Published in final edited form as:

Asia Pac Psychiatry. 2016 December ; 8(4): 309–311. doi:10.1111/appy.12240.

The symptom trajectories to clinical remission in Chinese patients with unipolar major depressive disorder

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Abstract

There is little understanding of how unipolar major depressive disorder (UMDD) symptoms evolve in response to antidepressant treatment. The present research examined the associations between symptom trajectories and clinical remission in Chinese patients with UMDD. A total of 165 outpatients with UMDD received treatment of fluoxetine (20mg/day) for six weeks and were assessed for symptom severity at week 1, 2, 4 and 6. We found that patients with UMDD show heterogeneity in treatment response to fluoxetine. Psychomotor retardation is a prominent symptom during the six weeks of assessment and its severity at baseline is negatively associated with clinical remission.

Keywords

Unipolar major depressive disorder; symptom; trajectory; clinical remission

In clinical settings, following treatment with an antidepressant, a significant proportion of patients with major depressive disorder (MDD) achieve only partial recovery. Moreover, clinical remission during acute depressive episode is often followed by subsequent recurrence (Paykel et al., 1995). Early improvement might predict stable efficacy at the end of treatment (Szegedi et al., 2003). A meta-analysis revealed that changes in depressive mood score and overall depression score in early HAMD measurements might predict eventual efficacy (Bech, 2001). It was also noted that early improvement in depressed mood and motor retardation predicted response to desipramine after 6 weeks of treatment. We

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Conflict of interest. The authors have no conflicts of interest to declare.

hypothesized and designed the present study to examine that, in Chinese patients with MDD, the improvement of certain symptoms during the early period of treatment could predict longer-term efficacy of the antidepressants. This study was approved by the Medical Ethic Committee of Second Xiangya Hospital of Central South University in China. Each patient provided the written informed consent prior to participation.

In the present study, a total of 165 outpatients with unipolar major depressive disorder (UMDD) (DSM-V) in China received treatment of fluoxetine (20mg/day) and were assessed by the *Hamilton Depression Scale-17 item (HAMD)*, the *Self-rating Depression Scale (SDS)* and the *Clinical Global Impression (CGI)* for the severity, the symptoms of depression, and the effect of treatment, respectively. Each subject was evaluated with these scales for five times: at baseline, week 1 (days 7±2), week 2 (days 14±2), week 4 (days 28±2) and week 6 (days 42±2) after initiating the treatment. 158 (95.8%), 139 (84.2%), 122 (73.9%) and 103 (62.4%) patients completed 1, 2, 4 and 6 weeks of treatment, respectively; 72 (43.6%) were males and 93 (56.4%) were females, with an average age of 33.9 (±12.1) years, ranging from 18 to 63 years; the current course of illness represented the first episode for 120 (72.7%) patients and a recurrence for 45 (27.3%) patients. There were no significant differences in the age, gender, years of education, recurrence rate and the mean overall HAMD and CGI scores at baseline between the patients who completed and those who did not complete the 6 weeks of follow-up (all $P>0.05$).

Therapeutic efficacy after 6 weeks of treatment was determined based on the measurement of overall HAMD score at the end of 6 weeks, with remitters achieving a total HAMD score 7. Of the 103 patients who have completed 6 weeks of follow-up in this study, 35 (34.0%) were categorized as remission group (35.7±9.7 years; ranging from 20 to 58 years; 17 males and 20 females), and 21 (20.4%) were categorized as non-remission group (35.7±14.8 years, ranging from 18 to 63 years; 10 males and 11 females). There were no significant differences in the age, gender, duration of illness, recurrence rate and the mean overall HAMD and SDS scores at baseline between the two groups (all $P>0.05$).

In the present study, most UMDD patients were experiencing their first episode of depression, and none of them received any antidepressant or psychotropic medications within one month before enrollment. As shown in Table 1, we found that the overall HAMD score, the cognitive disturbance, retardation and anxiety/somatization sub-scores were steadily reduced over the entire treatment period, and the difference between the scores of each of two consecutive evaluations was highly significant (all $P<0.001$). The mean total HAMD score was persistently significantly lower in remitters than non-remitters from the end of week 1 to week 6 of treatment (all $P<0.01$). Similarly, the CGI and SDS scores were also steadily reduced over the entire treatment, and the difference between the scores of each consecutive evaluation was highly significant (all $P<0.001$).

Among the HAMD symptom spectrum, retardation was the most severe among all domains and persisted through the follow-up. The mean retardation scores were significantly lower in remitters than non-remitters from baseline to the end of 1, 2, 4 and 6 weeks of follow-up (all $P<0.001$). This finding suggested retardation as a core and perhaps most-difficult-to-treat symptom in UMDD patient. The severity of retardation at baseline negatively predicts the

clinical outcome after 6 weeks of treatment ($\chi^2 = 7.445$, $P < 0.01$). It is possible that higher dosage of fluoxetine, other SSRI (Mallinckrodt et al., 2007), or antidepressants with noradrenergic actions (Artigas, Romero, de Montigny, & Blier, 1996) might be needed to obtain an effect on retardation symptom.

The improvement on several facets of depressive symptomatology manifested at the first week (Day 5–9) of treatment. The CGI, which reflects the overall clinical severity, and self-reported SDS symptoms, also improved significantly at the end of week 1 ($P < 0.05$). This suggested that medication-elicited symptom improvement can occur early. In non-remitters, all of symptom scores decreased at the end of the 1st and 2nd week, while showing minimal or no decrease from the end of the 2nd week to the end of 6 weeks of treatment. However, in remitters, all symptoms scores decreased more significantly at the end of the 1st and 2nd week, and continued to decrease significantly to the end of treatment, leading to full remission.

We found that mean anxiety/somatization scores were significantly lower from the 1st week in remitters ($P < 0.05$). Significant improvement of anxiety/somatization at the end of week 1 could predict better outcome of 6 weeks of treatment ($\chi^2 = 6.833$, $P < 0.01$), suggesting that antidepressants combined with anxiolytics in early period of treatment may be beneficial to patient with anxiety symptoms. Sleep disturbance was also significantly improved at the end of week 2 in remitters, and this efficacy sustained to the end of treatment (all $P < 0.05$ – 0.01), suggesting that this improvement in the first two weeks might be associated with better outcome too.

The mean cognitive disturbance score was significantly lower in remitters from the end of week 4 than non-remitters ($\chi^2 = 22.811$, $P < 0.001$), which might predict full remission. Cognitive symptoms responded less well or took longer to respond to pharmacotherapy. Therefore, cognitive psychotherapy combined with pharmacotherapy in the early period of treatment might accelerate the treatment efficacy.

Acknowledgments

This work was supported in part by National Institute of Health (NIH) grants R21 AA021380, R21 AA020319 and R21 AA023237. We thank Dr. Jessica A Baker for helpful comments.

References

- Artigas F, Romero L, de Montigny C, Blier P. Acceleration of the effect of selected antidepressant drugs in major depression by 5-HT_{1A} antagonists. *Trends Neurosci.* 1996; 19:378–383. [PubMed: 8873352]
- Bech P. Meta-analysis of placebo-controlled trials with mirtazapine using the core items of the Hamilton Depression Scale as evidence of a pure antidepressive effect in the short-term treatment of major depression. *Int J Neuropsychopharmacol.* 2001; 4:337–345. [PubMed: 11806859]
- Mallinckrodt CH, Prakash A, Houston JP, Swindle R, Detke MJ, Fava M. Differential antidepressant symptom efficacy: placebo-controlled comparisons of duloxetine and SSRIs (fluoxetine, paroxetine, escitalopram). *Neuropsychobiology.* 2007; 56:73–85. [PubMed: 18037817]
- Paykel ES, Ramana R, Cooper Z, Hayhurst H, Kerr J, Barocka A. Residual symptoms after partial remission: an important outcome in depression. *Psychol Med.* 1995; 25:1171–1180. [PubMed: 8637947]

Szegedi A, Muller MJ, Anghelescu I, Klawe C, Kohnen R, Benkert O. Early improvement under mirtazapine and paroxetine predicts later stable response and remission with high sensitivity in patients with major depression. *J Clin Psychiatry*. 2003; 64:413–420. [PubMed: 12716243]

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TABLE 1

The trajectories of HAM-D, CGI and SDS scores (M ± SD)

	Baseline (n=165)	Week 1 (n=158)	Week 2 (n=139)	Week 4 (n=122)	Week 6 (n=103)
Total HAM-D	28.38±5.89	23.01±7.02 ***	19.03±6.58 ***	14.72±6.02 ***	11.39±6.27 ***
Cognitive disturbance	4.79±1.89	3.78±1.81 ***	2.91±1.72 ***	2.02±1.57 ***	1.20±1.41 ***
Retardation	11.47±3.60	10.22±3.82 ***	8.98±3.88 ***	7.39±3.91 ***	6.29±3.95 ***
Anxiety/somatization	7.78±2.80	6.02±3.12 ***	5.25±3.05 ***	4.00±2.42 ***	2.68±2.42 ***
Sleep disturbance	3.68±1.79	2.58±1.97 ***	1.73±1.56 ***	1.31±1.44 **	1.16±1.84
Weight	0.64±0.75	0.25±0.49 ***	0.23±0.47 *	0.12±0.38	0.06±0.24
CGI	5.11±1.08	4.60±1.21 ***	3.88±1.19 ***	3.00±1.01 ***	2.20±1.17 ***
SDS	72.48±11.67	64.69±11.48 ***	59.54±13.01 ***	55.14±11.54 ***	50.32±11.73 ***

Note: Compared to its previous evaluation,

*** $P<0.001$,** $P<0.01$,* $P<0.05$