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Literature-Related Discovery (LRD): Potential treatments for Parkinson's Disease

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Abstract

Literature-Related Discovery (LRD) is the linking of two or more literature concepts that have heretofore not been linked (i.e., disjoint), in order to produce novel, interesting, plausible, and intelligible knowledge (i.e., potential discovery). The open discovery systems (ODS) component of LRD starts with a problem to be solved, and generates solutions to that problem through potential discovery. We have been using ODS LRD to identify potential treatments or preventative actions for challenging medical problems, among myriad other applications. The previous two papers in this Special Issue describe the application of ODS LRD to Raynaud's Phenomenon (RP) and to cataracts.

Parkinson's Disease (PD) is a progressive neurodegenerative disorder, affecting approximately 1% of individuals older than 60 years, and is characterized by resting tremor, rigidity, bradykinesia, and postural instability. We selected the subject of PD because of its global prevalence, and its apparent intractability to all treatments except for palliative remediation mainly through drugs or surgery.

Our first goal was to identify non-drug non-surgical treatments that would 1) prevent the occurrence, or 2) reduce the progression rate, or 3) stop the progression, or 4) maybe even reverse the progression, of PD. Our second goal was to demonstrate that we could again solve an ODS problem (using LRD) with no prior knowledge of any results or prior work (unlike the case of the RP problem). As in the 'cataract' example, we used the MeSH taxonomy of MEDLINE to restrict potential discoveries to selected semantic classes, and to identify potential discoveries efficiently. Our third goal was to generate large amounts of potential discovery in more than an order of

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magnitude less time than required for the RP study. The discovery generation methodology has been developed to the point where ODS LRD problems can be solved with no results or knowledge of any prior work.

Keywords: Text mining; Literature-Based Discovery; Document Clustering; Parkinson's Disease

1. Overview of study

The previous two papers in this Special Issue describe the application of ODS LRD to Raynaud's Phenomenon (RP) [1] and to cataracts [2]. The present paper presents a comprehensive approach for systematic acceleration of discovery, and demonstrates the generation of large amounts of potential discovery for treatment of PD. The definitions of discovery and innovation and the approach background were shown in the first (Introductory) paper of this Special Issue [3], and the approach methodology was shown in the second paper [4]. The present paper provides an overview of the etiology and treatment of PD, then proceeds to retrieve and analyze the core PD literature, and literatures related directly and indirectly to the core PD literature. These related literatures contain the seeds of potential discovery for PD, and some examples of potential discovery are presented for both classes of related literatures. Also, examples of interesting but non-discovery concepts from the core PD literature are presented, since they have practical value in their own right.

2. Purpose of study

We selected the subject of PD because of its global prevalence, and its apparent intractability to all treatments except for palliative remediation mainly through drugs or surgery. Our main goal was to identify non-drug non-surgical treatments that would 1) prevent the occurrence, or 2) reduce the progression rate, or 3) stop the progression, or 4) maybe even reverse the progression, of PD. A second goal was to demonstrate that we could again solve an ODS LRD problem with no prior knowledge of any results or prior work (unlike the case of the RP problem). Before proceeding to describe our approach and results, we summarize the medical issues and mainline treatments for PD.

3. Parkinson's Disease background

PD develops when a part of the brain known as the substantia nigra degenerates. [5]. The substantia nigra is located halfway between the cerebral cortex and the spinal cord. In healthy people, the substantia nigra contains nigral nerve cells that produce the chemical dopamine. Dopamine travels along nerve cell pathways from the substantia nigra to the striatum. In the striatum, dopamine activates nerve cells that coordinate normal muscle activity. In people with PD, nigral cells deteriorate and die at an accelerated rate, and the loss of these cells reduces the supply of dopamine to the striatum. Without adequate dopamine, nerve cells of the striatum activate improperly, impairing a person's ability to control movement [6]. Additionally, collections of proteins (Lewy bodies, a sign of nerve cell death) form in the nerve cells [7].

Dopamine and acetylcholine are two neurotransmitters in the brain that affect motor control. When there is reduced dopamine, the dopamine-acetylcholine imbalance makes motor control more difficult, and produces the symptoms of PD. Most of the mainline drug therapies are aimed at restoring this balance.