Brain Research 1642 (2016) 344–352

Contents lists available at ScienceDirect

Brain Research

journal homepage: www.elsevier.com/locate/brainres

Research Report

Protein profile changes in the frontotemporal lobes in human severe traumatic brain injury

Benhong Xu [a,b,1], Rui Tian [c,1], Xia Wang [b,1], Shaohua Zhan [b], Renzhi Wang [c], Yi Guo [a,d,*], Wei Ge [a,b,*]

[a] Department of Neurosurgery, Affiliated Hospital of Hebei University, Baoding 071000, China
[b] National Key Laboratory of Medical Molecular Biology and Department of Immunology; Institute of Basic Medical Sciences; Chinese Academy of Medical Sciences, Beijing 100005, China
[c] Department of Neurosurgery, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing 100730, China
[d] Department of Neurosurgery, Tsinghua Changgung Hospital, Beijing 102218, China

ARTICLE INFO

Article history:
Received 14 December 2015
Received in revised form
1 April 2016
Accepted 4 April 2016
Available online 8 April 2016

Keywords:
Severe traumatic brain injury
TMT (tandem mass tags)
Human
Proteomics

ABSTRACT

Severe traumatic brain injury (sTBI) is a serious public health issue with high morbidity and mortality rates. Previous proteomic studies on sTBI have mainly focused on human cerebrospinal fluid and serum, as well as on brain protein changes in murine models. However, human proteomic data in sTBI brain is still scarce. We used proteomic and bioinformatic strategies to investigate variations in protein expression levels in human brains after sTBI, using samples from the Department of Neurosurgery, Affiliated Hospital of Hebei University (Hebei, China). Our proteomic data identified 4031 proteins, of which 160 proteins were overexpressed and 5 proteins were downregulated. Bioinformatics analysis showed significant changes in biological pathways including glial cell differentiation, complement activation and apolipoprotein catalysis in the statin pathway. Western blot verification of protein changes in a subset of the available tissue samples showed results that were consistent with the proteomic data. This study is one of the first to investigate the whole proteome of human sTBI brains, and provide a characteristic signature and overall landscape of the sTBI brain proteome.

1. Introduction

Traumatic brain injury (TBI) is one of the most devastating types of injuries elicited by exogenous mechanical stress, especially in its most dramatic form, severe TBI (sTBI). With a rapid surge in motorization and economical liberation, sTBI has become a worldwide major public health issue with associated high morbidity and mortality rates (Puvanachandra and Hyder, 2009).

Brain damage in sTBI includes primary and secondary insult. The primary insult results in direct hemorrhage and injury to axons or cortical parenchyma (Davis, 2000). As for secondary insult, there are different kinds of secondary insult with close relationships with functional outcome (Chesnut et al., 1993). The neurological events of secondary injury include hypoxia (Carpenter et al., 2015), hydrocephaly (Godbolt et al., 2015), metabolic acidosis (Nongnuch et al., 2014), damage to the blood-brain barrier (Yang et al., 2015), excitotoxicity, steroidogenic stress response (Santarsieri et al., 2014; Wagner et al., 2011), post-traumatic coagulopathy (Tian et al., 2015) and inflammation (Kumar et al., 2014). Among the known biomarkers, interleukin-1β (IL-1β), IL-6, IL-10 and various cytokines play an important role in the acute and chronic inflammation stage during secondary insult (Woodcock and Morganti-Kossmann, 2013). Glial fibrillary acidic protein (GFAP), S100B, γ-enolase (NSE) and myelin basic protein (MBP), as well as other potential biomarkers from the cerebrospinal fluid (CSF) and blood have also been widely reported (Czeiter et al., 2012; Goyal et al., 2013). Biomarkers in CSF and blood show promising roles for evaluating neurotrophin status (Failla et al., 2016) and neurodegeneration (Maas et al., 2008; Rubenstein et al., 2015). However, the detailed molecular mechanisms involved during sTBI in the brain parenchyma are largely unknown.

Previous proteomic research used cerebrospinal fluid (Kulbe and Geddes, 2015) and serum (Cadosch et al., 2010) to demonstrate the above phenomenon and associated mechanisms in murine models, with an emphasis on the pathophysiology of TBI. However,

Abbreviations: sTBI, severe traumatic brain injury; TMT(s), tandem mass tag(s); GCS, Glasgow coma scale; MBP, myelin basic protein; CNP, 2′,3′-Cyclic-nucleotide 3′-phosphodiesterase; APO, apolipoprotein gene

* Corresponding authors at: Department of Neurosurgery, Affiliated Hospital of Hebei University, Baoding 071000, China.
E-mail addresses: ghuoyi@gmail.com (Y. Guo), wei.ge@chem.ox.ac.uk (W. Ge).
[1] These authors contributed equally to the article.

http://dx.doi.org/10.1016/j.brainres.2016.04.008
0006-8993/

understanding circulatory environment changes (serum and cerebrospinal fluid) of the traumatic brain tissue is insufficient for a complete understanding of sTBI. Direct insights into proteomic changes regarding biological functions and mechanistic pathways in post-traumatic brain are needed in human sTBI research.

The term 'proteomics' was first coined in 1997 (James, 1997) to refer to the large scale study of the entire set of proteins expressed by the genome at a given time. It is complementary to the transcriptional approach widely used in the genomic study, and emphasis is placed on protein structures and functions

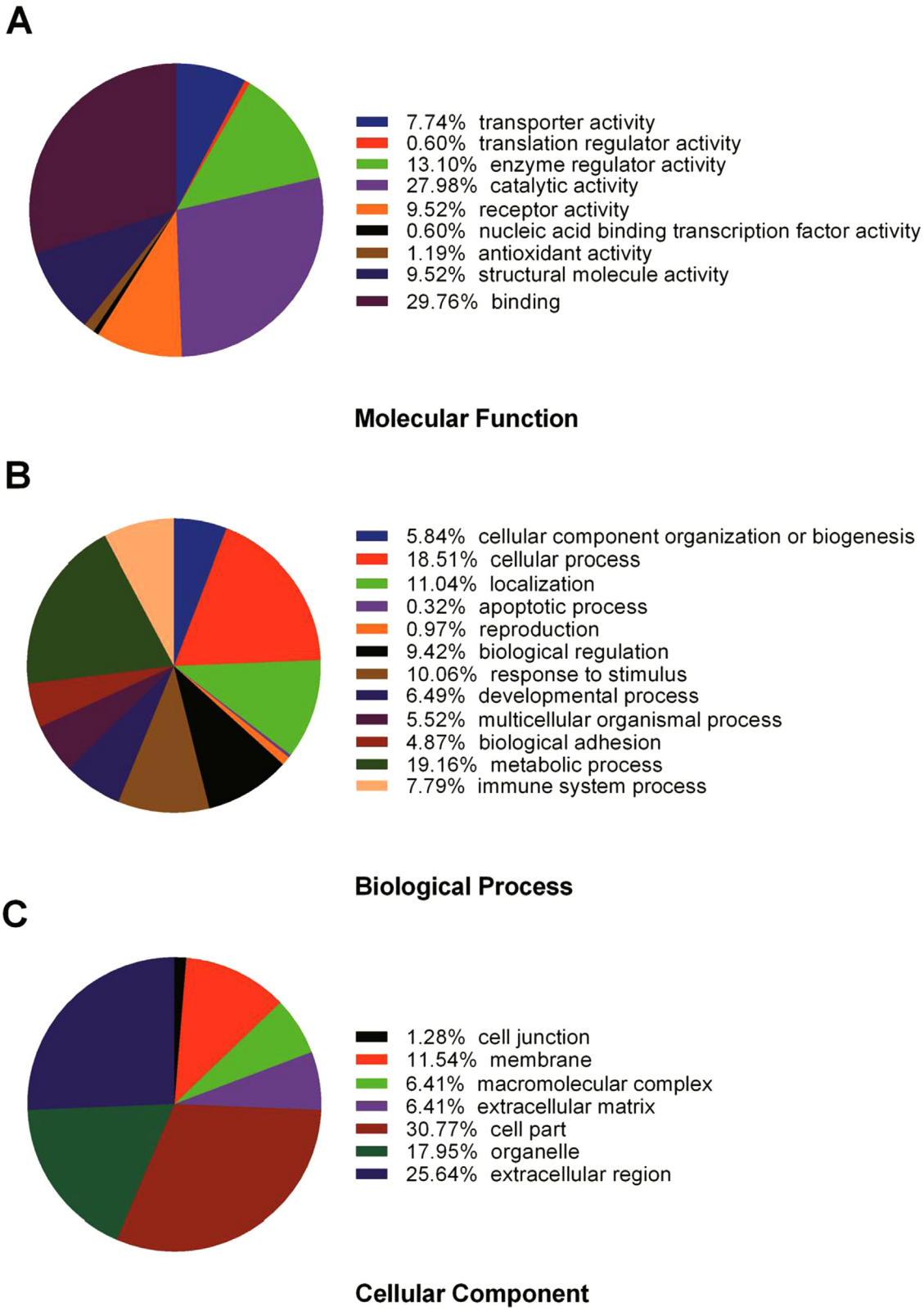

Fig. 1. Gene Ontology classification of altered proteins from sTBI brain tissue. Proteins were labeled with TMT labels and were identified with the PANTHER bioinformatics tool (http://www.pantherdb.org) under Gene Ontology categories. A) Molecular Function, B) Biological Process and C) Cellular Component.