

AlzPharm: A Light-Weight RDF Warehouse for Integrating Neurodegenerative Data

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Overview

- Data integration allows a better understanding of brain function by integrating different levels of brain data.
- Most of the neuroscience databases are neither integrated nor interoperable
- Diverse but related data are scattered in different Web-accessible resources and are formatted differently
- We present a Semantic Web approach to building a data integration framework, which involves using RDF as a standard data model to facilitate representation and integration of data

Neuroscience Database Gateway

The screenshot shows a web browser window titled "NDG-OL = Databases list - Microsoft Internet Explorer". The address bar contains the URL: http://big.sfn.org/NDG/site/eavObList.asp?c=81&menu_item=dblist. The page features a navigation menu on the left with links for Home, Background, Resources, Experimental data, Knowledge bases, Software tools, Bioinformatics, Materials, Links, All Databases, Linked Fields, Browse, and Search. The main content area is titled "Databases list" and includes a sub-header "A Gateway to Neuroscience Resources on the Web". Below this, there is a list of six databases with their names, descriptions, and URLs. The list is displayed in a table-like format with alternating row colors.

NDG
Neuroscience Database Gateway

A Gateway to Neuroscience Resources on the Web

Home
Background
Resources

Experimental data
Knowledge bases
Software tools
Bioinformatics
Materials
Links
All Databases

Linked Fields
Browse
Search

Databases list
Display fields [summary](#), or browse individual [fields](#).
Select a name for detailed view

Show: [\[All\]](#) [\[Next\]](#)

Name/ Description/ URL
1. a7 Database Biological aspects of alpha7 subunit of the nicotinic acetylcholine receptor http://www.lgics.org/a7/db/
2. Allen Brain Atlas Map of the Mouse Brain http://www.brain-map.org
3. ALZForum Alzheimer http://www.alzforum.org/
4. Alzheimer's Research Center Resource to disseminate information related to Alzheimer's Disease http://www.mcg.edu/centers/Alz/arc.htm
5. Array Express-European Bioinformatics Institute Public Repository of Microarray Data http://www.ebi.ac.uk/arrayexpress/
6. ASTD Audimotor Spike Train Database http://repositories.cdlib.org/mrrc/1

SOCIETY FOR NEUROSCIENCE

Internet

Current Issue

- No Links between related databases

[BrainPharm Web Portal](#)

Brain Pharmacological Database: Brain Pharmacological database

Home Parkinson's Epilepsy Alzheimer's NeuronDB	
Chemical	
Name:	Donepezil
Description	Cholinesterase inhibitor
Synonym	. Donepezil hydrochloride Show other
Full name	2-[(1-benzyl-4-piperidyl)methyl]-5,6-dimethoxy-2,3-dihydroinden-1-one hydro
Chemical formula	C ₂₄ H ₃₀ ClN ₃ O ₃
Structure	Download 0 Bytes
Molecular target	. Acetylcholinesterase Show other
Action site	Cholinergic synaptic cleft
Neuron affected	. Cholinergic neuron Show other . Cholinoceptive neuron Show other
Function affected	. Inhibit acetylcholine hydrolysis and enhance cholinergic synaptic transmission
Clinical usage	. Alzheimer Show other
Reference	

BrainPharm

AlzForum

The screenshot shows the AlzForum website interface. At the top, there is a navigation bar with links for Home, Contact Us, How to Cite, Become a Member, Your Profile, and Login. Below this is a search bar with a 'Search' button and a 'Get Newsletter' link. The main content area is titled 'PAPERS OF THE WEEK' and features a search form with fields for Keywords, Author, Comments By, Journal, Pub Date, and Sort By. The search results section displays a list of papers, including 'Pharmacological evidence of cholinergic involvement in adult hippocampal neurogenesis in rats' by Kotani S, Yamauchi T, Teramoto T, Ogura H, and 'Efficacy and safety of donepezil in patients with dementia with Lewy bodies: preliminary findings from an open-label study' by Mori S, Mori E, Iseki E, Kosaka K. The interface also includes a 'Forum Calendar' and 'KnowledgeBases' section.

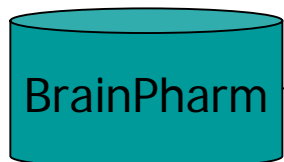
Semantic Web

- Exposes the semantics of Web-accessible data in a standard machine-readable way so that the data can be more easily interpreted and integrated by computer programs (or Web agents)
- Component technologies of Semantic Web:
 - Uniform Resource Identifiers (URI)
 - Ontology (machine readable)
 - Ontological Languages (RDF, RDFS, and OWL)
 - Semantic-Web-aware Tools (e.g., databases)

Oracle RDF Data Model

- Uses the Oracle RDF Data Model to build a Semantic Web data warehouse for integrating datasets extracted from two independently-developed neuroscience databases:
 - BrainPharm (a subdatabase of SenseLab)
 - domain-specific ontology modeling specific molecular details of drugs
 - SWAN (Semantic Web Applications in Neuromedicine)
 - a project to develop an integrated scientific knowledge infrastructure for the Alzheimer Disease (AD) research community enabled by Semantic Web technology. SWAN models domain-independent concepts including experiments, hypotheses, research statements, and publications

AlzPharm



Pathological mechanism [Go Back]	
Name:	Donepezil modulates potassium channels [synonyms] [Data]
Description	
Notes	This work was the first to show different effects of donepezil on two different types of potassium channels (I K(DR) and I K(A)) of molluscan neurons. At a low concentration (5 uM), the drug suppressed I K(DR) but augmented I K(A); at higher concentrations (10-100 uM), it reduced both current types. The ability of donepezil to reduce I K(DR) at low concentrations suggests the drug ability to prevent neurodegeneration in Alzheimer's disease.
Pathology	Alzheimer Show other
Pathological element	
Pathological action	
Channel(s)	I K Show other
Receptor(s)	
Transmitter(s)	
Pharmacological Agent	Donepezil Show other
Pharmacological Action	Modulates Show other
Neuron	
Cell model	Isolated neurons of the land snake Helix Show other
Cellular compartment	
Brain region	
Stage	
Citation	
PubMed ID	16485632

ALZHEIMER RESEARCH FORUM NETWORKING FOR A CURE

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Home: Papers of the Week

PAPERS OF THE WEEK

Papers: Search all papers

Keywords: donepezil any keywords all keywords

Author: Select Author (e.g. Doe, J)

Comments By: Select Commentator

Journal: Select Journal

Pub Date: From Month Year To Month Year

Limited To: Commented ARF Recommends Milestone

Sort By: Publication Date

Reset ARF Search

SEARCH RESULTS: PAPERS=SEARCH ALL PAPERS; ANY KEYWORDS=DONEPEZIL; COMMENTED

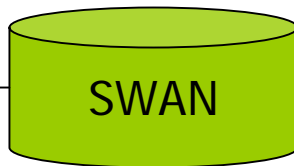
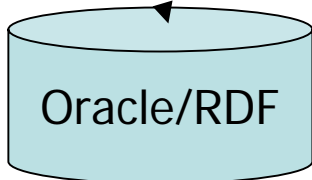
1 to 16 of 16 results

Kotani S, Yamauchi T, Teramoto T, Ogura H. **Pharmacological evidence of cholinergic involvement in adult hippocampal neurogenesis in rats.** *Neuroscience*. 2006 Aug 2; [PubMed Abstract](#)

Mori S, Mori E, Iseki E, Kosaka K. **Efficacy and safety of donepezil in patients with dementia with Lewy bodies: preliminary findings from an open-label study.** *Psychiatry Clin Neurosci*. 2006 Apr;60(2):190-5. [PubMed Abstract](#)

Bullock R, Bergman H, Touchon J, Gombina G, He Y, Nagel J, Lane R. **Effect of age on response to rivastigmine or donepezil in patients with Alzheimer's disease.** *Curr Med Res Opin*. 2006 Mar;22(3):483-94. [PubMed Abstract](#)

Van Dam D, Abramowski D, Staufenbiel M, De Deyn PP. **Symptomatic effect of donepezil, rivastigmine, galantamine and memantine on cognitive deficits in the APP23 model.** *Psychopharmacology (Berl)*. 2005 Jun 1;180(1):177-90. [PubMed Abstract](#)



BrainPharm/SWAN Semantic Gateway

Drug Name	Description	Journal	Title	PubMed ID
Donepezil	Cholinesterase inhibitor	Int J Clin Pract vol 56	Donepezil tolerability and safety in Alzheimer's disease.	12469988 [PubMed] [AlzForum]
		Am J Geriatr Pharmacother vol.2	Efficacy and tolerability of memantine in the treatment of dementia.	15903287 [PubMed] [AlzForum]
		N Engl J Med vol 352	Vitamin E and donepezil for the treatment of mild cognitive impairment.	15829527 [PubMed] [AlzForum]
		Drugs Aging vol.22	Causes of syncope in patients with Alzheimer's disease treated with donepezil.	16060718 [PubMed] [AlzForum]
		Br J Clin Pharmacol vol.46 Suppl 1	Pharmacokinetic and pharmacodynamic profile of donepezil HCl following single oral doses.	9839758 [PubMed] [AlzForum]
		Nucl Med Commun vol.21	Changes in the rCBF images of patients with Alzheimer's disease receiving Donepezil therapy.	10717900 [PubMed] [AlzForum]

AlzPharm: Collaboration between SenseLab, SWAN, AlzForum, and Oracle

- Publications

- Y.K. Lam, L. Marenco, T. Clark, Y. Gao, J. Kinoshita, G. Shepherd, P. Miller, E. Wu, G. Wong, N. Liu, et al. Semantic Web Meets e-Neuroscience: An RDF Use Case. Proceedings of International Workshop on Semantic e-Science, ASWC 2006. 2006. Beijing, China: Jilin University Press, pp. 158-170.

- Demo of AlzPharm

- <http://ontoweb.med.yale.edu/AlzPharm>

Conclusion

- Semantic Web technology benefits neuroscience data integration
- The Oracle/RDF system extends SQL to support semantic inferencing.

Future Directions

- Establish more linkages between SenseLab/BrainPharm and AlzForum/SWAN
 - Ontological overlap
 - Content overlap
- Interoperation with other BioRDF data sources (e.g., Entrez Gene)
- From RDF to OWL

Acknowledgment

- Hugo Y.K. Lam (CB&B Ph.D. Program)
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- Nian Liu (YCMI)
- Chiquito Crasto (YCMI)
- Tim Clark (Mass. General Hospital, Harvard University)
- Yong Gao (Partners)
- June Kinoshita (AlzForum)
- Elizabeth Wu (AlzForum)
- Gwen Wong (AlzForum)
- Gordon Shepherd (Yale Neurobiology)
- Tom Morse (Yale Neurobiology)
- Susie Stephens (Oracle)

Welcome to AlzPharm

at the Yale Center for Medical Informatics



Please select a drug name:
or enter your own drug name:

Note: AlzPharm is a demonstration of how to use the semantic web ([Oracle/RDF](#)) technology to integrate drug and publication information related to the Alzheimer's Disease. Such information is stored in two separate data sources ([SenseLab/BrainPharm](#) and [SWAN/AlzForum](#)). This demo is based on the following paper that was accepted for publication in [SeS2006](#):

[*Semantic Web Meets e-Neuroscience: An RDF Use Case*](#)

Authors: Hugo Y.K. Lam, Luis Marenco, Tim Clark, Yong Gao, June Kinoshita, Gordon Shepherd, Perry Miller, Elizabeth Wu, Gwen Wong, Nian Liu, Chiquito Crasto, Thomas Morse, Susie Stephens, and Kei-Hoi Cheung

AlzPharm

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		Am J Geriatr Pharmacother vol.2	Efficacy and tolerability of memantine in the treatment of dementia.	15903287 [PubMed] [AlzForum]
		N Engl J Med vol.352	Vitamin E and donepezil for the treatment of mild cognitive impairment.	15829527 [PubMed] [AlzForum]
		Drugs Aging vol.22	Causes of syncope in patients with Alzheimer's disease treated with donepezil.	16060718 [PubMed] [AlzForum]
		Br J Clin Pharmacol vol.46 Suppl 1	Pharmacokinetic and pharmacodynamic profile of donepezil HCl following single oral doses.	9839758 [PubMed] [AlzForum]
		Nucl Med Commun vol.21	Changes in the rCBF images of patients with Alzheimer's disease receiving Donepezil therapy.	10717900 [PubMed] [AlzForum]
		Jpn J Pharmacol vol.89	Research and development of donepezil hydrochloride, a new type of acetylcholinesterase inhibitor.	12083745 [PubMed] [AlzForum]
		Lancet vol.367	Donepezil in patients with severe Alzheimer's disease: double-blind, parallel-group, placebo-controlled study.	16581404 [PubMed] [AlzForum]
		Lancet vol.363	Long-term donepezil treatment in 565 patients with Alzheimer's disease (AD2000): randomised double-blind trial.	15220031 [PubMed] [AlzForum]
		Drug Metab Dispos vol.27	Absorption, distribution, metabolism, and excretion of donepezil (Aricept) after a single oral administration to Rat.	10570021 [PubMed] [AlzForum]
		Jpn J Pharmacol vol.81	Effect of donepezil hydrochloride (E2020) on extracellular acetylcholine concentration in the cerebral cortex of rats.	10591480 [PubMed] [AlzForum]

<u>Pharmacological agent</u>	
Name:	Donepezil
Description	Cholinesterase inhibitor

Other Categories that may reference "**Donepezil**"
Pathological mechanism: *Pharmacological Agent*



Pathological mechanism that have Donepezil as Pharmacological Agent

Name	
1	<u>Donepezil modulates potassium channels</u>
2	<u>Protective effect of donepezil against beta amyloid neurotoxicity</u>

AlzPharm

Drug Name	Description	Journal	Title	PubMed ID
Donepezil	Cholinesterase inhibitor	Int J Clin Pract vol.56	Donepezil: tolerability and safety in Alzheimer's disease.	12469988 [PubMed] [AlzForum]
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Petersen RC, Thomas RG, Grundman M, Bennett D, Doody R, Ferris S, Galasko D, Jin S, Kaye J, Levey A, Pfeiffer E, Sano M, van Dyck CH, Thal LJ, . **Vitamin E and donepezil for the treatment of mild cognitive impairment.** *N Engl J Med.* 2005 Jun 9 ; 352(23):2379-88. [PubMed Abstract](#), [Telemakus Biomarker Paper](#)

PRIMARY NEWS

[Early Intervention Trial Bears Little Fruit, but Sows Hope](#)

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Comments on Paper and Primary News

Primary News: [Early Intervention Trial Bears Little Fruit, but Sows Hope](#)

Comment by: [David Holtzman, ARF Advisor](#)

Submitted 15 April 2005

Posted 15 April 2005

Leon Thal and Ron Petersen presented data at the AAN meeting on 4/13/05 that was published today in the NEJM. It compared the effects of donepezil, vitamin E, and placebo in patients who met clinical criteria for amnesic mild cognitive impairment (MCI). The primary endpoint of the study was worsening of clinical outcome so that diagnosis converted to AD. There was no difference among the groups in primary outcome. However, donepezil-treated subjects performed significantly better than the other groups for a year on several cognitive measures. There was little to no appreciable effect of vitamin E. Further, more than half of the subjects were ApoE4-positive in the study. The effects of donepezil were more pronounced in this group, and the effects were seen for longer (18-24 months). Why the effect is more pronounced in ApoE4-positive subjects is not clear. One possibility is that a greater percentage of these patients actually have AD neuropathology underlying their cognitive change. It appears that the effects of donepezil are actually very similar in amnesic MCI to those... [Read more](#)

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Comment by: [Deborah Blacker](#)

Submitted 15 April 2005

Posted 15 April 2005

The possible effect of this study on the use of cholinesterase inhibitors is a complex issue because the widespread use of donepezil and other cholinesterase inhibitors is for established AD, not MCI, and the study doesn't speak to that. I believe use for AD will continue, although effects there are modest and time-limited, too. The impact of the results on the use of cholinesterase inhibitors for MCI is less clear. First, MCI is not often recognized clinically, and I doubt the term is used very often outside of Alzheimer centers and specialty memory clinics. In those settings, to my limited knowledge, these medications are widely used, and I'm not sure this study would change that, as it does show some limited benefits for donepezil. Given the recent FDA MedWatch for galantamine (based on excess deaths in large MCI trials), I don't think we can assume that all cholinesterase inhibitors will be treated the same. In any case, the big change in practice should be for vitamin E, also widely used, both by those with a diagnosis of MCI and those with memory changes who...

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