are there any similar articles or studies on this topic, MRI data only as a measure of hippocampal volume, related to Rapamycin use

Yes—there are a few directly relevant rapamycin/mTOR-inhibitor studies that use MRI-derived hippocampal volume as a primary or secondary structural endpoint, plus broader MRI hippocampal volumetry literature that can serve as methodological reference.

Rapamycin + MRI hippocampal volume

- **OXYS rat "brain aging" study (Kolosova/Blagosklonny, Aging 2013 / PMC3824413)**
  Senescence-accelerated OXYS rats were treated with dietary rapamycin (0.1 mg/kg) and underwent structural MRI with quantitative measurements of hippocampal area and lateral ventricular size. [1]
  - MRI showed enlarged hippocampal area and marked hydrocephalus (ventricular enlargement) in untreated OXYS vs Wistar controls. [1]
  - Rapamycin normalized hippocampal area (both absolute and relative "hippocampus/brain" %) and reduced ventricular volume, effectively erasing the structural differences between OXYS and Wistar rats. [1]
  - Authors explicitly link behavioral improvement to "normalization of brain structure revealed by MRI," including decreased size of enlarged hippocampus and abrogation of hydrocephalus. [1]
    This is the clearest preclinical example where MRI-derived hippocampal morphometry is used as a structural outcome in rapamycin treatment.
- **Poster: "Short-term Sirolimus Treatment Restores Hippocampus and Caudate Volumes and Global Cerebral Blood Flow" (Alzheimer's Imaging Consortium, 2024)**
  A human imaging poster (APOE4 carriers at risk for AD) reported that prescription sirolimus increased caudate and hippocampal volumes and cerebral blood flow measured by MRI. [2] [3]
  - APOE4 carriers had lower hippocampal and caudate volumes and reduced brain perfusion at baseline vs APOE3 carriers. [3]
  - After sirolimus, caudate and hippocampal volumes and blood flow in APOE4 carriers increased significantly; this effect was not seen in APOE3 carriers. [3]
    This is MRI-only volumetric data in humans, but as of now appears in poster / secondary summary form rather than a full peer-reviewed manuscript.
- **Rapamycin suppresses brain aging in OXYS rats (same dataset, more detailed report, PMC3824413)**

The full paper emphasizes MRI-based structural outcomes: cortical area, hippocampal area (absolute and relative), and ventricular size, all quantified from MRI. [1]

- Table 1 shows hippocampal area and relative hippocampal/brain percentage values with rapamycin vs control in both OXYS and Wistar rats. [1]
  This is essentially the same study but is useful for methodological detail.

Related rapamycin neuroimaging work (not strictly hippocampal MRI volume)

- **Phase 1 open-label rapamycin trial in MCI/AD (Gonzales et al., Nature Partner Journal 2025)**
  This pilot trial focuses on safety, CSF biomarkers, and broader neurodegenerative / inflammatory markers; rapamycin was not detected in CSF, but they report changes in multiple biomarkers from baseline to post-treatment. [4]
  From available summaries there is no clear statement that hippocampal MRI volumetry was a dedicated endpoint; structural MRI may have been acquired but not necessarily analyzed as hippocampal volume.
- **PET imaging study: single-dose rapamycin in Long-Evans rats (FDG + SynVesT-1)**
  This is primarily PET (glucose metabolism and synaptic density), with no mention of MRI-based volumetrics. [5]
  It is relevant mechanistically (acute rapamycin effects in brain), but not for hippocampal volume per se.

MRI hippocampal volumetry methodology references

For your interest in "MRI data only as a measure of hippocampal volume," independent of rapamycin:

- **Meta-analysis of MRI hippocampal volume in normal/MCI/AD (2023)**
  A recent meta-analysis compared hippocampal volumes across healthy controls, MCI, and AD using structural MRI. [6]
  It provides useful guidance on:
  - Standardization of hippocampal segmentation protocols.
  - Handling scanner differences and normalization (e.g., intracranial volume adjustment).
  - Typical effect sizes and variance in longitudinal hippocampal atrophy.
- **Longitudinal hippocampal volume change and cognitive decline (older adults, MRI)**
  A 2007 study examined change in hippocampal volume over time and its association with cognitive trajectories in non-demented older adults with and without depression. [7]
  This paper is helpful from a design standpoint (intervals between scans, test–retest reliability, covariate handling) if you're planning a longitudinal rapamycin study.

These non-rapamycin papers give you robust precedents for using MRI hippocampal volume as a structural biomarker, including segmentation techniques, normalization, and statistical modeling.

Practical implications for your work

- There is at least one **preclinical** rapamycin study where hippocampal morphometry from MRI is a central outcome (OXYS rats), with data on hippocampal area and relative hippocampus/brain metrics.[1]
- There is emerging **human** MRI volumetry evidence (sirolimus poster in APOE4 carriers) suggesting reversible hippocampal and caudate volume loss, but it is not yet a full journal article.[2] [3]
- For rigorous protocol design (especially human), you'll likely need to merge:
  - Rapamycin mechanistic and preclinical data (including the OXYS MRI work).[1]
  - Standard MRI hippocampal volume meta-analytic and longitudinal methodology from the broader neurodegeneration literature.[6] [7]

If you're designing or critiquing a study, would you be more interested in preclinical rodent protocols (dose, duration, segmentation methods) or in how to structure a human trial with MRI hippocampal volume as a primary endpoint under current regulatory expectations?

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mTOR inhibition and brain structural neuroplasticity mechanisms

mTOR inhibition modulates brain structural neuroplasticity by shifting the balance between growth/anabolism and maintenance/cleanup (autophagy), with effects on dendritic/synaptic structure, neural stem cell dynamics, and circuit-level remodeling that are highly context- and dose-dependent.[16] [17] [18] [19]

Core mTOR functions relevant to structure

mTOR exists in two main complexes, mTORC1 and mTORC2, integrating nutrient, energy, growth factor and neurotransmitter signals to regulate protein synthesis, cell size, metabolism, autophagy, and cytoskeleton dynamics.[20] [18] [16]
mTOR-dependent control of translation (via 4E-BP1/2, S6K, etc.) and autophagy directly shapes the capacity for structural plasticity: building and maintaining synapses, dendrites, and spines versus pruning and recycling damaged components.[17] [18] [16]

Synaptic and dendritic structural plasticity

mTOR signaling is a convergence node downstream of NMDA receptors, AMPA receptors, BDNF, dopaminergic inputs, and mGluRs that drive LTP/LTD and long-lasting synaptic changes.[21] [17]
Rapamycin and related mTORC1 inhibitors can block late-phase LTP and long-term facilitation, prevent activity-dependent dendritic spine enlargement, and reduce spine density when sustained or excessive, indicating that some forms of structural potentiation require intact mTOR-mediated local translation.[17] [21]

Conversely, pathological mTOR hyperactivation (e.g., TSC, NF1, PTEN mutations) produces abnormal spine morphology, excessive or miswired synapses, and network hyperexcitability;

targeted mTOR inhibition in these contexts can partially normalize spine structure and synaptic connectivity.[22] [23] [20]
This bidirectionality is key: modest, timed mTOR inhibition can restore structural homeostasis in hyperactive circuits, while strong or chronic inhibition can impair normal experience-dependent synaptic growth.[23] [20]

Neurogenesis, neural stem cells, and circuit remodeling

In development and adult neurogenesis niches, mTOR regulates neural stem cell (NSC) proliferation, survival, and differentiation into neurons and glia.[24] [18] [22]
Recent work shows that pharmacologic mTOR pathway inhibition alters NSC proliferation and lineage choice: reducing proliferation and changing differentiation patterns, with implications for long-term structural integration of new neurons into hippocampal and cortical circuits.[19]

In adult and aged brain, mTOR activity influences dendritic arbor complexity, axonal growth/regeneration, and the structural integrity of long-range connections; boosting mTOR can support axonal regeneration after injury, whereas inhibition is more beneficial for disorders driven by overgrowth, malformation, or tumorigenesis.[18] [16] [20]
Thus, structural neuroplasticity outcomes of mTOR inhibition depend on baseline mTOR tone, developmental stage, and whether the main problem is “too much” vs “too little” growth.[16] [20]

Autophagy, cytoskeleton, and neurodegeneration

mTOR inhibition robustly activates autophagy, enhancing clearance of protein aggregates, dysfunctional organelles, and damaged synaptic components, which can indirectly remodel circuits by pruning compromised synapses and stabilizing healthier ones.[18] [16]
By regulating lysosome and mitochondria biogenesis, mTOR also influences local energy supply and redox status in dendrites and spines, constraining which structural changes are energetically sustainable over time.[16] [18]

In neurodegenerative models, partial mTOR inhibition reduces toxic aggregate burden and can preserve neuronal and synaptic structure, but excessive suppression risks dendritic simplification and synaptic loss due to impaired protein synthesis needed for maintenance.[17] [18] [16]

This tension underlies ongoing debate about optimal “mTOR set-points” for aging brains, where modest inhibition may enhance structural resilience via improved quality control while still permitting activity-dependent growth.[18] [16]

Integrative view for rapamycin-like interventions

Taken together, mTOR inhibition reshapes structural neuroplasticity through overlapping mechanisms: reduced anabolic drive (translation, growth), increased catabolic/cleanup processes (autophagy), altered NSC behavior, and changes in cytoskeleton and synaptic signaling cascades.[19] [16] [17] [18]
The net structural outcome can range from normalization of pathological overgrowth and aberrant synaptic architecture (e.g., TSC, some epilepsies) to impaired structural learning and spine maintenance if inhibition is too strong or mistimed relative to plasticity demands.[20] [23] [18]

For the kind of gerontology-focused protocols you work on, the crucial question is not “does mTOR inhibition change structure?” but “under which dosing and timing regimes does it preferentially enhance structural *maintenance* and repair vs. suppressing healthy plasticity?”. [16] [18]

Would you like a more formal mechanistic map (e.g., pathway-level description from specific receptor inputs to structural outcomes in hippocampal circuits), or a translational synthesis focused on how these mechanisms constrain safe rapamycin dosing in middle-aged/older humans?

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1. https://pmc.ncbi.nlm.nih.gov/articles/PMC3824413/
2. https://www.rapamycin.news/t/poster-short-term-sirolimus-treatment-restores-hippocampus-and-caudate-volumes-and-global-cerebral-blood-flow/18234
3. https://www.nad.com/news/mtor-inhibitor-drug-reverses-neurodegeneration-in-individuals-at-risk-for-alzheimers-in-new-study
4. https://www.nature.com/articles/s43856-025-00904-9
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