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# Do Neurochemicals Reflect Psychophysiological Dimensions in Behaviors? A Transdisciplinary Perspective Based on Analogy with Maslow's Needs Pyramid.

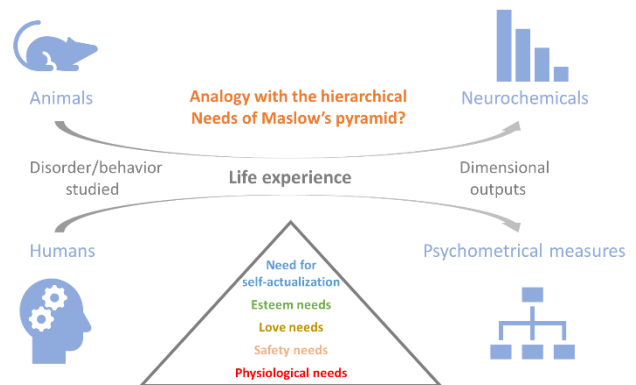
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**KEYWORDS:** *Neurochemistry, amino acids, monoamines, big data, multivariate analysis, behavior, psychometry, latent dimensions, Maslow's pyramid model.*

**ABSTRACT:** All behaviors, including motivated behaviors, result from integration of information in the brain via nerve impulses, with two main means of communication: electrical gap-junctions and chemical signaling. The latter enables information transfer between brain cells through release of biochemical messengers, such as neurotransmitters. Neurochemical studies generate plentiful biochemical data, with many variables per individual, since there are many methods to quantify neurotransmitters, precursors and metabolites. The number of variables can be far higher using other concomitant techniques to monitor behavioral parameters on the same subject of study. Surprisingly, while many quantitative variables are obtained, data analysis and discussion focus on just a few or only on the neurotransmitter known to be involved in the behavior, and the other biochemical data are, at best, regarded as less important for scientific interpretation. The present article aims to provide novel transdisciplinary arguments that all neurochemical data can be regarded as items of psychophysiological dimensions, just as questionnaire items identify modified behaviors or disorders using latent classes. A first proof of concept on non-motivated and motivated behaviors using a multivariate data-mining approach is presented.



Motivation is a powerful driver of dynamic behavior in humans. One way to “measure” psychological and motivational dimensions is by psychometric questionnaires, which are used in health, well-being, education, psychology and in human and social science studies in general. For instance, in health contexts, such questionnaires score the mental state of a patient suffering from a given pathology (e.g., cancer, brain hemorrhage, rare disease, etc.) or disorder (e.g., depression, stress disorder, autism spectrum disorder, etc.) by quantifying subjective answers to qualitative questions. The questions are designed by an expert group to explain one or several dimensions or “latent classes”: e.g., depression, fear or self-esteem (Figure 1A). To validate the classes of a psychometric test, the questions are first submitted to beta-testers and statistical tests are used to avoid doubletons between items or overlap between latent classes, by four main

methods: classical test theory, structural equation modeling, item response theory, or Rasch measurement theory. The questionnaire can then be adjusted, with new beta-testers, to meet statistical requirements such as reproducibility and accuracy, before being used at scale. Psychometric tests aim to obtain reliable data on targeted dimensions, with the most relevant variables. Although not always fully validated according to the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN)<sup>1-3</sup>, an impressive number of psychometric tests are available in the literature<sup>4</sup>. However, each questionnaire is valid for a specific subject profile, but often first tested on student populations, which are the most easily accessible for academic researchers. Consequently, extrapolation to other populations is hazardous: for example, it is a well-known textbook case in social science that a quality of life questionnaire item

on use of a bike would get quite different answers between the five continents. Despite efforts to minimize population bias, one has to keep in mind that there are potential biases inherent in tests that rely on self-reporting. As such additional measures, such as physiological tests, are often employed to validate the responses.

In humans, motivational aspects are also studied using neuroscientific approaches: electrophysiology (EEG, MEEG) or neuroimaging. Differences in brain activity between a study group and controls are recorded and additional machine learning approaches can help to find how the differences are encoded. However, neuroscience in humans is hindered by experimental and ethical limitations, which will be explained below, and the decoding of behavior is mainly studied in animal models, on the evolutionary assumption that all living creatures have much in common. However, animal motivation cannot be assessed on psychometric questionnaires, but only on behavioral tests based either on foraging approaches, the lowest common interspecies level of behavior, or, for example, on exploration/demotivation in depression/anxiety/fear models<sup>5</sup>. In addition to a plethora of behavioral approaches, electrophysiological recording is mainly used to study motivation in non-human primates, which provide better models to study higher motivated behaviors thanks to the anatomic similarities and phylogenic proximity to humans. In rodents, routine electrophysiological recording is mainly devoted to sleep disorder, because it is very difficult to apply multiple non-implantable electrodes on their skulls. Consequently, comparing results on psychometric questionnaires in humans with data obtained on animal models is not straightforward, despite the underlying brain processes and neurochemistry being the same (Figure 1B). However, if a behavior or disorder can be studied in terms of dimensions in psychology, the same behavior or disorder could be studied in terms of dimensions, on approaches applicable in animals. There are growing bodies of evidence suggesting that the neural dynamics observed in a given behavior are preserved across species<sup>6</sup>, so that dimensions appear highly relevant in modern neuroscience.

The purpose of the present article is to propose an original approach bridging neuroscience and psychology, through the prism of neurochemistry seen by multivariate analysis. Motivated or non-motivated behaviors result from integration of information by the brain. The two main mechanisms are chemical signaling, studied in biochemistry or neurochemistry, and its consequence, propagation of a nerve impulse, studied in electrophysiology. Brain cells mostly communicate via messengers released in extracellular space. The best-known compounds associated with motivation are dopamine and oxytocin, but brain communication is far more complex and involves two excitatory and inhibitory neurotransmitters (glutamate, GABA) and their neuromodulators (dopamine, noradrenalin, serotonin, acetylcholine, etc.) (Figure 1B). The present study provides a first proof of concept that neurochemical parameters assessed in animal models could reflect psychophysiological dimensions in motivated or non-motivated behaviors. After a brief introduction on neurochemical transmission and the parameters to be monitored, it is argued that neurochemical data obtained in animals, including numerous variables,

can fit a 5-level pyramid showing a strong analogy to Maslow's well-known motivational model. The study also suggests that neurochemicals analyzed in dimensions and big data approaches could be more relevant by considering individual life experience, in line with the dimensional outputs obtained from psychometric tests in humans.

### **Neurochemical transmission: what, where, how**

Brain communication involves propagation of information: chemical communication is triggered by electrical communication and electrical communication by chemical communication, and these exchanges of information occur all the time, from before birth to death. Briefly, electrophysiological signals are generated by ion exchanges underlying one-way propagation of nerve impulses. Once the electrical signal arrives at the presynaptic button (the end of the cell), through the axon, one or two neurotransmitters are released in the synapse (a space between neurons filled with interstitial extracellular fluid). Activation of specific excitatory and/or inhibitory receptors for this specific chemical message on the surface of a second neuron in the postsynaptic area modulates the nerve impulse of that second neuron and/or modifies intracellular messengers ("second messengers"). Ion diffusion underlies the nerve impulse, but all the cellular processes require energy, provided by glucose metabolism, to maintain homeostasis and enable the brain system to respond to any exchanged instructions. This very schematic picture is complicated by the combination of concomitant or subsequent events resulting from the release of neuroactive compounds by the various brain cells. Brain neurons are organized in bundles, creating complex networks between brain areas, or in groups of interneurons within a given brain area. Moreover, the other cells of the brain (glial cells, including astrocytes, microglia and oligodendrocytes) also release transmitters which act as neuromodulators. Finally, the brain is richly irrigated by blood vessels, and the mutual exchanges between brain tissue and blood are tightly controlled by the brain-blood barrier. Also, the extracellular space is yet another circulatory system for neurotransmitters and the target of neurons contacting the cerebrospinal fluid. Finally, if a neuron releases one or two neurotransmitters, the nature of the neurotransmitter in question can also change over the lifetime. Moreover, each neurotransmitter has not just one role in the brain (Figure 1B). Consequently, all these configurations and associated processes make both neurochemical and electrophysiological studies very tricky.

### **Which are the challenges and the current limits to the analysis of neurochemical transmission?**

One of the key questions in neurochemistry is how neuroactive molecules pass from one compartment to another. Four main compartments have to be considered: intracellular (in) vs extracellular (out), and, for the latter, intrasynaptic (in classical transmission) vs extrasynaptic (in volume transmission) – plus blood and plus glial cells, as mentioned above.

In humans, neurochemical tools are mainly non-invasive: urine or blood sampling, to quantify precursors or degradation products of brain neurotransmitters, which are very indirect and weak biomarkers of brain activity; and imaging tools. Cerebrospinal fluid analysis after invasive lumbar

puncture can also provide chemical information. Imaging techniques include positron emission tomography (PET), following one radiotracer in the whole brain after intravenous injection, and magnetic resonance spectroscopy (MRS), detecting compounds with high brain concentration thanks to the paramagnetic properties of the atoms; at present, only two neurotransmitters can be detected, GABA and glutamate, and the corresponding signals are either weak or not pure (Figure 1C). In contrast to PET, which studies one target of a neurotransmitter at a time by quantifying receptor occupancy, functional magnetic resonance imagery (fMRI) is based on oxygen or glucose consumption, providing indirect information on brain activity. Both techniques are used for monitoring or detection of brain pathologies, but little used to study motivation per se. They can be coupled to biopsies in the case of tumor. Only invasive tools (microdialysis/sensors) can provide more neurochemical information, but they can only be used ethically in a controlled context in neuropathological brain areas, such as following subarachnoid hemorrhage or brain trauma, and of course are never used to study behavior. For these reasons, it is difficult to study motivation neurochemically in humans, which is why animal models are predominant in this context. The alternatives to in-vivo experiments in humans are tissue and ex-vivo approaches (binding, mRNA of synthesis enzymes or receptors) which can be carried out on postmortem brain samples or brain cell cultures from biopsies (Figure 1C). Cell culture is used in very standardized conditions; postmortem samples, on the other hand, are collected just after a life experience (after the individual has produced a behavior), and are thus very relevant, because the brain signaling may have been altered, either by deleterious conditions impacting normal behaviors or by the variety or wealth of experience. However, in practice, postmortem approaches are limited to some psychiatric and neurological pathologies such as schizophrenia, major depression and related disorders, Alzheimer's disease or prion diseases, and never concern motivated behaviors. Technically speaking, as for psychometrical measurements, neurochemical measurements are often validated according to guidelines in analytical procedures<sup>7</sup>. They must adhere to criteria of reproducibility, linearity and accuracy, with precise limits of detection and quantification. Lastly, for all these neurochemical techniques, the amount of data that can be monitored depends on the number of parameters, number of brain areas, need for a brain area as reference, a priori relevance of the parameter being studied, etc. The literature on motivation studied by neurochemists is abundant in animal models; dopamine and oxytocin, two compounds that are strongly involved in motivational challenges, are certainly the most frequently studied molecules in the motivated brain with a view to application in humans, and dopamine alone accounts for almost 40% of neurochemical studies according to a comparison of the number of results from a PubMed search using the following keywords: "neurochemistry and neurotransmitter" vs "neurochemistry and dopamine". The neurochemical data presented in most of the papers focuses on very few variables, since the other molecules involved in neurotransmission, which could have been monitored simultaneously, often exhibit no changes or else changes that are difficult to interpret. Even so, if a disorder or a behavior can be studied by

dimensions in psychology, the same disorder or behavior could be studied by dimensions in neurochemistry (Figure 1D). To move in this direction, recent neurochemical studies by De Deurwaerdère's group<sup>8-10</sup>, quantifying dopamine and related compounds in a couple dozen brain areas, showed that, although ANOVA tests failed to demonstrate alterations in tissue concentrations in treated or transgenic vs control animals, correlations between some variables do exist and could explain the deficits observed in the animal models (mice, rats, monkeys). Multivariate analysis of neurochemical data, which is very rarely used or published in bioanalytical journals, in contrast to neuroscience journals (e.g. in Alzheimer's disease<sup>11</sup>), is highly relevant in this multiparameter context, to determine which chemicals are involved in a disorder or behavior (Figure 1D). Multivariate analysis is the basis of metabolomics studies in dementia and related neurodegenerative pathologies. The purpose of metabolomics is to determine the complete profile of the molecules (i.e. chemical fingerprints) present in fluids, cells, tissues or even whole organisms, to reveal and predict the specific biomarkers of a pathology from molecular signatures, and to study the interactions between the molecules. Neurochemistry can thus be regarded as a subfield of metabolomics.

#### **How could multivariate approaches be used in neurochemistry?**

While metabolomics deals with the molecular capacities of a cell, compartment, tissue or organism in order to predict, neurochemistry can be used not only as a tool to monitor chemical variations in the brain, as is perfectly done today, but also to encode and predict chemical communication in the brain. Only big data approaches could enable this to be done better and further, but have so far been very rarely used for neurochemicals, as explained above. The present article shows the first example of how to exploit neurochemical data from an ABC approach of data mining. In practice, considering  $n$  neurochemical variables creating a universe with  $n$  dimensions, visualization of the data is not possible since there is a great mass of data in a  $n$ -dimensional space, but an angle of view showing the longest distribution in the  $n$ -dimensional space allows projection to a new dimension in principal component analysis (PCA). Another angle of view, orthogonal to the new dimension, can show the data on another new dimension with a smaller length; then a third angle of view shows another new dimension, and so on. At the end of the process, up to  $n$  new neurochemical dimensions can be created, each composed of the initial  $n$  variables at different weights (factor contribution). The goal of PCA is to reduce the number of dimensions, so as to visualize the first new dimensions for analysis, because they represent a significant percentage of the data variance (scree plot). When more than two qualitative variables are also available (e.g., treatment, phenotype, age, food, pathology), factorial analysis of mixed data (FAMD) is appropriate, because firstly exactly the same dimensions will be generated as in the equivalent PCA, and secondly the residual variances provided by the qualitative variables will be "swept" from the last latent dimensions generated by the PCA into the first latent dimensions. This is the ABC methodology used when big data are available. Briefly, we ap-

plied FAMD on three datasets from brain tissues of drosophila, rats and mice respectively (Figure 2). Each neurochemical dataset, containing from 14 to 60 quantitative variables, was analyzed using the snowCluster package in the 'click button' R-based Jamovi 2.3.21 software. Five dimensions cumulating 100% of the variance, and obtained with no rotation, were generated on each dataset, as seen in the scree plots, here represented as 90°-rotated graphs to be visualized as 5-level pyramids (Figure 3A). To name the five new dimensions, we decided to select the initial variables with the greatest factor contributions (i.e., coordinates), to emphasize similarities between them, and for this simple numerical filtering was applied on each coordinate table. More precisely, we found that minimal thresholds of 0.4 or 0.5 in absolute values avoided having the same initial variable in two new dimensions as much as possible. The dimension names suggested by this filtering on one dataset were then compared to the dimension names suggested on the other datasets, to try to obtain the same 5-level pyramid model.

### **What neurochemical dimensions are revealed by multivariate analysis?**

We first worked with a dataset of amino acid contents from drosophila single brain samples collected in old and young animals at four time-points in the day/night cycle. The interest of amino acids is that they are involved in metabolic processes, are also precursors of neurotransmitters, and three amino acids (glutamate, GABA, aspartate) are neurotransmitters themselves (Figure 3A). Their roles are well-known, and data interpretation can be easy. Our analysis method revealed that the first new dimension fitted a dimension of physiological needs, because essential amino acids (provided by food) stood out. The second new dimension was related to responses to stress and hyperexcitation, by including the GABA inhibitory neurotransmitter and the arginine amino acid recruited in stressful conditions. The third new dimension brought together serine, which is a gliotransmitter in its D form, and alanine, which is the brain donor of ammonia in cell processes<sup>12</sup>. Glutamate precursor, glutamine, and aspartate, known to be an agonist of NMDA receptor signaling significantly contributed with time to the 4th dimension, while there was no strong amino acid contributor in the 5th new dimension. This representation in dimensions recalls the hierarchy of needs in Maslow's theory of human motivation, also popularized by a 5-level pyramid. In the light of this surprising analogy, two other datasets were also considered from animal models currently used to study motivated or non-motivated behaviors: one from adolescent rats used in a previous study of the immaturity of decision-making ability<sup>13</sup>, and one from a mouse model of Rett's syndrome, in which the transgenic animals exhibit defects in autonomic, cognition, motor functions and autistic traits<sup>14, 15</sup>. In adolescent rats, the FAMD, performed on dopamine, serotonin, noradrenalin and their related metabolites from four brain areas involved in goal-directed behavior, showed that three dimensions were generated from highly contributive variables (Figure 3A). The first concerned variables involved in the maturation of the dopaminergic system, in line with a dimension of "physiological needs", the second concerned metabolite variables in brain areas involved in control structures, in line with a "safety"

dimension. These two dimensions could be named, but the third dimension seemed to be very close to the second one. In the Rett model, in which both monoamines and neurotransmitter amino acids were quantified in five brain tissues, the five new dimensions were all interestingly associated with significant variable contributors (Figure 3A). The first mainly comprised variables and brain areas known to be involved in general metabolism. The second comprised contributive variables in areas controlling motor coordination or involved in anxiety. The third comprised respiratory and cardiac control, in line with the close interaction of these two vital systems. The fourth comprised hypothalamus GABA, controlling basic functions such as food intake, sleep and reproduction. And the fifth dimension was mainly based on cortical dopamine involved in action. The Maslow dimensions of love, esteem and self-actualization obviously cannot be used. However, to avoid anthropomorphism, the last three new dimensions could be named here as interdependency, body evaluation and action dimensions for these animals. Interdependency is defined as a condition of two or more variables depending on each other; body evaluation can be defined as the process of monitoring and controlling several variables in body functioning; and action means doing something. In contrast, the first two new dimensions match the physiology and safety dimensions.

To sum up, the FAMD revealed the existence of new neurochemical dimensions, which could be named, providing contributive variables in a 5-level pyramid model, according to a hierarchy of needs as theorized for motivated behaviors by Maslow. Although the data sets used in our preliminary observations do not match each dimension of Maslow's model in a perfect bijection, what heuristic, epistemic and methodological gains can be derived from this analogy?

### **Discussion**

The purpose of the present viewpoint was to propose an original transdisciplinary link between neurochemical data and psychometric measurements, so as to open up unexplored research perspectives. Multivariate approaches are particularly relevant in this context. The methodology is original, combining neurochemistry and evolutionary biology and analyzing all the data available for a given animal model, including neurochemical parameters that vary little and neurochemical changes that are difficult to interpret. With animals which have exhibited a given behavior, both physiology and psychophysiology are included in the multivariate approach. The approach develops a dimensional model analogous to Maslow's pyramid of needs, making quantifiable and coherent links with psychological features. The theory of human motivation based on five basic needs, developed by Maslow in 1943<sup>16</sup>, has been greatly enriched over 80 years, for instance with the conceptualization of human needs in terms of intrinsic motivation and self-determination by Deci and Ryan<sup>17</sup>, or with the two-process model of psychological needs proposed by Sheldon<sup>18</sup>; but Maslow's model, although a reductionist model for human motivation, not based on observational evidence, either when first published or after, is easy to grasp for non-specialists. It exhibits a structural logic allowing heuristic reflection on the relationship between the dimensions and the interest of using levels for the description of the initial variables. We do

not claim that Maslow's model realistically describes all the observed phenomena, but that it can help in interpreting data. The dimensions generated by the data are interpretable in a transversal and transdisciplinary perspective, by back-and-forth movements from one model to another, always keeping in mind that inter-species differences exist and can change the representativity of the psychometric dimensions. For instance, the first level of the pyramid concerns a biological dimension, which is a fundamental prerequisite for all the biological and social sciences. Secondly, the last level of the pyramid cannot be labeled "self-actualization" in our mouse study; however, finding a 5<sup>th</sup> dimension linked to action in a rodent model is consistent with the idea of accomplishment implied by self-actualization in the human model. Moreover, enrolling all the isolated factors into dimensions, and thus in conditions of interpretation that are closer to the complexity of living experience, enables the complexity of living experience to be taken on board. The porosity between the dimensions of the pyramid, for which Maslow's model has been criticized, is not an obstacle for applications in neurochemical multivariate analysis since neurochemicals themselves play various roles in brain functioning, as recalled in Figure 1B.

In practice, simple numerical filtering enabled the new dimensions generated by FAMD to be named in line with a Maslow-like 5-level pyramid; but other methodological and scientific points could further stabilize our suggested model. We first checked that numerous correlations between the neurochemical variables studied were obtained in each data set, to validate the use of factor reduction. Secondly, we checked that each neurochemical variable correlated with at least one other, in order to validate the use of FAMD. Then, we checked that the number of the new dimensions generated explained 80% of the variance, as recommended by biostatisticians. For this, a very common statistical practice is to consider the first three (unnamed) dimensions that fit the data, mainly because the factor reduction is good and allows easy interpretation. We are quite aware that the labeling of neurochemical dimensions and the foundation of the 5-level pyramid model need to be strengthened, because 3 or 4 main new dimensions were obtained from our experimental rat and drosophila data. However, it must be borne in mind that lab animals have a very poor social life and mainly exhibit basic behaviors such as foraging and sleep, with novelty responses only to a change of litter. In my opinion, this is why only the first two new dimensions in the present neurochemical data sets could be easily tagged, as physiology and safety dimensions (Figure 3B). In contrast, the tissue data from the transgenic Rett syndrome model generated many newer neurochemical dimensions than the other datasets, suggesting that life experience probably has a more significant impact on the dimensions than does the number of variables. Consequently, data obtained with or without altered conditions (e.g., genotype/phenotype/environment/behaviors) are likely to be more relevant than the basic data obtained to study the new neurochemical dimensions (Figure 3B). In practice, this means that neuroscientists should not study parameters in several distinct subsets of animals (one for neurochemistry, one for genetics, one for behavior, etc.), as is currently done, for example in the paper on adolescent

rats<sup>13</sup>, but rather should study many more parameters in the same animals so as to add life inputs, including behavioral measurements, and generate enough variance before reducing the factors. Comprehensive data collection, associating at least both neurochemical and behavioral quantification, would help better redefine the neurochemical variables from the brain structures in motivated or non-motivated behaviors, which is not entirely possible with only the neurochemical datasets available for this Perspective. Moreover, the consistency of the dimensions in which all the neurochemicals intervene from one experiment to another has to be carefully studied. From an evolutionary viewpoint, it is likely that a basic creature, that is nevertheless capable of learning, such as slime mold, will also exhibit the same new dimensions, as living creatures and basic needs have so much in common. Studying neurochemical parameters in other compartments than tissue (extracellular space, organelles such as mitochondria or blood) will probably generate latent dimensions that are useful for modeling the various biological compartments, and it cannot be excluded that the same dimensions as in tissue analysis may emerge.

The present study is not arguing for a-posteriori description and classification of data. Classifying neurochemical variables into dimensions does not make sense without looking at the interactions between the neurochemicals within a given dimension, if we do not know how the dimensions interact in motivated versus non-motivated behaviors. Therefore, identification of multifactorial changes should lead to a search for mechanistic links between the various factors involved, which may help answer outstanding questions in the context of motivation. Do the neurochemicals of an individual directly impact their motivation at any given level of the hierarchy of needs, or does motivation drive neurochemical changes instead? How does an individual's neurochemistry shift between different hierarchical stages following a significant life change e.g. trauma preventing their self-actualization, or stimulating activities contributing to a better well-being? To go further, this viewpoint calls for a comprehensive approach able to raise new hypotheses, study unexpected biochemical pathways, consider under-researched brain connections and highlight new neuropathophysiological mechanisms, in the study not only of motivation but also of normal and pathological brain functioning in general. In the era of multivariate approaches, data mining, machine learning, and deep learning, it is hard to understand why there is such a gap between neurochemistry, stuck with two-on-two comparisons, and the other neuroscientific disciplines exploiting their big data, such as neuroimaging and electrophysiology, which are very familiar with such data and already able to predict some brain signals.

In conclusion, interdisciplinarity is difficult to establish, but definitely needs new concepts coming from transdisciplinary viewpoints to defragment and unify the knowledge accumulated. In other words, links between animal models and human models exist and we need to explore them differently and more deeply. Data mining can be applied to neurochemical data; here is a first meaningful example, and further approaches based on machine learning and deep

learning could help model and understand the complexity of neurochemical processes.

## ASSOCIATED CONTENT

### Supporting Information.

Parrot-DoNeurochemicalsReflectPsychophysiologicalDimensions-Database-Rett-model, Parrot-DoNeurochemicalsReflectPsychophysiologicalDimensions-Database-Naneix (XLS).

## AUTHOR INFORMATION

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### Author Contributions

S.P. worked on the study design, development of ideas, data analysis and writing the manuscript.

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### Notes

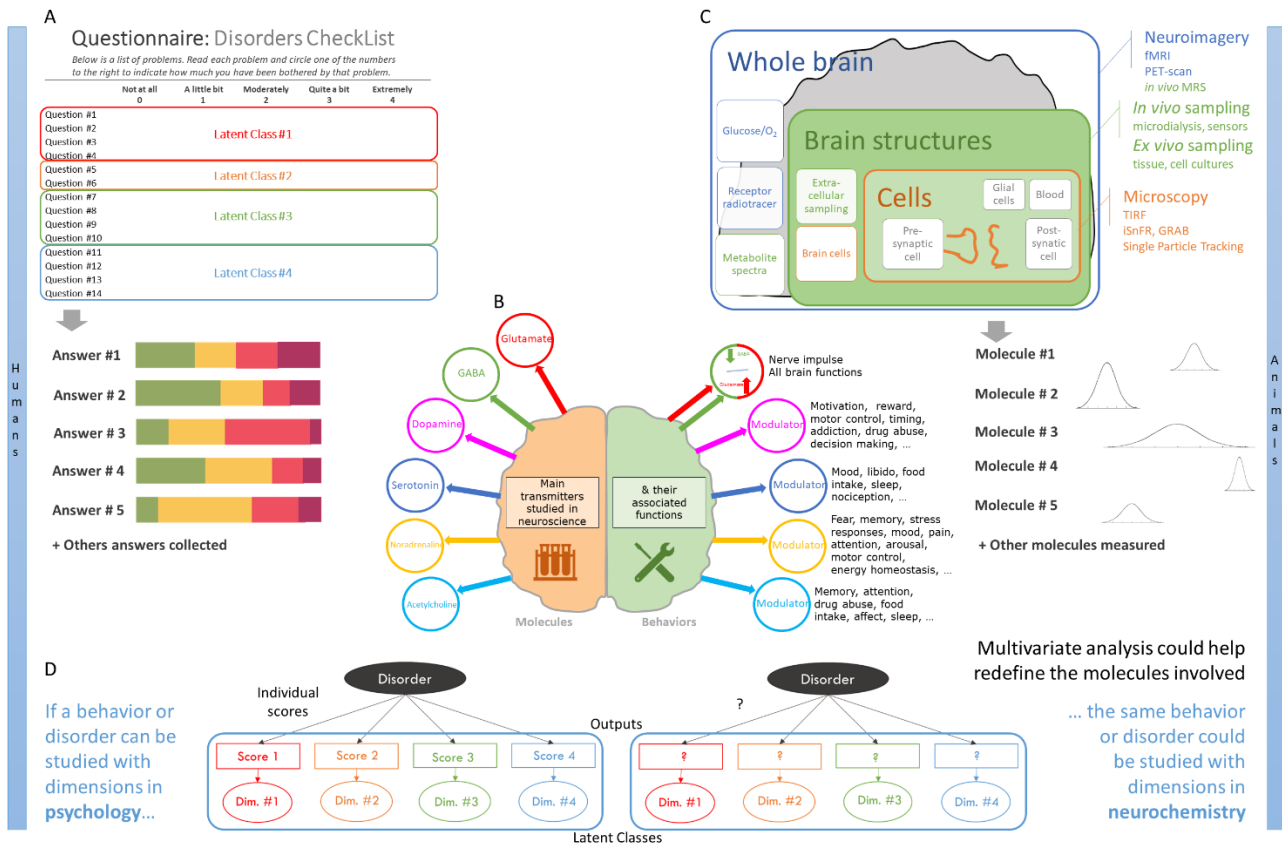
The original data on drosophila analyzed in this study were obtained by three collaborators, Matthew S. Thimgan, Jacob Crehan & Laurent Seugnet. Requests to access these datasets should be directed to Laurent Seugnet ([laurent.seugnet@inserm.fr](mailto:laurent.seugnet@inserm.fr)) and Sandrine Parrot ([sandrine.parrot@univ-lyon1.fr](mailto:sandrine.parrot@univ-lyon1.fr)). The other data analyzed for this study are reused data and available in the Supporting Information. The research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. The author also declares that her institutions never received payment or services from a third party for any aspect of the present work. The author declares no competing financial interest.

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## ABBREVIATIONS

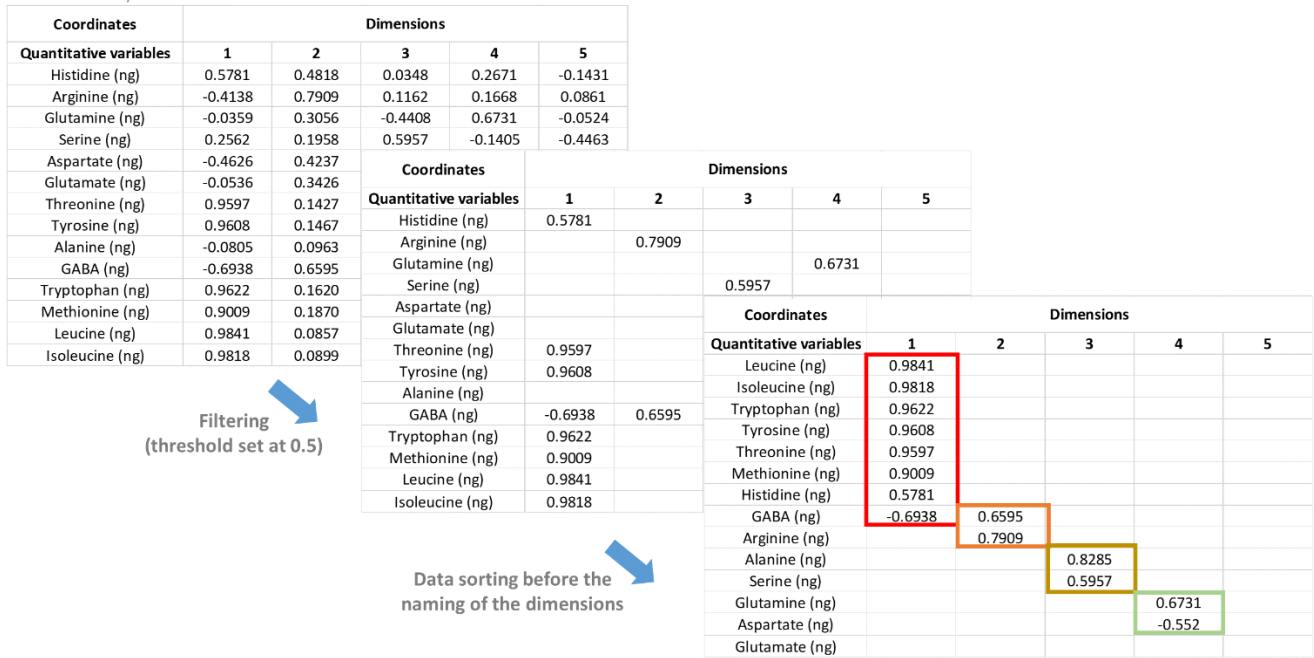
FAMD, Factor analysis of mixed data; PCA, Principal component analysis.



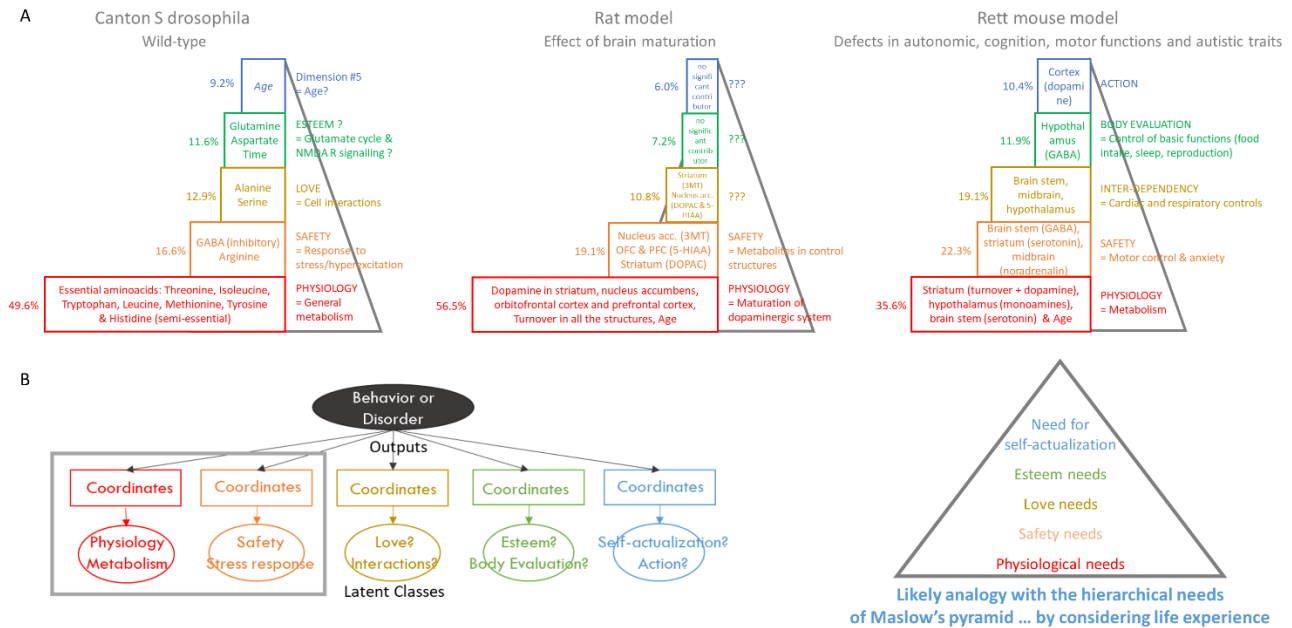
**Figure 1.** (A) Structures of the psychometric questionnaires with their outputs. (B) Main brain functions associated with the major neurotransmitters. (C) Schematic summary of the neurochemical techniques to study neurotransmitters and related neuroactive compounds and their related outputs. (D) Hypothesis of an analogy of the analysis between psychometric questionnaires and neurochemical measurements to study a behavior or disorder. Methodology to be used in neurochemistry: multivariate analysis.



## Factor Analysis of Mixed Data



**Figure 2.** Process of the methodology used to reduce the number of the neurochemical variables into five new dimensions using a FAMD analysis. An example of the data set containing 14 amino acid variables and obtained from drosophila single brain samples. More details in the main text.



**Figure 3.** (A) Latent dimensions represented as 90°-rotated scree plots following factorial analyses of mixed data (FAMD, cumulative: 100%) on three sets of neurochemical data. Drosophila model: 14 quantitative variables (tissue amino acid contents), 47 brains of old vs young individuals including 1 outlier, four collection times (11:00 am, 4:00 pm, 11:00 pm, 4:00 am), factor contribution > 0.5. Rat model: 45 quantitative variables (tissue contents in dopamine, serotonin, noradrenalin, and related metabolites) from four brain areas of 30 individuals at four adolescent ages, factor contribution > 0.5. Mouse model: 60 quantitative variables (tissue contents in dopamine, serotonin, noradrenalin, and related metabolites, glutamate, GABA, aspartate) from 32 wild-type or transgenic individuals, aged P35 or P55, from five brain areas, factor contribution > 0.4. Other details given in the graphs. (B) Naming the new dimensions generated by the FAMD exhibits similarities and likely analogies with Maslow's hierarchical needs, according to the life experience of the individuals.

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