

## Having gone **back** “in circulos suos”.

*«I was at the mathematical school, where the master taught his pupils after a method scarce imaginable to us in Europe. The proposition and demonstration were fairly written on a thin wafer, with ink composed of a cephalic tincture. This, the student was to swallow upon a fasting stomach, and for three days following, eat nothing but bread and water. As the wafer digested, the tincture mounted to his brain, bearing the proposition along with it».*

**«Gulliver's travels»**

We have not without a reason begun our story with this truly wonderful Jonathan Swift's predicting of future target experiments on memory transplantation. Since it's not a secret for anybody that the images, let's say, of an old man's terminating life which are being carried over to a baby, are completely equivalent, in fact, to the prolongation of the same life.

### I

So, the first domestic fundamental works in this area (and it happened almost half a century ago) started in Pushchino Institute of Biophysics – when a group of young enthusiasts led by cand. sc. Inna M. Sheyman was commissioned to conduct a series of the object experiments with planarians. Moreover that method was pretty guileless: worms were specially taught some simple defensive reflexes, after which their small sections introduced into the tissue of untaught brethren. And, curiously enough, involved fragments not only survived successfully but also imparted just purchased knowledge to their new owners.

Similar experiments were, in addition, performed by American psychologist James V.

McConnell at the same time with research assistant of the Lomonosov MSU Nina A. Tushmalova. McConnell, from his side, first was training planarians to respond to light, and then divided in two halves, placing into ribonuclease solution – a ferment that resolves RNA. After all, if the memory is really encoded in RNA, the reminiscences should be, in theory, disappearing both out the head and the tail. Well they, as a result, actually have flown, but... only out the tail. However maybe a head is just better protected than a tail from ribonuclease? Or, perhaps, it's not about nucleotides at all?.. And it was precisely the Muscovite Tushmalova who managed to convincingly demonstrate that ribonuclease prevents the development of only new reflexes, temporarily detaining the old ones. As literally in some couple of hours passed after it was injected and these remarkably enduring worms could recall everything they were taught before.

Planarians, besides capability to regenerate, also possess an inclination to cannibalism. And what if you feed bits of a trained planaria to an untrained? No sooner said than done. And again there was eventually achieved a firm positive result: cannibals who had eaten their smart fellows became much cleverer than those who had devoured the untaught specimens.

At the same time on one of Pushchino conferences dedicated to memory issues, the leading native specialist in planarians I.M. Sheyman told the participants about the way she was laboriously accustoming her nurslings to light and vibration. After which made cachets from skillful worms and injected them to test new-comers' several groups in different combinations. And those already had, accordingly, reaction either only on light, or on vibration, or for example, on both irritants simultaneously. «Well, quite may be all this is done not with RNA but, whatever it was, the memory is howbeit transmitted by chemical means, - it is beyond any doubt!» - with such enviable optimism Inna Moiseyevna summarized her report.

And just a couple of years have passed - and the identity of these miracle carriers has been felicitously established. The news came flying from Houston. A group of American research workers under George Ungar's guidance was performing

experiments with rats. Scientists were putting two boxes – dark and light - in front of each animal. And our domestic rodents, as known, adore gloom much even more than planarians. However, this time in the dark box the rat was waiting for an electric shock, so she had, of course, to get used gradually to the light one. After what the extract from her brain was injected to unlearned specimens – and those, as a result, began to avoid murk either.

When there engaged around ten of thousands of such sacrificial animalcules, an active principle (containing as associated with RNA complex) was isolated from their brain. It turned out to be a peptide of 15 amino-acids, which the authors of the study named “scotophobin” (deriving from Greek words «scotos» — dark and «phobos» — fear). And some time later biochemists, moreover, even managed to synthesize it in artificial way. This exogenous scotophobin has been injected into goldfishes – and latter, as expected, also became terribly afraid of gloom. While after marking it with radioactive iodine, the researchers had no problem to determine in what fish brain’s lobes it is concentrated.

A success? Undoubtedly! But, on the other hand, it’s not a secret these sensational Ungar’s experiments have required colossal costs of time, patience, soul energy and - not least of all – a truly incredible quantity of put to death laboratory animals (even having hitted, by the by, on this indicator to the Guinness Book of Records).

However, anyway, exactly starting from that moment nobody else had a desire to tackle such tiresome routine occupation – despite the fact now, in theory, a lot of the functions of the performed experiments’ accounting could already be entrusted to technically savvy IT-specialists.

Although certain smart alecks have tried nevertheless to find easier, I’d even say, unsophisticated approach in purely American style: were picking, particularly, peptides already used in medicine (as for example fragments of hypophyseal adrenocorticotrophic hormone) and testing them about neurotropic efficiency. And moreover given powerful informative support of modern computer systems, it actually brought rather fast and hopeful results. Similar neurobiological boom would,

quite possibly, continue to this day!.. If not for, alas, a well-known in science subjective factor of some concretely chosen (and still not at all accidental) personality. Because right here suddenly broke out a universal earthly psychosis around Alzheimer affliction – when latter was discovered in the old political senile Ronald Reagan. Indeed, such figure seems to be difficult even to imagine but key costs for investigation of this type of neurodegenerative dementia exceeded as much as 20 billion \$ at the whole. Needless to say, it was achieved by hurting the rest of important biological projects.

So what do we have finally to date? As before, at full speed there continue different kinds of screening explorations on the base of division and ulterior riddling peptide fractions from cerebral bio-extracts of cattle, pigs, marine mammals and apes – certainly, on orders of all the same unsinkable monsters of the notorious pharmacy business!.. By the way, this is prospering in domestic scientific centers too: particularly, at the Moscow Institute of Molecular Biology (Nickolas Myasoyedov's research group), at the Physiology cathedra of the Moscow National University (Andrey Kamensky's group), at the Gerontological Society of RAS (by its Vice-president Vladimir Khavinson), at the Bogomoletz Institute of Physiology (director – Nickolas Veselovsky) as well as by Anatoly Potopalsky (head of laboratory of the Institute of Genetics at NAS of Ukraine). In other words, nobody already is trying to find any new specific memory peptides now. Moreover, there is not even a unanimous conviction that they should be looked for at all. As after long and violent discussions in the late 1980s, the high scientific audience, frankly speaking, didn't support the idea of direct information encoding in a primary peptides' structure. Say, all this seems too "mechanistic", if we switch to the language of philosophy. Although in fact, the world science just isn't left the same desperate and a little maybe adventurous daredevils after McConnell, Ungar, Tushmalova and Sheyman. Yea, these people anticipated their time and moreover have done it quite notably. Since it's difficult to suppose when somebody will yet able, armed with new experimental data, to repeat corresponding investigations in such successful way.

Indeed, you can't even see those potential heroes who would easily risk their resources and reputation in order to step into this river completely dotted with insidious rapids. And apart from all the rest, no one pays, alas, money "for beautiful peep-holes" to scientists now, that's why the latter habitually prefer to have a banal titmouse in own cam by working hard in favor of rich pharmaceutical enterprises...

## II

Briefly speaking, we'll have to acknowledge that yet there is no unanimous opinion about the possibility of chemical encoding memory. And besides, there have been and still exist serious objections regarding also its direct interpretation which relates to targeted search of newly synthesized brain peptides. After all, even with the help of modern progressive techniques, the verification of this hypothesis requires immense efforts and facilities. That is, some qualitatively other biological models of operational learning and remembering will again be needed, let alone the latest methods of separation and purifying peptides.

So, unfortunately, biochemical transplantation of memory failed (well, at least, from financial side). However, it doesn't mean at all that given problem already thereby is out of agenda. You might ask: why? The reason lies in that all observed nowadays vain attempts of oligarchs to find such long-awaited immortality are inexorably run against the law of exponential growth of objective difficulties in a battle for each additionally lived year. That is, according to theory it's possible to rejuvenate oneself indeed; but what numberless expenses it will cost!.. And moreover this unpleasant picture is aggravated here by the fact the hopes which were before placed on the use of germinal stem cells, as it turned out quite recently, also did not come true in the end. As in the process of the Arnold Kaplan's purposeful experiments (not to mention highly extensive clinical practice) it was shown clearly that exogenous cells do not breed in a new organism, but just potentiate somewhat lost reparative abilities of the very recipient. In other words, stem-cell therapy really copes with the

adequate compensation of the defects appearing closer to old age; however it would be perhaps reckless to attribute purely rejuvenating functions to such.

Therefore, when having so unfavorable circumstances, the only salvatory straw in the hands of “homines morituri” may become, most likely, the transfer of memory from an ancestor to a descendant. But, alack, even in this case there are a lot of hidden and pretty slippery rocks waiting for us...

In particular, let's try to analyze the situation that results from solving this problem, as they say, head-on. For instance, we take as an acceptable model an ordinary domestic rat. Wherein one can imagine some extremely simplified scheme in the following way: development of a conditioned reflex – selection of an appropriate animal-recipient – localization of donor hippocampal neurons – transplantation of nerve tissue from donor to recipient – inducting the newly formed synaptic links – expressing of the neuro-physiological correlate of long-term memory – reproduction of the introduced behavior reflexes by animal-recipient. That is, at the first stage it's necessary a rat-donor to be developed a few standard conditioned reflexes with unconditioned reinforcement. At the second we are to perform the transplantation of nerve cells from donor into the animal-recipient's separate areas of hippocampus and frontotemporal lobes of neocortex - with the help of stereotaxic equipment and special micro-toolkit. The third one (after partial wound healing) is to identify the transferred neurons by immunohistochemical analysis - through positron-emission tomographic scanner and various immunofluorescent techniques as well as determining on the way the level of their vitality and functional activism. And, finally, at the closing stage, we only have to fix recipient's adequate behavior reactions which must coincide or at least notably correlate with the previous donor's.

It would seem everything is crisp and clear: a scalpel to hand - and forward! But still in this experimental scheme, two obvious miscalculations are striking. Moreover, though one of them has conceptual sense, the second is yet purely practical. First of all, we have to notice that in the process of its thorny polyfactorial evolution, nature created for live beings several variants of memory duplicating each other in many

aspects. And nevertheless, concluding from very rare cases of total amnesia, it would be quite logical to assume that certain type of memory stays inalterably dominant. As, when its damaging, a man often becomes completely helpless like a grass-blade neglected alone on a field. At that, by the way, he even loses somewhere a habitual for us emotional perception of reality. Thus, it seems to be clear that the very such “existential” memory must be the main operational target of neurosurgeons claiming to full-fledged transfer of “Ego” from pre-death individual to new-born. While all the rest tritely speeds up the learning process (as in notorious experiments with planarians or the same goldfishes).

But this is only one reason of inefficiency of the scheme described above. The second lays in fact neurons transplanted from alien organism, as a rule, have qualitatively different immunological characteristics either. Therefore, they will be actively sloughing by the recipient’s blood-lymph system. Although we could try to overpower this by some kinds of the suppressing pharmaceutical preparations but essence won’t change because such a healing tactic applied to a person is practically ill-suited.

That is, as you can see, again a resourceful Nature-queen put another pretty formidable obstacle on our exploratory way. So it is, but won’t really be found valiant enthusiast in a whole civilized world who should dare to break out from this ominous creative dead-lock?!..

Well, exactly this task was assigned themselves a few of years ago by employees of the capital Institute for Scientific Prognoses. Set – and immediately got down to business by performing a series of interesting experiments with hens and ostriches (namely – their fertilized ova), some laboratory rodents, and latterly even with dogs. The core of which was that the cells of “existential” (i.e. directly related to emotions) memory were introduced not to an adult individual but to an embryo. And as during the initial stages of development absolutely all the mammals don’t have protective-immunological barriers yet, then such, seemingly, alien cells survived felicitously and became afterwards recognized as 100% own. In addition to that, they were carrying,

in fact, the comprehensive information about the life of the deceased ancestor. Moreover, obtained data was then multiply verified for greater sure both by functional diagnosticians and ethologists (i.e. researchers of animals' behavior). And every time a-priori, and occasionally just sweeping criticism inevitably, as a result, yielded to sincere surprise. For many of growing animalcules at once have been turning out to be too confidential towards their "master", though had not seen him before at all: they wagged tail joyfully, poking own muzzle in the chin and visibly setting him preference over genuine parent who really brought up them from childhood. Because, as you might guess, exactly this "master" was imprinted forever in the previous donor's psyche (i.e. which sacrificed his "Ego" to some completely alien creature in the interests of science). At that, similar memory transfer from one generation to another, as shown by practice, wits no tangible boundaries. For a fetus itself, in addition, acts upon the neurons planted from outside in a rejuvenescent way. It is only important in this case to have an idea of what precisely kind of encephalic cells are to be extracted and where they should be transplanted afterwards. However it's already an issue of author's know-how.

Though yet the most essential is through such method of ours, the former eerie psychological chasm between life and death is leveled fully. That is to say, any person will be able to, sort of, just wake up after a deep sleep and continue to live for pleasure, going back "in circulos suos" and at the same time benefiting to other people as if nothing had happened.

### **Final section.**

However, what did, in fact, the McConnell's & K\* experiments with planarians give for better understanding problems of memory? And how productive appeared to be, in the end, the artless approach used by them: "eat a wise guy – and respectively become wiser yourself"?

It's the most important, of course, that similar hypothesis (and also the practical results obtained within it) was actively contributing into the development of universal



scientific attention to the nature of memory, stimulating thereby the progress of neurobiology for a couple of decades. Well as a quite regular effect is the laudable creative undertaking of this glorious international foursome, shown half a century ago, has found its deserving followers in our modern realities. Particularly, alike statement of a question is worked out now (and, moreover, did pretty good) by leading Ukrainian specialists either. Along the way, they comprehensively have analyzed, by the by, the topic of unlimited healthy longevity, which is no less relevant for everybody.

After all, in spite of today gerontologists already know nearly 300 theories of aging (and most of them are verifiable in different measure), still one doesn't see any immortal people at that around. Ok, we'll get ten-twenty years more as an addition to own life journey. And what's then? Sooner or later there follows a moment, when the rejuvenating procedures could be, in principle, continued but sums of money needed for that will already be just astronomic!.. Which is to say, if some multi-millionaire wishes to prolong his life again and again, it actually should be quite feasible. However the costs herewith will start growing not in linear progression but much more steep - exponentially.

That's why, without work at the level "in-vivo" (i.e. when keeping structural integrity of animate bio-organism), without the use of such sought after nowadays advanced nanotechnologies, as seems to me, it's impossible to do. For only in this case we'll be able before long to achieve truly convincing results worth comprehensive serious recognition. Generally, the closing chapter isn't at all finished yet here. And – believe me – it is neurobiology of the memory that will for sure still become the source of new amazing discoveries of the 3<sup>rd</sup> millennium!

**Emir E. Ashursky**

*/State Institute of Artificial Intelligence at NAS of Ukraine/*