2 Annotation guidelines study type labels

We only include studies in the field of neuroscience/neurology and psychiatry using the following search query on PubMed: "Central nervous system diseases[MeSH] OR Mental Disorders Psychiatric illness[MeSH]". A random sub-sample of xxx references sampled using the above mentioned search string are assigned one of fifteen study labels shown in Table 1. Those labels were defined based on our interest in finding studies that explore any kind of treatment for a neurological disease. The classification of studies relies on information from their titles, abstracts, and the journals in which they were published.
Studies which miss an abstract and studies where non-roman letters make up a substantial part of the text (i.e., except for the use of certain non-roman letters and characters in scientific formula) were excluded. The guidelines for the study labels in Table 1 shall be understood as such and not as necessary criteria that must be fulfilled for labeling.

The working definition for "intervention" is the following: An "intervention" includes a treatment, procedure, or other action taken to prevent or treat disease, or improve health in other ways.
We separate "non-drug-interventions" from "drug-interventions" according to the following definition: For the annotation on drug-based, respective chemical-based therapies, we follow the guidelines of the CHEMDNER corpus for annotating chemical mentions [13], as well as [14]. The basic rule for chemical entity annotation is that the chemical should have a specific structure. Non-drug-interventions include any therapeutic intervention not classifiable as drug, e.g., radiation therapy, physical therapy or complex diets. This also includes other substances, that cannot be associated to a clear molecular structure, such as olive oil, herbal extracts, cannabis, tea and nanoparticles (and others).

Studies which re-analyze data from former clinical trials shall be labeled as the respecitve clinical trial.
Pharmakokinetic studies shall be labeled as the respective drug-intervention study. Studies on long-term adverse events of therapies shall be labeled as the respective clinical trial. This applies only if the therapy is mentioned specifically. E.g., a study on dementia after aspirin-intake in humans would be labeled as "non-RCT drug-intervention" whereas a study on carotid sclerosis after irradiation would be labeled as "remaining" as "irradiation" is an unspecific description of a therpay (see below).

The lables are listed in hierarchical order except for "non-systematic review" which is the second-most important label. I.e., if more than one label applied to an abstract only the label found in the highest position in the table was assigned ("human, systematic review" > "non-systematic review" > "human, RCT drug-intervention" > "human, RCT non-drug intervention" > "human, RCT non-intervention", etc.).
Another exception applies for studies which are outside the realm of neuroscience/psychiatry, and clinical trials with unspecific mention of therapies: They are always labeled "remaining".

first word	label	working definition used (applies to title and/or abstract of study)
human,	systematic review	A structured and reproducible research summary of human participants. This also includes systematic reviews covering both human subjects and animals. An explicit mention of "systematic review", "we systematically review", "meta-analysis" and/or "we meta-analyze" in the title or abstract. Alternatively, the mention of at least 2 biomedical literature databases such as "PubMed", "Embase","Cochrane Library", "Web of Science", "Scopus" (or others) in the abstract and at least 2 authors would qualify as a systematic review.
	RCT non-drug-intervention	A scientific experiment in the form of a clinical trial with the distinguishing feature that participants are randomized into experimental groups. This study type needs a specific mention of randomization of a human population. Concretely, the aim of the study must be to test a non-drug treatment (e.g., radiation therapy, surgery, physical therapy, nanoparticles) in randomized fashion.
	RCT drug-intervention	A scientific experiment in the form of a clinical trial with the distinguishing feature that participants are randomized into experimental groups. This study type needs a specific mention of randomization of a human population. Concretely, the aim of the study must be to test a drug (e.g., aspirin, risperdal, lorazepam) in randomized fashion.
	RCT non-intervention	A scientific experiment in the form of a clinical trial with the distinguishing feature that participants are randomized into experimental groups. This study type needs a specific mention of randomization of a human population. Any RCT not annotated as "RCT drug-intervention" or "RCT non-drug-intervention" should be classified under this category.
	case report	A study type reporting clinical/imaging findings of one single human individual, e.g., by explicit mentioning of "case" or "case report". Case series with more than 1 participants shall not be classified under this category.
	non-RCT non-drug-intervention	A clinical study without explicit mention of randomization testing a non-drug intervention, e.g., observational or cohort studies. Also includes studies assessing participants which were sampled from a previous RCT.
	non-RCT drug-intervention	A clinical study without explicit mention of randomization testing a drug intervention, e.g., observational or cohort studies. Also includes studies assessing participants which were sampled from a previous RCT.
animal,	systematic review	A structured and reproducible research summary of animal studies only. An explicit mention of "systematic review", "we systematically review", "meta-analysis" and/or "we meta-analyze" in the title or abstract. Alternatively, the mention of at least 2 biomedical literature databases such as "PubMed", "Embase","Cochrane Library", "Web of Science", "Scopus" (or others) and at least 2 authors would qualify as a systematic review.
	non-drug intervention	Any study type testing a non-drug intervention such as radiation therapy, surgery, physical therapy or nanoparticles in animals, including experimental studies but also studies in companion animals (pets).
	drug intervention	Any study type testing a drug intervention in animals, including experimental studies but also studies in companion animals (pets).
	other	Any animal study not testing a therapeutic intervention, e.g., pathomechanistic studies, methods development, case series/reports (veterinary studies), studies testing diagnostic procedures in animals. This also includes exposure studies in animals (e.g., farm animals being exposed to certain environmental toxins).
	non-systematic review	A text reviewing/discussing a certain topic, can be very broad and includes editorials, perspectives and other types of texts with the goal to discuss any matter related to neuroscience/psychiatry. Does not generate original data but discusses previously published data. An explicit mention of "review", "expert review", "traditional review", "literature review", "review of literature" or "we summarize".
	remaining	Any other study which does not fit in any of the categories defined above. E.g., studies about medical history, epidemiology or other methodologies. Also includes studies which raters were uncertain how to label, clinical trials with unspecific mention of therapies (e.g., "antiepileptica"), studies published in the "Journal of Visualized Experiments" ("JoVE") and studies which are outside the realm of neuroscience/psychiatry.

Table 1: Annotation guidelines