Science & Technology Series

Neurodegenerative Disease Research

Mind, Matter and Medicine

Tradition of Excellence

Bar-Ilan University

Medicine

At Bar-Ilan, researchers are using a wide range of approaches to characterize how the brain is affected by neurodegenerative disease, and are devising new strategies to stop it.

Pictured from left to right:
Dr. David Anaki
Dr. Izhar Bar-Gad
Dr. Alon Korngreen
Dr. Sivan Henis-Korenblit
Dr. Avi Goldstein

Mind Matter and

Dr. Alois Alzheimer

Long before the turn of the last century, when German physician Dr. Alois Alzheimer identified a collection of brain cell abnormalities as a disease, neurodegeneration has been recognized as a major health problem. Conditions such as Alzheimer's and Parkinson's disease, as well as lesser-known conditions, affect millions of people and strike at the heart of what makes us human: the ability to think, to feel, to remember and to communicate with those around us.

There are no cures – and few treatments – for neurodegenerative disease. As a result, family members can only provide palliative care, while they watch their loved ones' mental and physical condition deteriorate. The direct costs of physically caring for the victims of these diseases runs in the billions of dollars. The emotional cost is incalculable. As the average age of the population in developed countries increases, this problem will only get worse, making the search for treatments and cures an ever-more urgent priority.

Bar-Ilan University encourages collaboration between researchers from varying disciplines who are investigating neurodegenerative diseases. Some of these researchers are examining specific diseases; others specialize in the biological factors common to many disease conditions. Some study the changes in the brain that mediate symptoms; others study genes and molecules known to be behind them. Some use stem-cell biology to develop replacements for damaged nerve cells; others use nanotechnology to create implanted devices that improve brain function. Finally, some groups are helping to design new molecules that will help deliver specially designed drugs to the parts of the brain affected by these diseases.

At Bar-Ilan, advanced, multi-disciplinary research is shining a new light on the dark mysteries of neurodegenerative disease. By working together, BIU scientists are closing in on uniquely integrated answers to critical neurological questions.

What Happens in Neurodegenerative Disease…

Bar-Ilan is home to one of Israel's foremost centers for neuroscience research: the Leslie and Susan Gonda (Goldschmied) Multidisciplinary Brain Research Center. Scientists associated with the Gonda Center are examining neurodegenerative disease on the molecular, cellular and network level – while collaborating with BIU experts on cognitive science and psychology.

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Dr. Edward Stern uses advanced electrophysiological and imaging techniques to examine how normal neurological activity is disrupted in the presence of Alzheimer's, Parkinson's and Huntington's disease. In addition to providing a more complete understanding of the normal and diseased brain, Stern's work is pointing the way toward novel therapeutics. Studying Alzheimer's in animal models, he has shown how structural damage to neurons can be halted or even reversed. This demonstrates that nerve cells can recover from disease-related damage even in brains of advanced age and reveals that the brain is more resilient than previously believed.

Dr. Izhar Bar-Gad studies Deep Brain Stimulation (DBS), a technique used to alleviate symptoms of Parkinson's disease. In DBS, a surgically implanted device – similar to a heart pacemaker – stimulates targeted areas in the brain, blocking the abnormal nerve signals that cause tremor and other Parkinsonian symptoms. While the benefits of DBS are undeniable, the underlying

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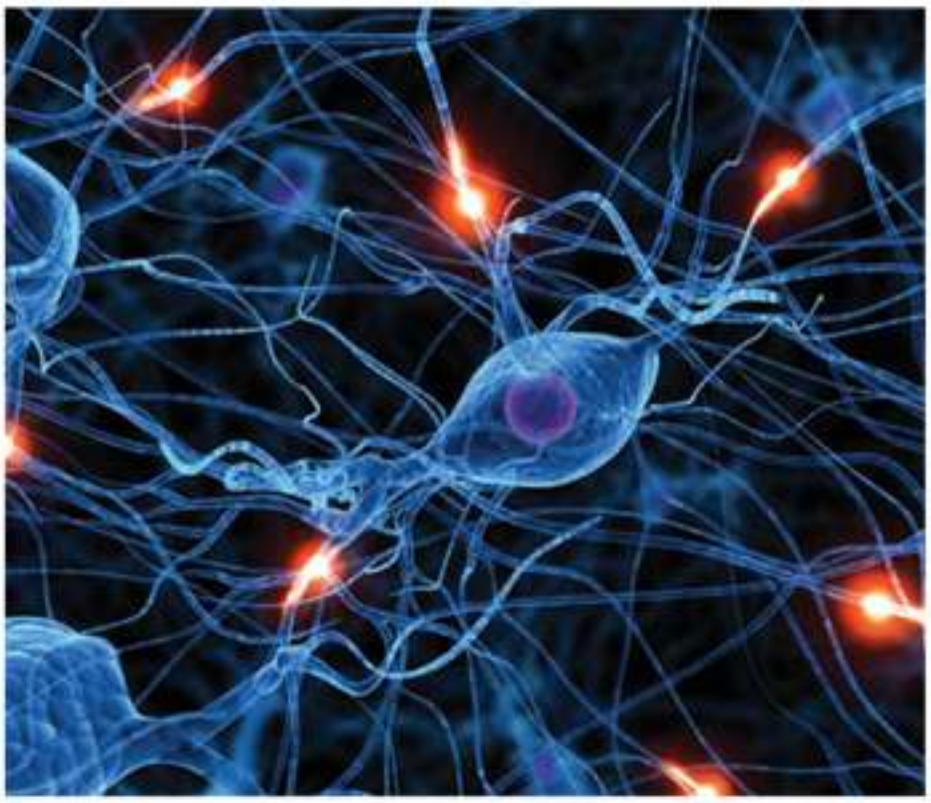
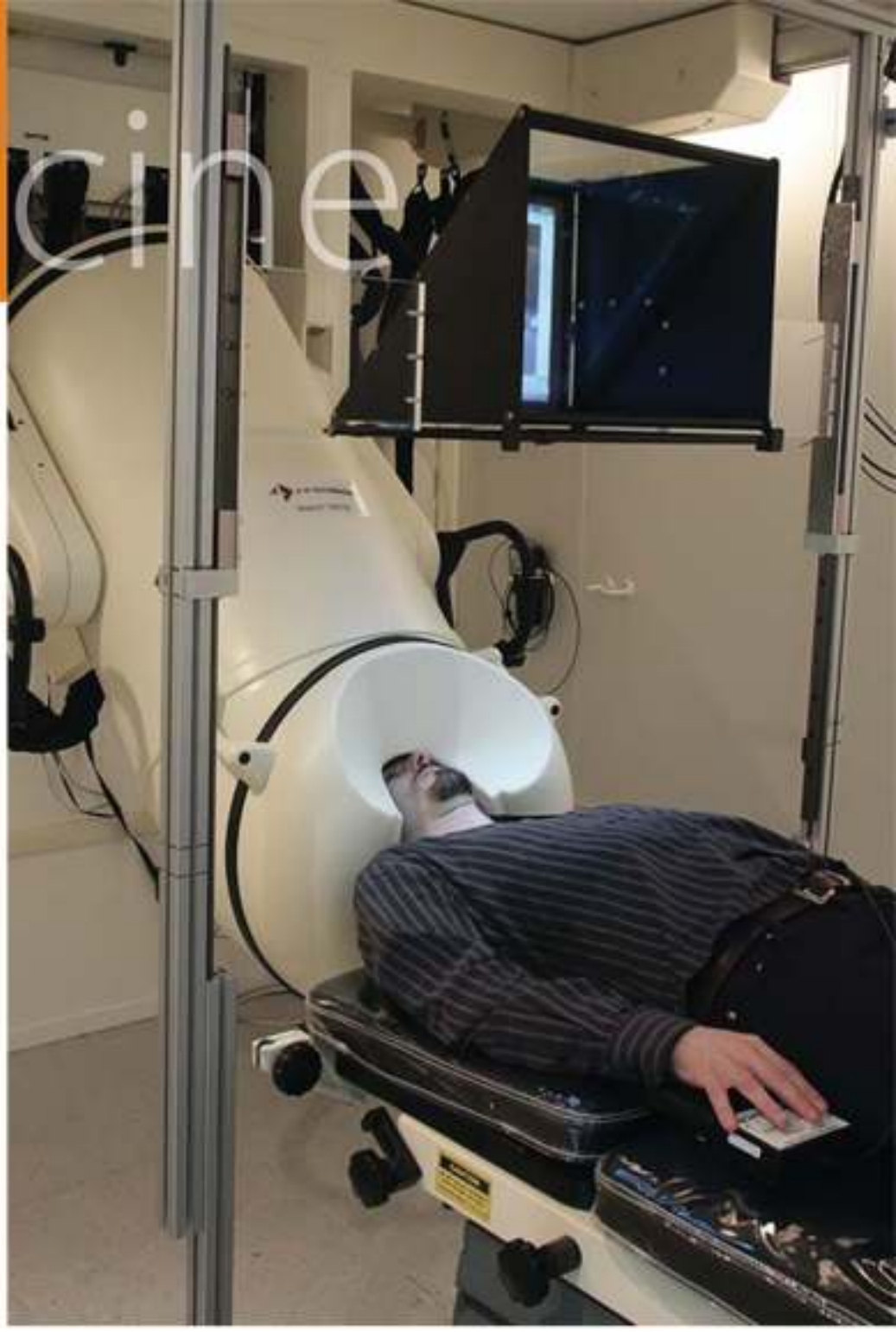
neural mechanisms that create clinical improvement are unknown. Dr. Bar-Gad studies the nerve-based interactions responsible for the effects of DBS, and is creating new protocols for advanced DBS-based therapeutics.

Dr. Alon Korngreen is a biophysicist who uses electrophysiological techniques to make dual and triple simultaneous recordings of nerve cells' electrical activity. He is particularly interested in how this activity is altered by DBS. By linking the changes that occur at the cellular and network level to changes in symptoms, Korngreen is helping to identify DBS stimulation patterns that are of most benefit to patients.



Dr. Avi Goldstein, Head of BIU's Electromagnetic Brain Imaging Unit, is clarifying how the human brain performs cognitive tasks – and how this process is altered in the presence of neurodegenerative disease. Using an advanced imaging technique called magnetoencephalography, or MEG, Goldstein tracks faulty transmission of neural signals that cause brain activity to become erratic and unsynchronized. MEG imaging can reveal such non-synchronized brain activity long before any behavioral or cognitive symptoms appear. Goldstein is currently developing MEG-based protocols for measuring brain synchrony as a tool for early diagnosis.



Another BIU researcher using technology to study brain activity is Prof. Michal Lavidor. Lavidor studies the brains of brain damaged patients, as well as healthy elderly individuals who are experiencing cognitive difficulties. Lavidor – an expert in language processing – uses a non-invasive therapy called transcranial direct current stimulation, or tDCS. In tDCS, two electrodes placed on the skull provide sub-threshold stimulation that increases the likelihood that neurons will "fire." Lavidor has demonstrated that this enhancement of brain activity – together with interactive training – can significantly improve cognitive and linguistic performance.

Also studying neurodegeneration from the perspective of cognitive neuroscience is Dr. David Anaki. A member both of the Gonda Center and BIU's Department of Psychology, Anaki examines how progressive atrophy of the posterior part of the brain affects visual tasks such as reading and identifying faces. In another project, Anaki is using statistical methods to assess individuals suffering from mild cognitive impairment in order to determine whether their difficulties constitute a precursor of Alzheimer's disease.

...And How Might We Stop It?

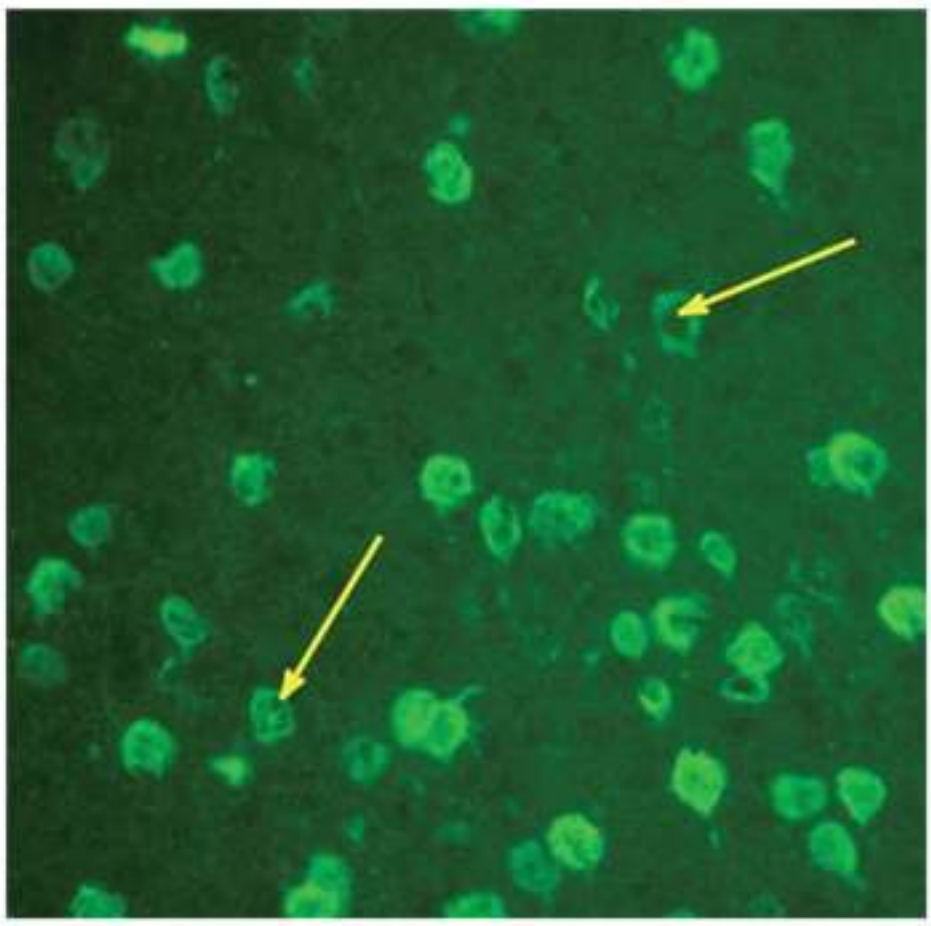
BIU researchers are pursuing a wide range of projects that may improve the medical community's ability to understand and treat neurodegenerative disease.

Molecular geneticist Dr. Sivan Henis-Korenblit of the Mina and Everard Goodman Faculty of Life Sciences is looking at how genes related to aging affect the body's tendency to succumb to neurodegenerative conditions. Working with a model system called C. elegans – the very first animal whose genome was sequenced completely – Henis-Korenblit hopes to clarify the link between gene-based mechanisms of age regulation and specific neurodegenerative disorders, paving the way toward novel therapeutic approaches.

Also in the Faculty of Life Sciences, Prof. Ron Goldstein is pursuing research related to the repair and regeneration of damaged nerve cells. In 2005, Goldstein's lab was the first to successfully coax human embryonic stem cells into generating human peripheral sensory neurons – the cells responsible for sensation. Today, he is using these lab-generated neurons for the first-ever molecular studies of the regeneration of human axons – the long extensions of a nerve that carry impulses away from the body of the cell. Using advanced microscopy and molecular techniques, Goldstein is identifying genes whose activity changes after axon damage. This work may provide new genetic targets for enhancing nerve re-growth after trauma, which could enhance nerve repair in patients with nerve damage, and potentially, spinal cord injury, as well.

Prof. Benjamin Sredni – who in addition to his work in the Faculty of Life Sciences is former Chief Scientist of the Israeli Ministry of Health – has designed a specific compound that protects neurons from the degeneration process. Called AS101, this non-toxic compound – developed together with Prof. Michael Albeck – has been shown to improve motor function in animal models of Parkinson's disease. In another animal-based study, Sredni has demonstrated how AS101 reduces brain damage associated with ischemic stroke. Sredni's compound reduces swelling, and helps to limit the area in which neural damage occurs in the brain. It also improves post-stroke neurological function.

In the Department of Chemistry, Prof. Bilha Fischer has identified and synthesized protective agents that may minimize the devastating effects of Alzheimer's. Unlike other potential drugs that target individual factors associated with this disease, Fischer's protective agents are capable of addressing several molecular targets at once. In protein- and cell-based studies, Fischer has demonstrated how her protective agents work to prevent oxidative damage to neurons, as well as the pathological build-up of plaques – excess fibers and proteins that, in Alzheimer's patients, cause brain cells to die.



Another researcher working on Alzheimer's drugs is Dr. Shai Rahimipour, who uses computers to narrow down the compounds most likely to block Alzheimer's-related processes. The focus of Rahimipour's research is on the synthesis of small molecules that bind to soluble amyloid beta protein, which accumulates in the brain of Alzheimer's patients. Rahimipour's molecules inhibit the aggregation of amyloid beta proteins

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and reduce their toxicity. He has also discovered compounds that dissolve pre-formed protein fibers that contribute to neurodegeneration. In another project, he has synthesized molecules that – in addition to blocking amyloid aggregation – stimulate the body's immune system to combat this biological process.

Prof. Elisha Haas of the Faculty of Life Sciences is examining alpha-synuclein – a protein that collects in specific nerve cells and disrupts their normal function in several neurodegenerative diseases. Focusing on the mechanism by which soluble synuclein is converted into its toxic, aggregate form, Haas is characterizing the earliest and most dynamic phase of this transition under various conditions on the structural level. Haas has revealed new and potentially important targets for drugs designed to combat the protein aggregation associated with neurodegenerative diseases.

One Mind at a Time

At Bar-Ilan University, research cuts across traditional academic departments and disciplines to focus on mechanisms of neurodegeneration, neuroprotection and brain repair. With a team that combines world-renowned experts with young, innovative scientists, BIU's groundbreaking research is de-mystifying neurodegenerative disease, and speeding the transition from basic research to life-saving clinical treatment.

For more about the research of BIU faculty listed in this brochure go to: www.biu.ac.il and click Research.

The Leslie and Susan Gonda (Goldschmied) Multidisciplinary Brain Research Center

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Bar-Ilan University

Science and Technology

Bar-Ilan University stands at the forefront of cutting-edge research. Bar-Ilan researchers are making breakthroughs that improve life around the globe in areas such as drug-development, nanotechnology, medical research, bio-engineering, microscopy, optics, communications, energy, security, and more. As part of a national program to combat Israel's brain drain, BIU has taken the lead by committing to absorb dozens of returning experimental scientists within its world-class research infrastructure, and has added state-of-the-art physical facilities in engineering, brain sciences and nanotechnology to house these innovative initiatives. The Science and Technology Series highlights some of the University's most exciting research endeavors.

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