OFFICE OF THE UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

PERSONNEL AND
READINESS

DEC 17 2012

The Honorable Daniel K. Inouye
Chairman
Subcommittee on Defense
Committee on Appropriations
United States Senate
Washington, DC 20510

Dear Mr. Chairman:

The enclosed report responds to section 723 of the National Defense Authorization Act for Fiscal Year 2012 (Public Law 112-81) that requires the Secretary of Defense submit to the congressional defense committees an assessment of neuroimaging research for the purpose of improving the identification and diagnosis of post-traumatic stress disorder (PTSD). Activities related to PTSD fall under my purview, and I am pleased to provide the enclosed report.

The report reveals that current research findings do not support the specific use of neuroimaging techniques to identify or diagnose PTSD in individual patients. However, while the use of neuroimaging for these purposes is still experimental, research findings have significantly improved our understanding of the brain abnormalities in groups of patients with PTSD. Future brain imaging research could help identify individuals at risk for developing PTSD, categorize different types of PTSD, serve as a diagnostic tool for PTSD, and assist in making informed choices about individualized treatment with medications or psychotherapy.

A similar letter has been sent to the chairmen and ranking members of the other congressional defense committees. Thank you for your interest in the health and well-being of our Service members, veterans, and their families.

Sincerely,

Jessica L. Wright
Acting Principal Deputy

Enclosure:
As stated

cc:
The Honorable Thad Cochran
Vice Chairman

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PERSONNEL AND
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DEC 17 2012

The Honorable Carl Levin
Chairman
Committee on Armed Services
United States Senate
Washington, DC 20510

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Acting Principal Deputy

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cc:
The Honorable John McCain
Ranking Member

OFFICE OF THE UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

PERSONNEL AND
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DEC 17 2012

The Honorable Howard P. "Buck" McKeon
Chairman
Committee on Armed Services
U.S. House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

The enclosed report responds to section 723 of the National Defense Authorization Act for Fiscal Year 2012 (Public Law 112-81) that requires the Secretary of Defense submit to the congressional defense committees an assessment of neuroimaging research for the purpose of improving the identification and diagnosis of post-traumatic stress disorder (PTSD). Activities related to PTSD fall under my purview, and I am pleased to provide the enclosed report.

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Jessica L. Wright
Acting Principal Deputy

Enclosure:
As stated

cc:
The Honorable Adam Smith
Ranking Member

OFFICE OF THE UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

PERSONNEL AND
READINESS

DEC 17 2012

The Honorable Harold Rogers
Chairman
Committee on Appropriations
U.S. House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

The enclosed report responds to section 723 of the National Defense Authorization Act for Fiscal Year 2012 (Public Law 112-81) that requires the Secretary of Defense submit to the congressional defense committees an assessment of neuroimaging research for the purpose of improving the identification and diagnosis of post-traumatic stress disorder (PTSD). Activities related to PTSD fall under my purview, and I am pleased to provide the enclosed report.

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Sincerely,

Jessica L. Wright
Acting Principal Deputy

Enclosure:
As stated

cc:
The Honorable Norman D. Dicks
Ranking Member

OFFICE OF THE UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

PERSONNEL AND
READINESS

DEC 17 2012

The Honorable Jim Webb
Chairman
Subcommittee on Personnel
Committee on Armed Services
United States Senate
Washington, DC 20510

Dear Mr. Chairman:

The enclosed report responds to section 723 of the National Defense Authorization Act for Fiscal Year 2012 (Public Law 112-81) that requires the Secretary of Defense submit to the congressional defense committees an assessment of neuroimaging research for the purpose of improving the identification and diagnosis of post-traumatic stress disorder (PTSD). Activities related to PTSD fall under my purview, and I am pleased to provide the enclosed report.

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The Honorable Lindsey Graham
Ranking Member

OFFICE OF THE UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

PERSONNEL AND
READINESS

DEC 17 2012

The Honorable Joe Wilson
Chairman
Subcommittee on Military Personnel
Committee on Armed Services
U.S. House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

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As stated

cc:
The Honorable Susan A. Davis
Ranking Member

OFFICE OF THE UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, DC 20301-4000

PERSONNEL AND
READINESS

The Honorable C.W. Bill Young
Chairman
Subcommittee on Defense
Committee on Appropriations
U.S. House of Representatives
Washington, DC 20515

DEC 17 2012

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Ranking Member

REPORT TO CONGRESS

National Defense Authorization Act for Fiscal Year 2012, Section 723

Report on Research and Treatment of Posttraumatic Stress Disorder

October 2012

Preparation of this report/study cost the Department of Defense a total of approximately $19,000 for the 2012 Fiscal Year.
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EXECUTIVE SUMMARY

Current research findings do not support the specific use of neuroimaging techniques to identify or diagnose Posttraumatic Stress Disorder (PTSD) in an individual patient. However, neuroimaging research has advanced our overall understanding of PTSD with the potential to impact diagnosis in the future.

Neuroimaging research findings have significantly improved our understanding of the brain abnormalities in groups of patients with PTSD. Future brain imaging research has the potential to help identify those at risk for developing PTSD, categorize different types of PTSD, serve as a diagnostic tool for PTSD, and assist in making informed choices about individualized treatment with medications or psychotherapy (talk therapy).

The DoD currently funds 23 neuroimaging research projects in the areas of PTSD and traumatic brain injury (TBI), headed by principal investigators from the Department of Veterans Affairs (VA), academia, and Draper Laboratory (see Appendices for discussion and list of studies). The VA and the National Institute of Mental Health (NIMH) currently fund 8 and 14 neuroimaging studies in PTSD, respectively.

INTRODUCTION

The National Defense Authorization Act for Fiscal Year 2012, Section 723, required that the Secretary of Defense submit a report assessing the benefits of neuroimaging research in an effort to identify and improve the diagnosis of PTSD. This report also considers the potential benefits of research using techniques for wounded, ill, and injured Service members with PTSD and explores collaborative interagency and extramural research in this area.

Despite the increasing prevalence of PTSD in Service members from the Operation IRAQI FREEDOM, Operation ENDURING FREEDOM, and Operation NEW DAWN conflicts, there is no objective lab-based test that can accurately diagnose PTSD. Currently, a diagnosis of PTSD is made by a trained clinician, based on a comprehensive clinical interview and assessment of an individual's self-reported symptoms. A diagnosis of PTSD can be made if an individual meets 8 out of 19 symptom criteria for PTSD (according to the Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition, Text Revision), and experiences either significant distress or impaired functioning for more than one month. Neuroimaging techniques can identify changes in the brain associated with mood and anxiety disorders, and have been investigated as a potential diagnostic tool for PTSD.

In response to the Congressional requirement for this report, the DoD conducted an extensive review of the PTSD literature using PubMed.gov (National Center for Biotechnology Information, U.S. National Library of Medicine). Conclusions in this report are based on the literature reviewed (Appendix E) and input from subject matter experts in the DoD and VA.

DISCUSSION

I: Benefits of Neuroimaging Research in an Effort to Identify and Improve the Diagnosis of PTSD

Seven neuroimaging techniques were critically evaluated for their potential use in diagnosing PTSD. Peer-reviewed publications in PTSD and structural magnetic resonance imaging (MRI), functional MRI (fMRI), diffusion tensor imaging (DTI), magnetic resonance spectroscopy (MRS), positron emission tomography (PET), single-photon emission computed tomography (SPECT), and magnetoencephalography (MEG) were examined (See Appendix C for bibliography). Each of these techniques provides a unique set of data that can be used to assess potential differences between groups of patients with and without PTSD.

Neuroimaging technologies detect average differences in brain structure (the anatomy or how the brain is built) and function (what each part of the brain does) between groups of patients with and without PTSD. However, the brain imaging abnormalities that are reported in PTSD are often inconsistent, partly due to variations in study design and other methodological limitations. The most consistent brain changes in PTSD are related to the smaller size of the hippocampus (brain structure related to memory), increased function of the amygdala (brain structure related to processing of fear), and the smaller size and decreased function of the medial prefrontal cortex and the anterior cingulate cortex (brain structures related to control of emotions including fear). To summarize, the brain imaging research provides a possible biological explanation for the key symptoms in PTSD, including memory problems, increased fear response, and a decreased ability to inhibit this response.

Despite significant group differences, it is important to note that the size of the hippocampus (and other regions of interest) of an individual with PTSD could be similar or even identical to the size of the hippocampus of an individual without PTSD. Since there is a significant overlap in brain structure and function between individuals with and without PTSD, neuroimaging techniques cannot be used currently to diagnose this disorder. (See Appendix E for bibliography).

II: Potential Benefits of Research Using Neuroimaging Techniques for Wounded, Ill, and Injured Service Members with PTSD

Neuroimaging techniques have contributed to the recognition of structural and functional brain abnormalities in PTSD, and helped us understand how this disorder develops after trauma exposure. Structural and functional changes confirmed by neuroimaging techniques can potentially be used to target these abnormal brain regions for treatment. Neuroimaging may also help predict individuals who are at risk of developing PTSD, and could help with the development of new treatments that prevent PTSD. Since evidence indicates that there are likely many types of PTSD, reliable identification of the different PTSD types through use of neuroimaging techniques could improve the ability to predict the progression of this disorder, and determine the response to varied treatments. Neuroimaging research is currently underway to identify predictors of response to PTSD treatment. Unique brain patterns associated with successful and unsuccessful PTSD treatment could help clinicians and patients make informed choices about individualized treatment with medications or psychotherapy (talk therapy). Neuroimaging techniques may also help differentiate PTSD from other disorders that present with similar symptoms, such as mild Traumatic Brain Injury (mTBI) and depression. An accurate method to distinguish and accurately diagnose disorders with overlapping symptoms is critical, as these conditions have different disease progressions, and therefore require different types of treatment and rehabilitation.

III: Collaborative Interagency and Extramural Research on the Use of Neuroimaging in PTSD Diagnosis

The DoD currently collaborates with researchers from the VA, academia, and Draper Laboratory to investigate PTSD using neuroimaging techniques. Detailed tables that list the principal investigator, institutional affiliation, institutional collaboration, proposal title, types of imaging techniques, and imaging targets can be found in Appendices B, C, and D. The DoD currently funds 23 ongoing neuroimaging studies on PTSD and TBI. Four studies focus on differentiating PTSD from mTBI, six studies focus on identifying those at risk for developing PTSD, six studies evaluate predictors of response to treatment, and seven studies evaluate brain changes in PTSD (Appendix B). The VA and the NIMH funded 8 and 14 PTSD neuroimaging studies, respectively (Appendices C and D). The DoD collaborates with the VA and the NIMH to regularly review the research portfolios of their respective agencies. This coordinated review ensures oversight of currently funded DoD, VA, and NIMH research studies, and prevents duplication of funding allocation for similar projects.

CONCLUSIONS

- Current research does not support the use of neuroimaging to identify or diagnose PTSD in an individual patient.
- The use of neuroimaging in PTSD should currently be considered in the realm of research, and not for use in the diagnosis or care of an individual patient in the clinic.
- Neuroimaging research findings have confirmed that PTSD is associated with structural and functional abnormalities in the brain regions related to memory and fear response, and have helped facilitate an understanding of the biology and development of PTSD.
- Future neuroimaging research has the potential to identify those at risk for PTSD, determine different types of PTSD, and develop new tools that can help match patients with optimal treatments.
- Neuroimaging research has the potential to help accurately diagnose PTSD by distinguishing it from other conditions with overlapping symptoms, such as mTBI.
- The DoD is currently collaborating with the VA, academia, and Draper Laboratory by funding 23 research studies in PTSD and related conditions to investigate the utility of neuroimaging in the diagnosis, biology, and treatment of PTSD.

Appendix A – DoD-Funded Neuroimaging Studies in PTSD*

Funded Principal Investigator	Institutional Affiliation	Institutional Collaborations	Study Title	Type of Imaging	Brain Region Targeted
McCaslin-Rodrigo	University of California, San Francisco	San Francisco VA	Functional Brain Mechanisms of Mutual Maintenance of PTSD and Chronic Pain: A Pilot fMRI Study	fMRI	Amygdala
Hendler	Tel Aviv University	-	Prospective EEG/fMRI Evaluation of Neuro-Feedback for Military Stress Regulation	EEG, fMRI	Amygdala
Germain	University of Pittsburgh School of Medicine	Harvard Medical School & Massachusetts General Hospital	Effects of Dose-Dependent Sleep Disruption on Fear Responses and Reward Processing	fMRI	Amygdala, Cingulate, Hippocampus
Matthews	University of California, San Diego	San Diego VA	Understanding the Brain Mechanism Underlying Depression in Combat-Related Traumatic Brain Injury	MRI, fMRI	Amygdala, Other (Anterior Cingulate Cortex)
Eman	Center for Integration of Medicine and Technology, McLean Hospital, Harvard Medical School	-	Novel Predictors of Pharmacotherapeutic Outcomes using Functional Reciprocity between Heightened Stress Reactivity and Emotional Numbing in PTSD	fMRI	Amygdala, Other (Nucleus Acumbens)
Rauch	University of Michigan	Ann Arbor VA	Randomized Trial of Sertraline, Prolonged Exposure Therapy and their Combination in OEF/OIF with PTSD	fMRI	Amygdala, Prefrontal Cortex

Funded Principal Investigator	Institutional Affiliation	Institutional Collaborations	Study Title	Type of Imaging	Brain Region Targeted
Germain	University of Pittsburgh School of Medicine	Pittsburgh VA	Neurobiology of Sleep and Sleep Treatments in PTSD (NOS-STIP)	PET	Amygdala, Prefrontal Cortex
Forster	University of South Dakota	Avera Sacred heart Hospital; Sioux Falls VA Hospital	Neural and Behavioral Correlates of PTSD and Alcohol Use	fMRI	Cingulate Gyrus, Amygdala
Bergold	Research Foundation of the State University of New York	University of Texas; Southwestern Medical Center	Interhemispheric Information Transfer: A New Diagnostic Method for Mild Traumatic Brain Injury	DT-MRI	Corpus Callosum
Sutula	University of Wisconsin, Madison	-	Prediction, Detection, and Prevention of Post-Traumatic Epilepsy and PTSD in Genetically Susceptible Rats	DT-MRI	Hippocampus
Wolkowitz	The Regents of the University of California, San Francisco	VAMC Brox, NY;VAMC San Francisco; University of California, San Francisco; Mt. Sinai Hospital, NYC	Allostatic Load as a Mechanism of Increased Physical Disease Risk in Combat-Related PTSD	MRI	Hippocampus
Liberzon	University of Michigan	Ann Arbor VA	Mindfulness and Self-Compassion Meditation for Combat Post-Traumatic Stress Disorder: Randomized Controlled Trial and Mechanistic Study	fMRI	Medial Prefrontal Cortex

Funded Principal Investigator	Institutional Affiliation	Institutional Collaborations	Study Title	Type of Imaging	Brain Region Targeted
Papanicolaou	University of Texas Health Science Center, Houston	Baylor College of Medicine; Michael E. Debakey VAMC; Ben Taub General Hospital; Memorial Hermann Hospital	Mission Connect Mild TBI Translational Research Consortium	MEG, DT-MRI	Prefrontal Cortex, White Matter Tracts
Young	Texas A&M University	Brooke Army Medical Center; Baylor College of Medicine, VA Waco Center of Excellence; Darnell Army Medical Center; Resilience and Restoration Center	The Root Cause of PTSD and Developmental Stress Disorder	MRI	Prefrontal Cortex, Amygdala
Rao	Cleveland Clinic	Baylor College of Medicine; Louis Stokes VAMC; Metro Health System; Michael E. Debakey VAMC; Memorial Hermann Hospital	Neural and Behavioral Sequelae of Blast-Related Traumatic Brain Injury	fMRI, DT-MRI	White Matter Fiber Tracts within the Brain Associated with Memory and Executive Function

Funded Principal Investigator	Institutional Affiliation	Institutional Collaborations	Study Title	Type of Imaging	Brain Region Targeted
Sponheim	Minneapolis VAMC	-	The Effects of Explosive Blast as Compared to PTSD on Brain Function and Structure	DT-MRI	White Matter in the SupraCallosal, Inferior Frontal and Superior Frontal Brain regions
Levin	Baylor College of Medicine	University of Texas Health Science Center; Michael E. Debakey VAMC; Ben Taub General Hospital, Memorial Hermann Hospital	Mission Connect Mild TBI Translational Research Consortium	EEG, DT-MRI, MRI	Whole Brain
Lin	Brigham and Women's Hospital	Draper Laboratory, USARIEM	Identifying Biomarkers that Distinguish PTSD and mTBI using Advanced Magnetic Resonance Spectroscopy	MRS (1D & 2D)	Whole Brain
Kamimori	Walter Reed Army Institute of Research	Banyan Biomarkers	Brain Injury Biomarkers and Behavioral Characterization of mTBI in Soldiers following Repeated, Low-Level Blast Exposure	DTI, MRI	Whole Brain
Levin	Baylor College of Medicine	Louis Stokes VAMC; Michael E. Debakey VAMC	Neural and Behavioral Sequelae of Blast-Related Traumatic Brain Injury	MRI, fMRI, DT-MRI	Whole Brain (Structure and White Matter Tract Integrity)

Funded Principal Investigator	Institutional Affiliation	Institutional Collaborations	Study Title	Type of Imaging	Brain Region Targeted
Seibyl	The Institute for Neurodegenerative Disorders	-	SPECT Imaging to Evaluate Post Traumatic Stress Disorder	SPECT	Whole Brain
Simmons	Veterans Medical Research Foundation of San Diego	University of California, San Diego; VAMC San Diego	Using fMRI to Measure Brain Response to Exposure-Based Psychotherapy in Individuals with Combat-Related PTSD	fMRI	Whole Brain, with Focus of Regions of the Brain Associated with Affective Response
Keshava	Draper Laboratory	Brigham and Women's Hospital	Identifying Biomarkers that Distinguish PTSD and mTBI using Advanced Magnetic Resonance Spectroscopy	MRS (1D & 2D)	Whole Brain

*All studies listed in Appendix B assess PTSD although some of them do not mention PTSD in the title

Appendix B – VA-Funded Neuroimaging Studies in PTSD*

Funded Principal Investigator	Institutional Affiliation	Institutional Collaborations	Study Title	Type of Imaging	Brain Region(s) Targeted
Morey	Durham VAMC	-	Imaging-Genetics of PTSD in OEF/OIF Veterans	fMRI	Dorsal Frontoparietal, Ventral Frontolimbic Regions
Scott	VA CT Health Care System	-	Neural Response to Cognitive Overload in Posttraumatic Stress Disorder	fMRI	Neural Correlates of Working Memory Overload
Verfaellie	VA Boston Health Care System	-	Neural and Cognitive Sequelae of Blast-Induced Traumatic Brain Injury	DTI	Whole Brain and White Matter Abnormalities
Williams	Michael E Debakey VAMC	-	Neuroimaging the Impact of Treatment on Neural Substrates of Trust in PTSD	fMRI	Neural Substrates Associated with Interpersonal Dysfunction and Social Functioning
Yehuda	Bronx Veterans Affairs, James J Peters VAMC	-	Neural and Cognitive Correlates of Glucocorticoid Responsiveness in PTSD	FDG-PET	Hippocampus, Amygdala
Bremner	Atlanta VAMC	-	Memory and the Hippocampus in Vietnam Twins with PTSD	MRI, PET	Hippocampus, Whole Brain

Funded Principal Investigator	Institutional Affiliation	Institutional Collaborations	Study Title	Type of Imaging	Brain Region(s) Targeted
Simmons	VA San Diego Health Care System	-	Neural Correlates of PTSD in Veterans with Blast-Related TBI	DTI, fMRI, PET	Whole Brain
Phan	VA Ann Arbor Health Care System	-	Neurofunctional Markers of SSRI Treatment Responses in PTSD	fMRI	Amygdala, Ventral Medial Prefrontal Cortex

*All studies listed in Appendix C assess PTSD although some of them do not mention PTSD in the title

Appendix C – NIMH-Funded Neuroimaging Studies in PTSD*

Funded Principal Investigator	Institutional Affiliation	Institutional Collaborations	Study Title	Type of Imaging	Brain Region(s) Targeted
Bremner, J. D.	Emory University	-	Neural Circuits in Women with Abuse and PTSD	MRI	Hippocampal Volume
Bremner, J. D.	Emory University	-	Biological Correlates of Traumatic Stress (Mentoring Program)	MRI, PET	Hippocampus, Medical Prefrontal Cortex, Amygdala
Hayes, J. P.	Boston University Medical Campus	-	Neuroimaging of Trauma Memory and Cognitive Reappraisal in PTSD	fMRI	Neural Networks Involved in Trauma Memory Encoding and Emotional Regulation of Trauma Memories in PTSD
Neria, Y. Y.	New York State Psychiatric Institute	-	Brain Circuitry and Psychological Predictors of PTSD	fMRI	Neural Circuitry of Symptomatic Improvement in Response to Prolonged Exposure Treatment
Shin, L. M.	Massachusetts General Hospital	-	Twin Study of Biologic Markers for PTSD	fMRI	Anterior Cingulate Cortex, Amygdala
Bearer, E. L.	University of New Mexico Health SCIS Center	-	Live Imaging of Brain Circuitry in Mouse Models of PTSD	MRI	Whole Brain

Funded Principal Investigator	Institutional Affiliation	Institutional Collaborations	Study Title	Type of Imaging	Brain Region(s) Targeted
Morey, R. A.	Duke University	-	fMRI Assessment of Attention and Memory in PTSD	fMRI	Neural Correlates of Attention and Memory
Huff, N. C.	Duke University	-	Neural Mechanisms of Fear Renewal in Humans	fMRI	Amygdala
Germain, A.	University of Pittsburgh at Pittsburgh	-	Neurobiology of PTSD during REM Sleep	PET	Whole Brain and Neurobiological Correlates of PTSD during REM Sleep
Etkin, A.	Palo Alto Institute for RES &EDU, INC.	-	The Neurobiology of Psychotherapy: Emotional Reactivity and Regulation in PTSD	fMRI	Whole Brain, Neural Circuitry of Reacting to and Regulating Negative Emotion and Prefrontal Cortex
Bruce, S. E.	University of Missouri-St. Louis	-	Neural Correlates of PTSD Treatment Outcome: An fMRI Study	fMRI	Amygdala and Prefrontal Cortex
Osuch, E. A.	Henry M. Jackson FDN for the ADV MIL/MED	-	Functional Neuroimaging of Acute Stress Disorder and PTSD	fMRI	Amygdala, Hippocampus and Prefrontal Cortex
Pitman, R. K.	Massachusetts General Hospital	-	Twin Study of Biologic Markers for PTSD	fMRI	Amygdala
Rauch, S. L.	Massachusetts General Hospital	-	Prefrontal Mechanisms in Retention of Fear Extinction	fMRI	Prefrontal Cortex

*All studies listed in Appendix D assess PTSD although some of them do not mention PTSD in the title

Appendix D – Bibliography

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