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LETTERS TO THE EDITOR

## Serum levels of catecholamine metabolites and return to work in patients with major depression: a preliminary study

Reward processing comprises three components: reinforcement learning, reward responsiveness, and motivation to obtain a reward. Reward processing recovery is associated with recovery from major depression (MD), including return to work (RTW).[1,2] Reward processing and recovery from major depression are both related to the catecholaminergic system.[3] Thus, we investigated the relationship between serum levels of 3-methoxy-4-hydroxyphenylglycol (MHPG), a major metabolite of noradrenaline and homovanillic acid (HVA), a major metabolite of dopamine, at baseline (T0) and at week 8 (T8), and the outcome of RTW in patients with MD. This study included 27 patients who met the DSM-5 criteria for MD (M/F: 12/15, age: 29–60 years). We evaluated the severity of depressive state using the Hamilton Rating Scale for Depression (HAMD) at T0 and T8 following treatment with antidepressants. All patients achieved remission within week 12 (T12). The patients who succeeded in RTW within 6 months following remission were categorized as the succeeding group, whereas the others were categorized as the failure group. All blood samples were taken at 7:00 am before breakfast (at least 12 h following the last medication) at T0 and T8 following treatment with antidepressants. Fifteen milliliters of venous blood was drawn, with the patient in the supine position, after the patient had rested overnight. The serum samples were quickly separated in a centrifuge (2000 g, 10 min, 4 °C) and stored at −80 °C until assay. The serum levels of MHPG and HVA were measured by high-performance liquid chromatography according to previously reported methods.[4] The study protocol was approved by the Ethics Committee of the University of Occupational and Environmental Health, Kitakyushu, Japan (approval number: H25-13; May 8, 2013) and was conducted while upholding its ethical standards. All the participants of the study signed an informed consent document explaining the study protocol and the potential risks involved. All patients were administered selective serotonin/serotonin noradrenaline reuptake inhibitors, and achieved remission within T12. The HAMD at T0 was higher in the successful group (22.94 [2.58], mean [standard deviation]) than in the failure group (19.9 [1.91], $p = 0.003$).

**Table 1** Odds ratio for return to work (RTW) and variable factors in patients with major depression (MD).

| | OR (95% CI) | *p*- Value |
|---|---|---|
| Sex(Male) | 0.34 (0.05–2.50) | 0.29 |
| Age | 0.99 (0.90–1.10) | 0.89 |
| Changes in serum HVA | 1.75 (0.34–8.87) | 0.50 |
| Changes in serum MHPG | 2.63 (0.50–13.8) | 0.25 |

OR = Odds ratio, CI = Confidence interval, MHPG = 3-methoxy-4-hydroxyphenylglycol, HVA = homovanillic acid.

Logistic regression analysis was performed with RTW success or failure as the objective variable. Sex, age, changes in serum HVA levels, and serum MHPG levels were independent of RTW. The preliminary results indicate that peripheral levels of catecholamine metabolites during the acute phase of MD did not predict the success or failure of RTW within six months following remission. Further studies to analyze more metabolites or account for the relationship between the drugs used and their influence on noradrenaline and dopamine metabolites, and to reconfirm the preliminary results are warranted (Table 1).

### Ethical considerations

The study protocol was approved by the Ethics Committee of the University of Occupational and Environmental Health, Kitakyushu, Japan (approval number: H25-13; May 8, 2013).

### Conflict of interest

The authors have no conflict of interest to declare.

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### Author contributions

RY, NO, YK, and AI contributed to conception and design, were involved in the clinical investigations, and wrote the manuscript. All authors have read and approved the final manuscript.

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