -5 | 6.52 |

研究成果の刊行に関する一覧表

書籍

| 著者氏名 | 論文タイトル名 | 書籍全体の編集者名 | 書籍名 | 出版社名 | 出版地 | 出版年 | 頁 |
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P.128の「研究成果の刊行に関する一覧表」をご参照ください。