BME 201 (Biomedical Engineering Design)
Spring 2008

Project #13: Development of a Device for Neurochemical Sample Collection from Freely Moving Monkeys

MID-SEMESTER REPORT

March 12, 2008

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Abstract

The goal of this design project is to develop and construct a device to provide protection for the microdrive unit, an apparatus which is used in microdialysis experiments conducted on non-human primates. This would allow the experiments to be conducted without restraining the monkeys in a chair, providing them with a more comfortable and realistic experimental setting. Currently, there are no existing devices in the market specifically catered for this purpose. In accordance with the client's requirements, the team considered three design alternatives, and ultimately chose to pursue the Cushion and Shell design. In the future, the team seeks to address the potential problems identified and to continue to work on and develop the proposed solution.

Problem Motivation

Microdialysis allows for real-time *in vivo* measurements of various substances in the body[2]. In particular, direct measurements of neurochemical substances in the brain from free-moving non-human primates is significantly important for understanding complex brain function and developing treatment strategies for brain disorders in humans. A modified microdialysis method has been developed for application to Rhesus macaques (*Macaca mulatta*). However, it requires restraining the monkeys in chairs for up to 12 hours while samples are collected. Although this is considered a norm and the monkeys have been appropriately conditioned, the situation is less than ideal since the monkeys are subjected to a certain amount of discomfort due to the restricted movement and long period of chairing. The data collected might also not be representative of a monkey in its natural environment, since it is confined to a chair. One way to address this problem is to allow the monkeys to be free from chairing while the experiments are being conducted. Besides alleviating the discomfort experienced by the monkeys, it would also better simulate the monkey's natural environment since it would be free to move around, albeit within the confines of a cage. Additionally, this method would allow the experiments to be conducted without the 12-hour limit imposed by chairing. More time would be available for sample collection and safety inspections to be conducted, allowing the experiments to be carried out more smoothly and safely. However, allowing the monkeys to move freely introduces the risk of them tampering with the experimental apparatus (called a microdrive unit), thus compromising the experimental procedure. Hence, a protective device must be constructed to protect the microdrive unit during the experiment. This device must be compatible with the monkeys such that it will not incur greater discomfort than is necessary or encumber the experimental process. There are currently no products in the market that specifically address this issue, so a suitable device must be designed and constructed.

Background

RHESUS MACAQUE

The Rhesus macaque, also known as the Rhesus monkey, is one of the best known species of Old World monkeys. Rhesus macaques have an extensive geographic distribution and are found ubiquitously throughout mainland Asia, ranging from Afghanistan to India and Thailand to southern China. They range in color from brown to grey and have little fur, if any, on their reddish-pink faces[5]. On average, adult males measure approximately 53 cm and weigh 7.7 kg. Females are smaller, measuring 47 cm and weighing 5.3 kg on average. Their tails are of medium length, averaging between 20.7 and 22.9 cm, and are not prehensile (i.e. the tails are not adapted to be able to grasp and/or hold objects). Typically, Rhesus macaques have a lifespan of about 25 years[10].

Because of their anatomical and physiological similarity to humans, as well as the relative ease at which they can be maintained and bred in captivity, Rhesus monkeys have long been an ideal choice to carry out research on non-human primates. As a result, they have become the most studied non-human primate, both in the field and in laboratory settings. Some examples of research involving Rhesus monkeys include the experiments on maternal deprivation carried out by comparative psychologist Harry Harlow in the 1950s, development of rabies, smallpox, and polio vaccines, and the creation of drugs to manage HIV/AIDS[5]. As with all other macaques, the *Herpesvirus simiae* (B virus) is endemic among Rhesus monkeys, but could be deadly if spread to a human. Thus, extra care must be taken when interacting with them.

CLIENT'S RESEARCH

A faculty member at the University of Wisconsin-Madison Department of Pediatrics, the client is interested in understanding how growth and development are controlled in humans. One particular focus is on the role of the brain in triggering puberty[3, 4]. In order to investigate this, the client studies neuroendocrine function by measuring the release of neuropeptides, neurotransmitters, and neuromodulators from the hypothalamus in the brain. Currently, this research is being carried out on Rhesus monkeys, due to their anatomical and physiological closeness to humans. It is hoped that through these neuroendocrine studies on the monkeys, a better understanding of complex brain function in humans can be achieved. Since the studies revolve around the events occurring during puberty, the monkeys used for the experiments are generally young and pubertal. Unlike adult Rhesus monkeys, these monkeys generally range from 2.5 to 5 kg in weight[1].

MICRODIALYSIS & EXPERIMENTAL PROCEDURE

In order to study the release of substances from the hypothalamus of the Rhesus monkeys, a technique known as microdialysis is employed. Microdialysis is widely used in clinical research in areas such as neuroscience (to study the neurochemical bases of brain disorders) and pharmacology (to study drug metabolism, drug delivery, and the effects and efficacy of drugs) [6]. In general, microdialysis entails inserting a probe into the extracellular fluid of a particular part of the body. The probe contains a semi-permeable membrane for substances to diffuse in/out based on a concentration gradient. The inlet of the probe is connected via tubing to a pump which infuses a physiological salt solution. Exchange of substances occurs at the semi-permeable membrane, and the desired samples are collected by a fraction collector connected via tubing to the outlet of the probe[2, 9].

A brief outline of the experimental setup used in the client's research is shown in Figure 1. Before experiments can be conducted on the monkeys, a cranial pedestal (head cap) must be implanted into their skulls and secured using dental cement. This allows the microdrive unit to be fitted onto their heads. The purpose of the microdrive unit is to properly position the microdialysis probe for insertion. On the day of the experiment, the monkey is anesthetized and placed in a stereotaxic apparatus. The microdrive unit with a guide cannula are attached and positioned precisely to the specific area desired for testing. Accurate placement is ensured using radiographic visualization. The monkey is then transferred to a primate chair (Figure 2), which it has been conditioned and well-adapted to prior to the experiment. Apart from moving its hands to feed itself and turning its head a little, all other movements of the monkey are restricted by this chair. Once the monkey has been put in place, the guide cannula is removed and the microdialysis probe is inserted. The pump is used to perfuse cerebrospinal fluid (CSF) through the probe and the exchange of substances occurs at the semi-permeable membrane (which is in the vicinity of the hypothalamus). The perfusate containing the desired substances which have diffused into the probe are collected by a fraction collector and immediately frozen for storage. The entire experimental process takes approximately 12 hours, and the monkeys are confined to the chair throughout this time[1].

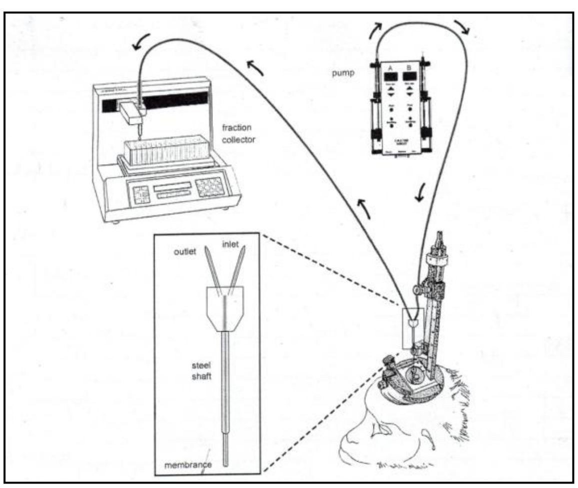

Figure 1: Experimental Setup for Microdialysis

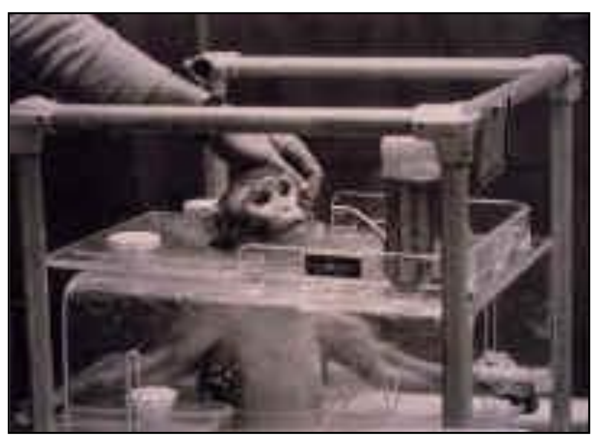

Figure 2: Rhesus Monkey in a Primate Chair[8]

Client's Requirements & Design Constraints

The device must be strong enough to provide protection for the microdrive unit such that the monkeys will not be able to tamper with it during the experimental process. This means that the device must be rigid and cover the entire microdrive unit. Taking into account any forces that the monkey may apply, it should also be able to withstand a force of 100 N. This value was an estimate based on human arm strength[7].

Given that the monkeys are generally smaller in size than the average adult Rhesus monkey, the microdrive unit already imposes a considerable amount of weight on the monkey's head. As such, the materials used to construct the protective device must be lightweight (not more than 0.5 kg as determined by the client) to minimize the additional weight to be imposed.

The design of the device must be simple such that it can be easily integrated with the current experimental apparatus, so as not to interfere with or impede the data collection process. Yet, a certain degree of complexity must be incorporated to prevent the monkeys from dismantling the device. Also, there must not be any sharp edges or protrusions that can possibly harm the monkey or researcher during the experimental setup and process.

The device should be detachable, so that adjustments to the experimental apparatus can be made during the experiment if needed. This will also allow the device to be cleaned and sterilized prior to subsequent use. In addition, the design and construction of the device must comply with USDA regulations and NIH guidelines, subjected to approval by the attending veterinarian.

Design Alternatives

JACKET & METAL RING

The first possible design is the Jacket & Metal Ring design (Figure 3). This is composed of a nylon fabric mesh jacket, an attached metal pole that extends up from the back of the jacket, and a metal ring that fits tightly around the monkey's head. Additionally, there is a protective metal dome welded to the ring that covers the base of the microdrive unit and a PVC tube to cover the upper portion of the microdrive unit. Since the monkey's head would have to be restrained vertically, nylon straps would be used around the chin and neck to prevent the monkey from moving its head.

The mesh jackets have already been designed to fit the monkeys. They fit like a T-shirt with short sleeves and a hole for the neck. They are secured with two, layered zippers on the back making it difficult for the monkey to escape. However, the jackets are not incredibly tight-fitting, and the monkeys have been known to maneuver the jackets on their bodies, even flipping them around such that the jacket was on backward. An additional strap around the monkey's abdomen prevents the pole and ring device from bending away from the monkey's head or body.

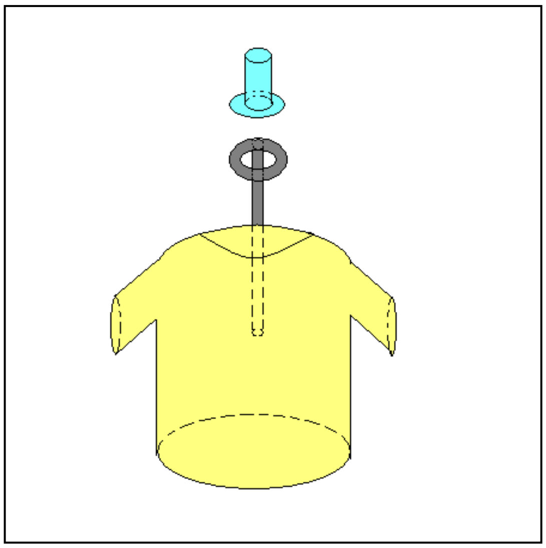

Figure 3: Jacket & Metal Ring Design

A metal rod attaches to the jacket and extends up to the monkey's head. This rod is secured to the jacket in an additional sleeve, which is sewn on directly to the back of the jacket. The rod extends along the back and is welded to a metal ring that sits atop the monkey's head. The ring is interchangeable with other rings prior to the experiment, and fastens to the rod with an Allen wrench. The monkey's head is locked into place next to the rod and ring by nylon straps. Two straps extend down from the ring around the monkey's chin, and a third strap, connected at the chin to the first two, wraps around the neck and connects to the metal rod. This will prevent the monkey from turning or moving its head during the experiment.

On top of the ring, a metal dome with a hole in the top will be welded to the ring. The dome encompasses the entire base of the microdrive unit, the dental cement, and will extend down to the metal ring. None of the dome touches the microdrive unit or the monkey, and it is only secured to the metal ring around the monkey's head. The PVC cylinder fastens to the hole in the top of the dome. This protects the top part of the microdrive unit. The PVC connects to the tether that houses the tubing.

This device would need to be put on in two stages. First, the jacket would be secured on the monkey before it is anesthetized. Then, after the microdrive unit has been attached, the ring and rod device would slide down atop the whole monkey with the tethered connection being made after the microdialysis probe has been inserted.

Advantages to this design are that the weight of the device is distributed throughout the monkey's body and that the housing apparatus is very durable. The pole connected to the rest of the device distributes the weight around the abdomen through the abdominal strap. The head straps are mainly to prevent movement of the monkey's head down and out of the metal ring. The device can be heavier because the weight is distributed. This allows the rest of the housing to be made of more durable metals.

The disadvantages are that the mesh jackets are not tightly secured to the monkey's body. This means that the monkeys are able to slip around inside the jackets and stretch them in places. They have also been known to pick at the zippers in order to escape. Also, the experimental procedure while the monkey is anesthetized is quite rushed, and the jacket takes a while to put on. Adding the metal rod, ring, and straps may cause the procedure to take too much time for this option to be viable.

HELMET

The second alternative is the Helmet design (Figure 4). It resembles a bicycle helmet with a PVC pipe sticking out at the top. It is the most simple of the three designs and has only three main components: PVC cylinder, dome helmet, and straps.

The main part of the helmet is made out of carbon fiber. Carbon fiber is lightweight and very strong, so it will be good for protecting the monkey without adding too much extra strain to the monkey's neck. The helmet will have an inner rim, which rests closer to the head cap and provides additional support and friction to help the helmet stay centered on the head. The helmet will cover the entire base of the microdrive unit with its dome shape, and have a hole at the top for the upper portion of the microdrive unit.

The upper portion will be a PVC tube similar to that used in the Jacket & Metal Ring design. It will cover the upper portion of the microdrive unit. Again, it connects to the hole in the top of the helmet and to the tether through which the sampling tubes are passed. The entire device stays on the head mainly due to straps around the chin and neck. Nylon straps, tightened at the helmet, extend down and around the chin. This strap is connected to another strap that wraps around the neck to the back of the head and connects from there to the back of the helmet. This second strap prevents the monkey from pulling the first strap up far enough to get it into its mouth and possibly chew on it.

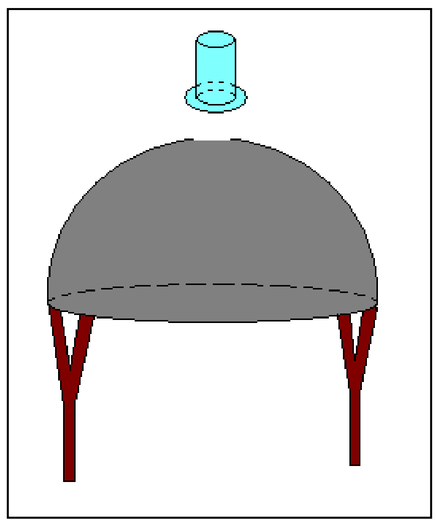

Figure 4: Helmet Design

After the microdrive unit is secured and the sampling tubes have been inserted, the helmet slides over top of the monkey's head. The PVC tube would be attached to the tether, but could slide along it and be removed for cleaning. The entire helmet device would be secured to the tether so that it can no longer slide along the tether.

One advantage of this design is that it is very simple. The design only has 3 different parts and the helmet and PVC portions are both very easy to make. The straps may be a bit more difficult to engineer, but all three designs have a similar component, so this is not a disadvantage when compared to the other two. Also, it is the smallest and lightest of the three designs.

Unfortunately, the straps alone may not be enough to keep the helmet from sliding around on the monkey's head. If the helmet can move enough to touch the protective device, this design would not achieve its intended purpose. Also, fastening of the PVC to the tether during the experimental set up would take some time, and this might deter the researchers from wanting to use it.

CUSHION & SHELL

The third design alternative is the Cushion & Shell design. This design is composed of three hard outer casings that surround a soft inner core. The protective device is secured to the head of the monkey by nylon straps that attach to the outer casing and extend around the monkey's chin. The three outer casings, made from aluminum, provide protection to the microdrive unit. The soft inner core, made from a polymer, provides added protection to the microdrive unit in addition to providing stability to the protective device.

The base of the microdrive unit is protected by two half disks. A representation of one of the half disks is shown in Figure 5. The two half disks are attached together by Allen screws allowing the protective device and the soft inner core to be placed on the monkey's head after the microdrive unit is already in place. This is important because there would be no way to insert a soft inner core into the outer shell if the two half disks were fused into one piece. Lastly, nylon straps attach to the outside of the two half disks and extend down and around the monkey's chin to secure the casing to the forehead of the monkey. Additional straps are used as needed to prevent the monkey from biting through the nylon straps.

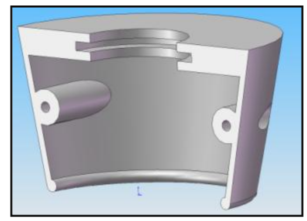

Figure 5: Half Disk

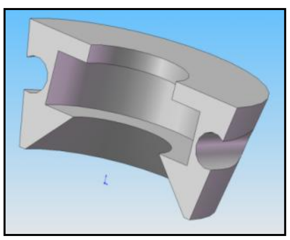

Figure 6: Soft polymer core

The soft inner core lies within the two outer casings that protect the base of the microdrive unit. It is made up of a polymer that is molded to the inside surface of the hard outer casing. In addition, the soft inner core has a cavity within it that is molded to the shape of the base of the microdrive unit (Figure 6). The soft inner core provides additional protection to the microdrive unit by padding the microdrive unit from the hard outer shell. Also, the cavity that is molded to the shape of the microdrive unit helps to keep the entire protective device correctly aligned on the monkey's head.

The upper cylindrical shell protects the remainder of the microdrive unit. It is simply a cylindrical shell constructed from aluminum that has a lip on one end and an attachment for the tether at the other end (Figure 7). The lip fits perfectly within the slots that are machined into the top of the two half disks. The lip-groove relationship secures the upper cylindrical shell to the other two half disks when the disks are fastened together using an Allen wrench. The tether, on the other hand, is attached to the cylindrical shell directly using multiple Allen screws. A representation of the entire Cushion & Shell Design is shown in Figure 8.

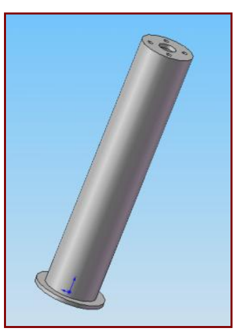

Figure 7: Cylindrical Shell

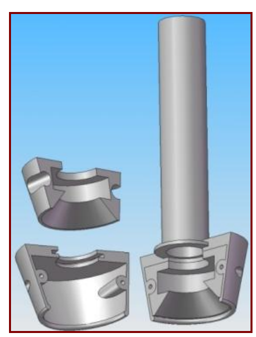

Figure 8: Cushion & Shell Design

The advantages of this design include its soft inner core and its ability to clamp around the microdrive unit. The two half disks that clamp around the microdrive unit allow a soft inner core that is molded to the shape of the microdrive unit to be imbedded within it. The soft inner core provides additional protection to the microdrive unit that is lightweight, and it also helps to keep the protective device correctly aligned on the monkey's head.

Disadvantages of the Cushion & Shell design include its complexity and how it distributes its weight onto the monkey. The complexity of this design comes from the three hard outer casings, the soft inner core, the various nylon straps, and the Allen screws. This could make construction of this design very challenging. Also, this design puts all of its weight on the head of the monkey instead of distributing it to other areas of the monkey. Consequently, the protective device would need to be constructed out of a lightweight material that would reduce the strain on the monkey's head.

Design Matrix

In order to evaluate the three design alternatives, a design matrix was created with several weighted criteria and the designs were ranked in each category (Table 1).

The first criterion is security from the monkey. Monkeys are very clever animals capable of fine motor movements. As a result, the monkeys must not be able to unscrew the device, take it off, or otherwise interfere with the function of the system. For the first design, the available jackets are made of a mesh material and have many zippers. With this setup, the monkeys have been able to chew on the mesh and undo some of the zippers, which would not make the device very secure from the monkey. However, both the Helmet and Cushion & Shell designs are secured by straps and Allen wrench connections. This system is much more difficult for the monkey to interfere with since they cannot undo things put together with Allen wrenches and the straps will be under the chin and neck preventing them from putting the straps into their mouth.

Another important factor in the design is the security from slip. While the device is on the monkey's head it cannot move around and forcefully hit the microdrive unit and knock it out of place. For the Jacket & Metal Ring design, the jacket does not fit tightly on the monkey's body, so it is likely that it would cause the entire device to slip since the device is anchored by the jacket. The Helmet design is anchored by straps which would be a more stable securing point, and the Cushion & Shell design has the straps along with the close molding to provide more support.

The ability of the device to withstand force is a key aspect of the designs. Rhesus monkeys are strong and capable of hitting the device with their hands or on the side of the cage. As a result, the device must be able to withstand these forces without breaking. All of the design alternatives were ranked the same for this criterion since all have the same cylinder column extending up over the microdrive unit, which is the main piece that will need to withstand force. The ranking was also quite high since the materials planned to be used (PVC or aluminum) are both strong materials.

Ease of use is a less important component of the designs, but still is something that needs to be taken into consideration. It would be ideal to have the monkeys anesthetized for the least amount of time possible and the researchers have a lot on their minds when conducting the experiment, so creating a system that is easy to implement is important. The Jacket & Metal Ring design has a lot of different parts that would be hard to put on the monkey. A jacket with a metal rod, ring, and dome attached to it would be very difficult to maneuver. The Cushion & Shell design would be easier to use since it involves less parts and only has attachments on the head. The easiest to use would be the Helmet design since the researchers would just need to strap it on and pull down the protective PVC cylinder.

Another criterion is the ease of construction. The chosen design must be constructible so it can be used by the client and possibly reproduced if successful. The Jacket & Metal Ring design involves many different pieces, creation of metal parts, welding, and attachments to different jackets for different size monkeys. All of this is quite complex and would be difficult to create. The Cushion & Shell design would be easier to create since it involves fewer parts; however, specialty metal parts need to be made which adds difficulty to its manufacturing process. The Helmet design would overall be the easiest to create, but there would be challenges in finding how to create a helmet that would appropriately fit the monkey's head.

Safety is the last criterion used to decide among the design alternatives. A checkmark system was used for this factor since any device that is chosen to be pursued must be safe for both the monkeys and the researchers. It cannot be toxic, have sharp edges, or involve small pieces that may fall off. All of the design ideas received a checkmark for this category since they do not involve any of the aforementioned concerns.

	Jacket & Metal Ring	Cushion & Shell	Helmet
Security from Monkey (30)	15	18	18
Security from Slip (20)	7	15	10
Ability to Withstand Force (30)	25	25	25
Ease of Use (10)	3	7	8
Ease of Construction (10)	3	5	6
Safety	✓	✓	✓
Total	**53**	**70**	**67**

Table 1: Design Matrix

Proposed Solution

When the numbers of the design matrix were added together, the Cushion & Shell design came out on top. This is the design that will be pursued for the rest of the semester. The chosen design is the best not only according to the analysis using the design matrix, but it also intuitively seems to be the design that will allow for the most support and protection of the microdrive unit. The entire device will be relatively secure from the monkey with its Allen wrench connections and strap system. It will also be stable on the monkey's head, since it is secured by both straps and the tight molding. The aluminum is very strong and will allow for the device to withstand large amounts of force. Lastly, the device will be easy enough to use and construct, although there might be some challenges.

Potential Difficulties

There are a few potential problems with the Cushion & Shell design. One problem lies with the strapping system. The straps need to be tight around the monkey's head in order to provide adequate stability. However, the veterinarian may not want the straps extremely tight for the comfort of the monkey, so there may be less security with the straps than preferred. If this does become a problem, a more elaborate strapping system might be needed. Another potential problem is with the security of the screws in the monkey's head. When the cranial pedestal is implanted, screws are put into the monkey's skull to keep it in place, and dental cement is put over the screws. At this point, no one knows the amount of stress the screws can handle and the Cushion & Shell design may put too much strain on them. If this turns out to be the case, more of the stability will have to rely on the straps or the design will have to be significantly modified.

Future Work

The next step is to determine the exact dimensions of the chosen design. This has been a challenge since access to the monkeys is very limited and all of the monkeys have different head sizes. An old Rhesus monkey skull might be available at the National Primate Research Center that could be used to help visualize the exact dimensions of the device. The skull, along with measurements made by the researchers will be the sources for attaining the dimensions. Once these dimensions have been determined, the necessary materials will be ordered, including the aluminum, silicon, and nylon straps. When the materials arrive, the construction of the device will begin. Help will be enlisted with the shop worker at the National Primate Research Center (who is skilled with metals) to aid in the construction of the special metal shell pieces. After the device has been created, the testing phase will begin. The strength and stability of the device are the two main properties that need to be evaluated. The strength will be tested by applying forces to the device in a controlled manner that is equivalent to 100 N of force. The stability will be tested by attaching the device to a model of a monkey head. The device will then be hit from all angles to see how well it stays on. To see how much force the screws in the monkey's skull can withstand, it is possible that a fresh dog skull will be fitted with a metal ring and screws like the monkeys are, and from there it can be tested to see how much force is required to remove the screws. Once testing is complete, any modifications will be made and retesting will be done if necessary.

Conclusion

The goal of this project is to produce a device that protects the experimental apparatus used in neuroendocrine research. The device will be designed for young Rhesus monkeys that undergo the experiment so that they no longer have to be confined to a chair for 12 hours. After considering several designs including the Jacket & Metal Ring design and Helmet design, the Cushion & Shell design was determined to be the best and will be pursued for the rest of the semester. To begin, the exact dimensions will be determined, and then the device will be built, tested, and modified as needed. Hopefully by the end of the semester there will be a prototype that can be reviewed by the necessary boards to obtain approval for use in non-human primate research.

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APPENDIX: PRODUCT DESIGN SPECIFICATIONS

PROJECT TITLE:

Development of a Device for Neurochemical Sample Collection from Freely Moving Monkeys
(Project Number: 13 / Project Code: neurochemical_sampling)

INITIAL PROBLEM STATEMENT:

Direct measurements of neurochemical substances in the brain from free moving non-human primates is significantly important for understanding complex brain function and developing treatment strategies for brain disorders in humans. Accordingly, we have modified an existing microdialysis method for application to rhesus monkeys (Frost et al., in press). However, this method requires restraining monkeys in chairs for up to 12 hours while we collect samples. Thus, the purpose of the project is to develop a device allowing monkeys to be free from chairing while experiments are conducted. Although a similar device is available for other studies involved in blood sampling in non-human primates, the development of the device for microdialysis experiments may require creativity and intellectual exercise.

REVISED PROBLEM STATEMENT:

To construct a device that protects the microdialysis apparatus used during cranial experiments on non-human primates. This device will free the monkey from the constraints of chairing while the experiment is conducted and will provide a more comfortable and realistic environment for the monkey. The device should be lightweight, durable, and removable to meet the needs of both the researcher and the subject.

CLIENT REQUIREMENTS:

- Material must be lightweight so as not to impose too much weight on the monkey's head.
- Material must be strong enough to withstand forces that the monkey may apply.
- The device must not interfere with the data collection process.
- The device must be able to be easily integrated with the current microdialysis apparatus being used.
- The monkey must be able to move freely with the device attached to it.
- There should be limited space between the device and the microdialysis apparatus.
- The device must be detachable from the apparatus after use.
- The device should be sterile and reusable.

Design Requirements:

1. Physical & Operational Characteristics

a. **Performance Requirements:** The device must be strong enough to withstand 100 N (based on human arm strength estimate) to protect the microdrive unit from any forces that the monkey may apply.

b. **Safety:** The device must not contain sharp edges or other protrusions that may injure the monkey or researcher. The materials that are used must not be toxic.

c. **Accuracy & Reliability:** The device must provide reliable protection for the microdrive unit by being able to withstand a force of 100 N for 10 consecutive hits within a time period of 10 s.

d. **Life in Service:** The device must be able to withstand at least 12 hours of use at a time, and must be sterile so that it can be reused.

e. **Shelf Life:** At least 5 years.

f. **Operating Environment:** Normal laboratory environment for non-human primate research.

g. **Ergonomics:** The device must not restrict the monkey's motion except for the head and neck.

h. **Size:** The base of the protective device should be no larger than 10 cm in diameter and 5 cm in height. The cylinder above the base should be smaller in diameter but the exact dimensions have yet to be determined. The entire device should be no longer than 20 cm.

i. **Weight:** Not more than 0.5 kg so as not to impose too much weight on the monkey's head (as determined by client).

j. **Materials:** Aluminum for the outer casing and a soft polymer (e.g. silicone) for the inner moldable core.

k. **Aesthetics, Appearance & Finish:** The device must be aesthetically pleasing and look "humane" so as not to create a public outcry.

2. Production Characteristics

a. **Quantity:** 1 reproducible device.

b. **Target Product Cost:** Not more than USD1000.

3. Miscellaneous

a. **Standards & Specifications:** The design and construction of the device must comply with USDA regulations and NIH guidelines, subject to approval from the attending veterinarian.

b. **Customers:** Primarily the client, but can be potentially extended to any research institution that is involved with cranial microdialysis studies on non-human primates.

c. **Patient-Related Concerns:** The device must be sterilized before use with a different primate. It should not cause more discomfort to the monkey than the current experimental apparatus (i.e. the primate chair) does.

d. **Competition:** No currently known products specifically address the need to protect the microdrive unit during cranial microdialysis studies on non-human primates.