Translational Medicine: Using Systems of Differential Equations to Identify Patterns in Symptom Remission in Response to Treatment and the Underlying Dynamics of their Interactions

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Abstract

Systems of differential equations (neural networks) were constructed to study the Major Depressive Disorder treatment response. The methods included statistical tests of patient's response times and parameter fits based on methods derived from optimal control theory. We modeled changes in overall severity (HDRS total) and severity of, and interactions among, seven symptom factors derived from the Hamilton Depression Rating Scale (HDRS) during the initial six weeks of treatment in two patient groups. The dynamics of the recovery process revealed different clinical symptom remission patterns for desipramine (DMI), and cognitive behavioral therapy (CBT). These results have implications for clinical practice and for continued integrative interdisciplinary research.

Introduction

Depression is a serious and sometimes fatal illness for ten percent of those affected, depression results in suicide. Although antidepressant treatments are available, depression remains prevalent (Gwynn, et al, 2008).

Methods

Network Architecture

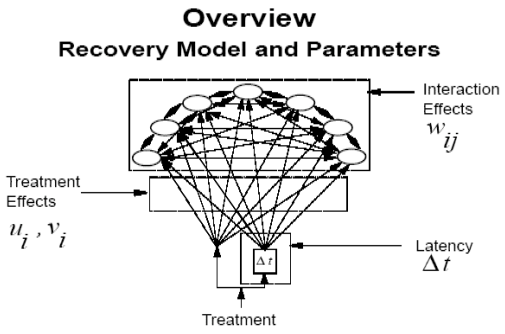

Figure 1. Overview of the recovery model. Ellipses represent symptom factors; arrows between the symptom factors indicate each symptom factor can influence every other symptom factor.

The architecture comprises a network of connections among variables corresponding to treatment and symptom-factors derived from the HDRS modeling brain region activity. Three characteristics of the response pattern were studied: (1) direct effect (from treatment to symptoms); (2) interaction effects (between pairs of symptoms, those not directly caused by the treatment); and (3) latency, defined as the average time that elapses, from the start of the treatment to a 50 percent improvement in the symptom. Differential equations were used to describe the dynamics of the model.

Results

The dynamics of the recovery process revealed different clinical symptom remission patterns for desipramine (DMI), and cognitive behavioral therapy (CBT) ($p<0.05$, two-tailed).

Discussion

Both the model and analysis of the patterns of recovery capture trends and variability in recovery based on initial state and treatment. The method eliminated much of the noise in individual clinical data. The model provides an explanation for the seemingly paradoxical situation of a depressed person committing suicide after treatment with an antidepressant drug. If the treatment pattern shows that the energy symptom improves before cognitions, a person with suicidal thoughts and low energy could regain the energy to act on those thoughts.

References

1. Gwynn RC, McQuistion HL, McVeigh KH, Garg RK, Frieden TR, Thorpe LE.. Prevalence, diagnosis, and treatment of depression and generalized anxiety disorder in a diverse urban community (2008). Psychiatr Serv. Jun; 59 (6):641-7.

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